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The Hippocampus and Structural Learning

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Abstract

The hippocampus has been implicated in the learning and memory of arrays of spatial cues. Certain theories of the function of the hippocampus have stressed the importance of the hippocampus in learning about configurations of stimuli that have non-linear associations. Recent evidence has suggested that the hippocampus may not be responsible for learning about unique configurations but rather the unique spatial relationships formed by a configuration of visual cues. This thesis examines the effects of hippocampal lesions on visual configural discriminations, in which the solution relies on learning the features that are necessary for configural learning, and also discriminations in which the solution of the task relies on learning the spatial structure of the features that form the configurations. It was found that hippocampal lesions made after acquisition impaired performance of a structural discrimination. Hippocampal lesions did not impair performance of previously acquired configural discriminations. A probe test revealed that although hippocampal lesioned and control rats do not differ on performance of a configural discrimination that does not require learning structural information, control rats learn the structural features of the configurations to a greater extent than hippocampal lesioned rats. Hippocampal lesioned rats were impaired at learning structural information when a task explicitly demanded, and when the structural features were incidental to the requirements of a task. The results are discussed with regards to a configural account of hippocampal dependent allocentric spatial learning, and also theories of hippocampal dependent stimulus representation.

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1.2 The involvement of the hippocampus in the encoding of allocentric spatial cues

1.2.1 Spatial navigation by the use of allocentric cues

It has been found that cells in the hippocampus selectively respond when an animal is exploring a specific location in an environment (O'Keefe and Dostrosvsky, 1971; Olton, Branch and Best, 1978). O'Keefe and Nadel (1978) concluded that the hippocampus is responsible for encoding spatial environments with regards to the spatial relationships between cues (i.e. the distance and angle between landmarks), so that a 'cognitive map of the environment is formed. Lesion studies have supported the 'cognitive map' hypothesis by finding that hippocampal damage impairs performance of spatial tasks that require learning the allocentric cues in an environment.

Morris et al. (1982) found that hippocampal lesioned rats were impaired at learning the location of a hidden platform (place learning) in a circular water maze. Rats were placed in the pool at random start locations and were able to learn the location of a fixed platform by the use of the room cues. However, when the platform was made visible (cue learning), lesioned rats were able to swim to the platform in a manner that did not differ from controls. When the platform was once again hidden, hippocampal lesioned rats were again impaired compared to controls, thus, demonstrating that lesioned rats were not able to use the room cues to navigate to the platform. These results are typical of the ability of rats with hippocampal system damage to show successful cue learning but impaired place learning in the Morris water maze (de Bruin, Moita, de Brabander and Joosten, 2001; Devan, Goad and Petri, 1996; Oswald, spatial relationships between cues (Muller, Poucet, Fenton and Cressant, 1999; O'Keefe and Conway, 1978). Shapiro, Tanila and Eichenbaum (1997) have demonstrated different that cells appear to encode local cues in an environment and other cells encode distal cues. Altering the spatial relationships between local and distal cues (but maintaining the spatial relationships within sets of local and distal cues) resulted in altering the firing response of neurones and eventually new place fields were formed. Also altering the topological relationships between a set of distal or local cues resulted in cells switching their firing response, and replacing the cues with a novel set of stimuli resulted in either the formation of new place fields or cells ceasing to fire (Shapiro et al., 1997).

It has been shown that hippocampal cells encode information about the geometry of an environment (O'Keefe and Burgess, 1996). Within an environment some cells fire at fixed distances from walls and other cells are controlled by a fixed proportion of distance between walls. Cells responded to the geometric features of the environment even when the environment was rotated, thus ruling out the encoding of odours (O'Keefe and Burgess, 1996). Also, the place field response of a cell in two geometrically distinct environments diverges as a consequence of exposure to the environments (Lever, Wills, Cacucci, Burgess and O'Keefe, 2002).

In contrast to the evidence for cells in the hippocampus encoding the spatial location of an animal it has been shown that some cells respond to the perceptual, behavioural and cognitive demands of a task regardless of the location of the animal within an environment (Wood, Dudchenko and Eichenbaum, 1999). In a study by Wood, Dudchenko, Robitsek and Eichenbaum (2000) rats were trained to perform a continuous T-maze alternation task. It was found that cells that fired when the rat was located in the central stem of the T-maze fired differentially depending on whether the animal's correct response was to turn left or to turn right (Wood et al., 2000). Therefore, there is evidence that suggests that cells in the hippocampus can encode more than just the spatial location of animal. This has lead to the suggestion that the hippocampus may have a general function of encoding events which occur in the same or distinct locations and ultimately the memory for specific episodes of experience (Eichenbaum, Dudchenko, Wood, Shapiro and Tanila, 1999).

Whether cells in the hippocampus encode spatial locations to form a 'cognitive map' of an environment (O'Keefe and Nadel, 1978) or have a more general function in memory (Eichenbaum et al., 1999) the work on place cells suggests that the hippocampus can encode configurations of cues with respect to the spatial relationships between cues such as the distance and angle between cues (Fenton, Csizmadia and Muller, 2000).

1.2.2 Object-in-place tasks

1.2.2.1 The effects of hippocampal system damage in rats

Recent evidence has pointed towards the hippocampus playing an important role in learning of object-in-place tasks (Aggleton and Pearce, 2001). Whereas tasks such as the Morris water maze, radial-arm maze and T-maze alternation depend on learning about an array of room cues, in object-in-place tasks, successful performance depends on learning that an object appears in a specific location within an environment. Therefore, it is possible to examine the effects of hippocampal lesions on responses that are explicitly directed to objects within an environment without the necessity to also tax use of cues for navigation.

Chapter One

General Introduction

1.1 Introduction

The hippocampus has been implicated in playing an important role in learning and memory. Cases of damage to the hippocampus in humans have revealed that pathology in this region results in severe anterograde amnesia (Scoville and Milner, 1957; Zola-Morgan, Squire and Amaral, 1986). In the case of patient YR, it has also been found that damage to the hippocampus impairs learning that uses allocentric spatial cues (Holdstock, Mayes, Cezayirli, Issac, Aggleton and Roberts, 2000). This finding is consistent with the wealth of evidence showing that the rat hippocampus is vital for normal allocentric spatial learning. This thesis builds on these findings by examining how the rat hippocampus encodes spatial relationships between visual cues.

Lesion studies suggest that the rat hippocampus plays an important role in the learning and memory of spatial tasks that require processing of allocentric cues (Morris, Garrud, Rawlins and O'Keefe, 1982). It has been argued that the hippocampus specifically encodes spatial relationships formed by allocentric cues to form a cognitive map of an environment (O'Keefe and Nadel, 1978). In contrast to this specific model, Sutherland and Rudy (1989) proposed a more general model of hippocampal function that could not only account for impaired allocentric spatial learning following hippocampal lesions, but also for deficits found on certain non-spatial tasks. It was proposed that the hippocampus was responsible for learning and memory of 'configural associations' and these same associations also underlie allocentric spatial learning (Sutherland and Rudy, 1989; Rudy and Sutherland, 1995).

Bannerman, Yee, Rawlins, Honey and Good, 2003; Packard and McGaugh, 1992; Save and Poucet, 2000).

Hippocampal lesioned rats are also impaired at learning radial-arm maze (Olton, Becker and Handelmann, 1979) and T-maze alternation (Aggleton, Hunt and Rawlins, 1986) tasks. In the radial-arm maze task, rats are typically required to obtain food from the end of eight arms that extend from a central start position. An error is counted as returning to an arm that has previously been visited. Successful performance of the task requires remembering which arms have been visited. In the T-maze alternation task, for a sample run a rat is forced to turn left or right down an arm to obtain food. In the choice run, rats are placed in the start arm of the maze and are required to turn down the arm that was not visited in the sample run. These two tasks are believed to tax the ability to learn about the room cues even though other cues may be used for the performance of these tasks. Probe tests have revealed that when the maze is rotated 45° after a rat has visited half of the arms, when returned to the maze rats show a preference for entering the arms that are in a place that have not been visited (Bussey, Muir and Aggleton, 1999; Olton and Samuelson, 1976). Therefore, rats predominately rely on the extra-maze cues rather than the intra-maze cues for successful performance of the radial-arm maze task. For the T-maze alternation task egocentric strategies can also be tested against allocentric learning. Rotating the maze 180° in between the sample and choice run still results in rats showing a preference for the arm in the spatial location that was not previously visited (Lui and Bilkey, 1998; Restle, 1957).

Further to the work of O'Keefe and Dostrosvsky (1971) recording of cells in the hippocampus have demonstrated that a place field can be manipulated by altering the

The purpose of this thesis is to test the prediction that lesions of the hippocampus will impair performance of a specific form of configural association task, namely a 'structural discrimination' (George, Ward-Robinson and Pearce, 2001; George and Pearce, 2003). A structural discrimination requires the ability to differentiate between two configurations that contain identical visual features, but differ in their spatial arrangement (i.e. A to the left B versus B to the left of A). The performance of a structural discrimination will be compared with other tasks that do not require the structural features of a configuration to be discriminated. By testing this prediction it may also be possible to specify better the nature of learning spatial relationships that are believed to be hippocampally dependent.

This chapter will begin by discussing the impairments caused by damage to the hippocampus on spatial tasks that require the processing of allocentric cues and, subsequently, how the 'configural association' theory proposed by Sutherland and Rudy (1989) might account for these findings. Unless stated, throughout this thesis, the term hippocampus is used to refer to the dentate gyrus, the hippocampal fields CA1, CA2 and CA3, and the subiculum. The limitations of the 'configural association' theory will then be discussed with regards to the findings of spared performance on a variety of configural tasks, and the specific revised assumptions of hippocampal function (Rudy and Sutherland, 1995) will be considered. Finally, it will be argued that the hippocampus is responsible for learning the specific spatial relationships between cues, and the prediction will be made that lesions of the hippocampus will impair performance of a configural task that requires the spatial structure of the component features of the stimulus configuration to be discriminated.

Although there has been some controversy, research has shown that for rats, the hippocampus is often not responsible for tasks that require objects to be remembered in recognition tests (Aggleton et al., 1986; Winters, Forwood, Cowell, Sakisda and Bussey, 2004; Mumby, Wood, Duva, Kornecook, Pinel and Phillips, 1996; Mumby, Wood and Pinel, 1992; Mumby, 2001). However, when learning about objects is incorporated with learning about an object in a particular location, it has been found that fornix lesions, which disrupt functioning of the hippocampal system, impair rats on such tasks (Bussey, Duck, Muir and Aggleton, 2000). Similarly, it has been found that rats with anterior-dorsal hippocampal lesions show normal habituation in their exploratory behaviour to an array of objects presented in an arena, but show no discernable increase when a subset of the objects was moved to new locations compared to controls (Save, Poucet, Foreman and Buhot, 1992). When one of the familiar objects was replaced by a novel object, exploratory behaviour towards the novel object increased for both the hippocampal group and a control group (Save et al., 1992). These finding have been supported by Mumby, Gaskin, Glenn, Schramek and Lehmann (2002) who found that familiar objects moved to a novel location in a familiar environment did not produce a novelty preference in the exploration of hippocampal lesioned rats.

Complementary to the object-in-place research, it has been found that hippocampal lesioned animals have impaired memory for the spatial location of stimuli, but not necessarily for the stimuli themselves. Therefore, it appears that spatial learning can be dissociated from learning simple associations between stimuli and reward.

For example, in a novel one-trial paired-associate learning task, Day, Langston and Morris (2003) found that blocking of *N*-methyl-D-aspartate (NMDA) receptors in the hippocampus impaired encoding of a spatial location cued by the presentation of a food that had previously been consumed in that particular location. Blocking of hippocampal α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) receptors, resulting in neuronal inactivation blocked both encoding and retrieval of the location and food association. Therefore, hippocampal function is crucial for learning about the spatial location of where a stimulus was encountered. Similarly, hippocampal lesioned rats are not impaired at learning to approach odours associated with reward (Wood, Agster and Eichenbaum, 2004), but when memory for a reward is contingent on learning spatial locations rather than odours, hippocampal lesioned rats are impaired (Dudchenko, Wood and Eichenbaum, 2000).

1.2.2.2 The effects of hippocampal system damage in monkeys

The role of the monkey hippocampus in learning object-in-place associations has also been examined. It has been shown that hippocampal lesions that spare the rhinal cortices need not affect non-matching to sample of object stimuli (Murray and Mishkin, 1998), however, lesions of the hippocampus can impair the ability to match-to-sample when the stimuli are spatial locations and objects that appear in specific locations (Parkinson, Murray and Mishkin, 1988). In contrast to the finding of Parkinson et al. (1988), it has been subsequently found that lesions of the hippocampus that spare the posterior parahippocampal regions fail to produce spatial and object-in-place deficits using a matching-to-sample task design (Malkova and Mishkin, 2003; Murray and Mishkin, 1998). Therefore, there is some controversy as to the role of the hippocampus in object-in-place associations.

Gaffan (1994) reported that monkeys with fornix lesions are impaired at learning discriminations in which a response is required to be made to a particular object that is always presented in a particular location on a particular background. For this reason, optimal performance is thought to depend on object-in-place learning. In contrast, fornix lesioned monkeys were not impaired when the task required objects, regardless of their location, to be discriminated (Gaffan, 1994).

In an experiment using 3 dimensional objects, monkeys were rewarded for choosing object A but not object B when they were placed facing the objects in one direction, but when placed facing the objects in another direction, object B was rewarded but not object A (Gaffan and Harrison, 1989). Monkeys with fornix lesions were impaired on this spatial conditional task, but were not impaired on a similar task in which objects were only rewarded in unique locations in which the same spatial scenes could not be seen. Therefore, both tasks required spatial environments to be learned for the solution of the discrimination, but fornix lesioned monkeys were only impaired when spatial environments with overlapping features was used (Gaffan and Harrison, 1989).

The work of Gaffan (1994) and Gaffan and Harrison (1989) highlights that monkeys with lesions of the hippocampal system are able to acquire tasks that have a spatial dimension, but are only impaired when knowledge of the spatial information is crucial for correct responding to an object stimulus. It is the combination of object and spatial information that is necessary to produce hippocampal system lesion deficits.

1.2.2.3 The role of the hippocampus in human subjects

Hippocampal damage in humans also results in impairments on some spatial tasks (Henke, Kroll, Behniea, Amaral, Miller, Rafal and Gazzaniga, 1999; Holdstock et al., 2000; Turrizani, Calresimo, Perri, Tomaiuolo and Caltagirone, 2003). The role of the intact hippocampus in spatial learning has also been demonstrated by the use of functional imaging studies in humans. The recollection of routes and knowledge of spatial layouts results in activation of the right hippocampus (Maguire, Frackowiak and Frith, 1997; Maguire, 1997).

Similar to the studies of hippocampal damage in rats (Bussey, Duck et al., 2000; Mumby et al., 2002; Save et al., 1992) it has been found that the hippocampus in humans plays a role in learning object-in-place associations. Lee, Bussey, Murray, Saksida, Epstein, Kapur, Hodges and Graham (2005) found that patients with hippocampal damage could discriminate visual objects, but were poor at discriminating spatial scenes. In one case study, the patient K.C. who has bilateral hippocampal damage was found to have normal performance on tests of allocentric spatial memory, but had memory impairments for specific landmarks (Rosenbaum, Priselac, Kohler, Black, Gao, Nadel and Moscovitch, 2000). Similarly, functional imaging has shown that the hippocampus, as well as parahippocampal regions, is activated during recall of landmarks in a spatial context, but recalling of landmarks without knowledge of their spatial context did not result in hippocampal activation (Maguire, 1997).

1.2.3 Hippocampal neuronal activation due to novel spatial arrangements of familiar visual cues

Immediate early gene (IEG) activation studies have added evidence supporting the involvement of the rat hippocampus in the encoding of spatial relationships between stimuli. The increase of IEG activation is seen as a correlate of neuronal activation.

By examining IEG activation it is possible to test the effect of experimental manipulations on activation in different brain areas in intact rats.

Experiments by Wan, Aggleton and Brown (1999) and Jenkins, Amin, Pearce, Brown and Aggleton (2004) have examined the neural substrates underlying encoding of configurations of visual stimuli. These experiments highlight the role of the hippocampus in detecting novel spatial arrangements of stimuli, indicating that the hippocampus may play a role in the discrimination of the structure of stimuli presented in compound. These experiments will be described in detail.

In a study by Wan et al. (1999) the effects of exposure to novel objects and to novel spatial arrangements of objects was tested. The IEG c-*fos* was measured in different areas of the medial temporal lobe as a result of activation from the presentation of different stimuli. It was found that there was an increase in the Fos protein in the hippocampus after presentation of familiar visual stimuli in a novel spatial arrangement. In contrast, presentations of individual novel visual stimuli did not cause increased c-*fos* activation in the hippocampus but did in the perirhinal cortex (Wan et al., 1999). Figure 1.1 illustrates an example of the stimuli used.

In the experiments by Wan et al. (1999), rats were trained to approach an observing hole in a wall. In close proximity to the hole was a tube that dispensed juice, so that rats would be motivated to approach the observing hole. Running perpendicular from the hole were two partition walls, which were placed at angles so that their apex met just in front of the rat's nose. Viewed from the observation hole were two computer monitors. When looking through the observation hole, only one eye could view one computer monitor. This meant that within-subject comparisons could be made with the presentation of familiar or novel stimuli, because viewing of a stimulus in one associative strength. In a water maze task in which a rat is placed into a circular pool and is required to swim to a hidden platform by the use of the spatial cues, it is possible to imagine that configurations of stimuli are more reliable at predicting an outcome than individual stimuli. Perception of a cue may not be associated with the reward when the subject is in a certain location in the pool, but perception of the same cue may be associated with reward when in a different location in the pool. Therefore, it is important for animals to form configurations of the cues for successful navigation to the hidden goal.

Sutherland and Rudy (1989) also claim that navigation to a goal requires the 'conditional linkage of specific movement sequences with specific views of the environment' (p133). Thus, spatial learning requires the use of conditional responses towards series of configurations of room cues. Spatial learning can be seen as a complex discrimination in which configurations of stimuli elicit a response that is dependent on the presentation of other configurations. For example, a rat may perceive the configuration of AB followed by AC for approach, compared to if a rat perceives AB followed by AD then avoid.

Although the assumptions made by Sutherland and Rudy (1989) about how normal animals solve a spatial task have not been directly tested, there is evidence that when only a single cue is available for locating a hidden goal in a water maze, hippocampal lesioned rats are not impaired on the task (Pearce, Roberts and Good, 1998). Pearce et al. (1998) trained rats to locate a hidden platform that changed location session by session. Even though the location of the platform changed each session, a landmark was also present at a fixed distance and angle from the platform. Hippocampal lesioned rats learned to locate the platform by use of the landmark and their and non-reinforced. This discrimination cannot be acquired because neither of the stimuli reliably predicts an outcome. However, the configural association system would be able to solve the discrimination task, because when the stimuli are presented in compound they form a unique representation that is different from their individual representations. Sutherland and Rudy (1989) claim that hippocampal lesioned rats are impaired at solving a negative patterning task due to the loss of function of the configural association system, but the simple association system is left intact allowing for elemental learning to still be possible.

1.3.3 Configural associations and spatial learning of allocentric cues

The 'configural association' theory of Sutherland and Rudy (1989) accounts for the findings of Morris et al. (1982), in which hippocampal lesioned rats were found to be impaired on a standard Morris water maze reference memory procedure, by making the assumption that navigation to a goal requires subjects to form configural representations of the allocentric cues that are present in an environment. Approach towards a spatial cue in one trajectory may result in reward but approach to the same cue in a different trajectory may not result in reward. Therefore, single cues will fail to gain associative strength due to the inconsistent pairings with different outcomes. Consequently, learning can not be supported by a simple association system (Sutherland and Rudy, 1989). Configurations of stimuli will come to gain associative strength by providing a high reliability of predicting an outcome. For example, approaching the configuration AB may consistently lead to reward, whereas approaching AC may not lead to reward. It is not simply that the stimuli B and C become conditioned exciters or inhibitors, respectively, because it is possible that all stimuli may have excitatory and inhibitory associations that cause them to fail to gain

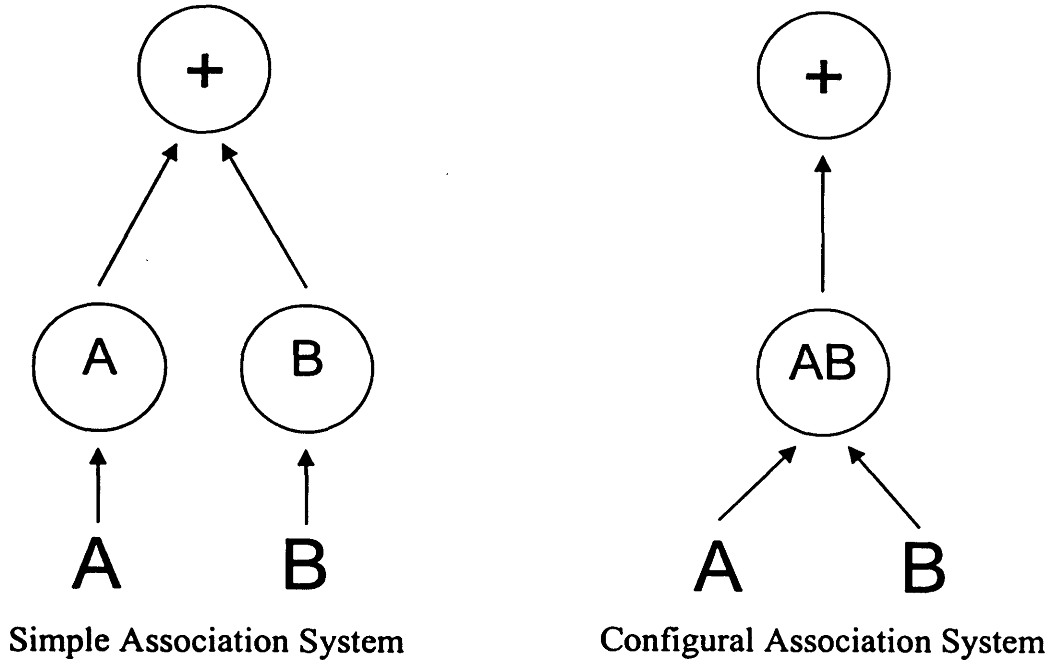

Figure 1.2. The association formed by the 'simple' and 'configural association' systems, as a consequence of rewarded training of a compound (AB), according to Rudy and Sutherland (1995). The left column depicts the learning of the 'simple association' system. Each stimulus enters into an association with reward. Like the elemental theory of Rescorla-Wagner (1972), the associative strength of the compound is equal to the algebraic sum of the associative strengths of its elements. Therefore, individual presentation of elements would result in less responding than to the compound. The right column depicts learning of the compound by the 'configural association' system. The representation of the compound as a unique configuration, AB, enters into an association with reward. Once the configural representation of the compound is acquired, individual presentation of the elements would come to only partially activate the representation of the configural cue, similar to the configural learning theory of Pearce (1994).

By the use of discrimination tasks that have a non-linear solution, Sutherland and Rudy (1989) claim that learning between these two systems can be dissociated. For the case of a negative patterning task, A+ B+ AB- (Woodbury, 1943), a simple association system would fail to learn this task due to stimuli being equally reinforced association' theory interpretation of spatial learning and tests of the predictions of Sutherland and Rudy (1989) will subsequently be discussed.

1.3.2 Simple and configural association systems

The 'configural association' theory of the hippocampus (Sutherland and Rudy, 1989) claims that there are two mechanisms within the brain for learning associations: a simple association system and a configural association system. The simple association system is capable of learning about elemental associations in which a stimulus can come to predict an outcome. This notion is similar to the Rescorla-Wagner (1972) model of associative learning in which individual elements compete for associative strength that can be gained from presentations of a reward contingency. In contrast, the configural association system treats multiple elements that may be associated with an outcome as one unique representation that will come to acquire associative strength during the course of learning. The simple and configural association systems differ in how they treat representations of stimuli. For example, if two stimuli A and B are both presented on a training trial, the simple association systems allows A and B to individually accrue associative strength, whereas the configural association system would treat A and B as forming a representation of A and B together (AB), and the configuration AB would come to accrue associative strength. The associations that would be formed by the 'simple' and 'configural association' systems (as predicted by Rudy and Sutherland, 1995), as a consequence of training with the compound AB are depicted in Figure 1.2.

system will be evaluated. The tests of Sutherland and Rudy's (1989) theory will be discussed with reference to a revised 'configural association' theory of Rudy and Sutherland (1995).

Negative Patterning
A+ B+
AB-

Feature-Neutral
A+ BC+
AB- C-

Transverse Patterning
A+ B-
B+ C-
C+ A-

Biconditional
AB+ CD+
AD- CB-

Figure 1.3. The design of four discrimination tasks that require a configural solution. For the negative patterning task, elements are reinforced when presented individually and non-reinforced when presented in compound. For the feature-neutral task, the element A is reinforced and the element C is non-reinforced. When elements A and C are presented with the element B, the reinforcement contingencies are reversed. For the transverse patterning discrimination pairs of the elements, A, B and C are presented simultaneously and elements within the pair are differentially reinforced. Each element is equally reinforced and non-reinforced over the three discriminations. For the biconditional discrimination, pairs of the stimuli A, B, C and D are required to be discriminated. Across the four compounds, each element is equally reinforced and non-reinforced.

As well as the negative patterning task there are several configural discriminations that have been used to test the function of the hippocampus. These tasks include transverse patterning, feature-neutral discrimination and biconditional discrimination. The designs of these tasks are described in Figure 1.3. According to Sutherland and

Rudy (1989) a discrimination task requires the integrity of the hippocampus if it has a non-linear solution. Thus, in a non-linear discrimination, no one stimulus can reliably predict an outcome, only the unique configurations of stimuli are able to enter into associations with a reward.

1.3.4.2 Negative Patterning

The negative patterning task (Woodbury, 1943), as described previously, requires a configural solution due to each stimulus being reinforced when presented individually and non-reinforced when presented in compound. This task can be assumed to be of a high level of difficulty due to the summation of the individual elements' associative strength, when presented in compound, being in conflict with the required inhibition of responding to the compound AB. The task cannot be explained by elemental models of learning, such as the Rescorla-Wagner model (1972) without attributing additional unique cues that are present when stimuli are presented in compound. An elemental model of learning would claim that unique cues can acquire the negative associative strength that would result in inhibition of responding to the compound (Rescorla, 1973). It is of interest to note that when presented with a complex negative patterning discrimination, A+, BC+, ABC-, pigeons show a greater discrimination of A from ABC, than for the discrimination BC from ABC (Redhead and Pearce, 1995). This contradicts the predictions of the Rescorla-Wagner model (1972) that claims that due to the sum of the associative strengths of BC, responding will be greater to BC than for A, which is presented alone. The results of Redhead and Pearce (1995) can be explained in terms of a configural theory of learning, that claims that responding will be based on the extent of generalisation of reinforced configurations from non-reinforced configurations (Pearce, 1994). Therefore, A is less similar than BC to the performance was not disrupted by the location of the platform changing each session. In contrast, control rats showed evidence of learning within a session, inferring that they were using the room cues to locate the platform (Pearce et al., 1998). This gives credence to the hypothesis that the 'simple association system' functions independently of the hippocampus.

The appeal of the 'configural association' theory (Sutherland and Rudy, 1989) lies in the fact that it can account for a variety of results which at face value do not appear to be related. The proposed unitary function of the hippocampus mirrors the systematic regularities of the neuroanatomical structure and appeals to parsimony. The importance of the 'configural association' theory (Sutherland and Rudy, 1989) for this thesis, lies in its ability to account for impairments on spatial learning tasks that require learning of allocentric cues, and also for its account of non-spatial discrimination tasks that require non-linear solutions. The theory makes precise, testable predictions for the learning of discrimination tasks in which configural associations must be acquired. Therefore, it is possible to falsify the assumptions made about spatial learning by testing hippocampal lesioned rats' ability to solve configural discriminations.

1.3.4 Learning of configural associations

1.3.4.1 Non-linear discriminations

A variety of discrimination tasks that are claimed to require configural learning have been used to test the 'configural association' theory (Sutherland and Rudy, 1989). These tasks will be described, and the ability of the 'configural association' theory to predict impairments following lesions of the hippocampus and the hippocampal unlikely, due to there not being an activation in the hippocampus following presentation of novel visual features in Experiment 1. Therefore, it can be assumed that the activation in the hippocampus was caused by the novel spatial arrangement of the familiar visual array.

In a related study by Jenkins et al. (2004), to test the validity of the findings of Wan et al. (1999), rats were trained to solve a radial-arm maze task with visual stimuli hung at equal distances from the maze on a curtain that surrounded the apparatus. On a test trial, the visual stimuli were rearranged so that stimuli still occupied the same locations, but were now in a novel spatial arrangement. The design ensured that the rats were learning about the stimuli rather than being behaviourally passive, as in the experiments of Wan et al. (1999). The experiment used a between-subjects design which benefits from eliminating the influence of cross-hemispheric connections on the level of c-*fos* expression. It was found that rats that were exposed to the novel arrangement showed significant increase in activation in the hippocampus, compared to a group that was exposed to the familiar arrangement used for training of the task. A behavioural control experiment was used to show that rats were using the visual stimuli (Jenkins et al., 2004). The presentation of novel spatial arrangements results in increased activation in the hippocampus in a task in which learning of the cues is explicitly required for successful performance. Even though there was activation in the hippocampus caused by novel spatial arrangements of stimuli, this may not necessarily reflect the necessity of the hippocampus for learning a task that would require distinguishing between compounds that have the same features but are presented in differing spatial arrangements.

amount of activation in the hippocampus in the ipsilateral hemisphere (Wan et al., 1999) (see Figure 1.1). Therefore, the novelty inherent in the different visual stimuli did not produce activation in the hippocampus.

In a second experiment (Wan et al., 1999), the same procedure was used, but this time rats were exposed to an array of visual stimuli presented in a particular spatial arrangement. An array would consist of visual stimuli similar to the stimuli used in the previous experiment, but now items would be presented in different locations on the computer monitor. An array would include three stimuli presented diagonally from the top right to the bottom left of the computer monitor. Rats were exposed to these arrays of stimuli repeatedly so that they became familiar. On a test session, rats were presented with the familiar stimuli to one eye, and for the other eye the same arrays were presented, but now the spatial locations of the stimuli were novel. The same locations on the computer were used, but now if stimulus A had been previously been located in the top right, it would now be presented in either the centre or the bottom left corner, and so on for the other two stimuli. Neither the stimuli nor the locations of stimuli were novel, only the conjunction of a stimulus in a location and the spatial relationship between the stimuli were novel. It was found that this produced a significant amount of c-*fos* activation in the hippocampus in the hemisphere contralateral to the eye to which the novel spatial arrangements had been presented, compared to the hippocampus in the ipsilateral hemisphere (Wan et al., 1999) (see Figure 1.1). It is possible that the novelty was not caused by the novel arrangement of the items, but could be due to rats only attending to only one spatial location of the array. Therefore in the test stage, a stimulus that had been previously presented to the rats, but which may not have been attended to, would appear in a novel location, and would consequently be novel to the rats. This, however, seems visual field would have an effect on the contralateral hemisphere, but would have less of an effect on the ipsilateral hemisphere.

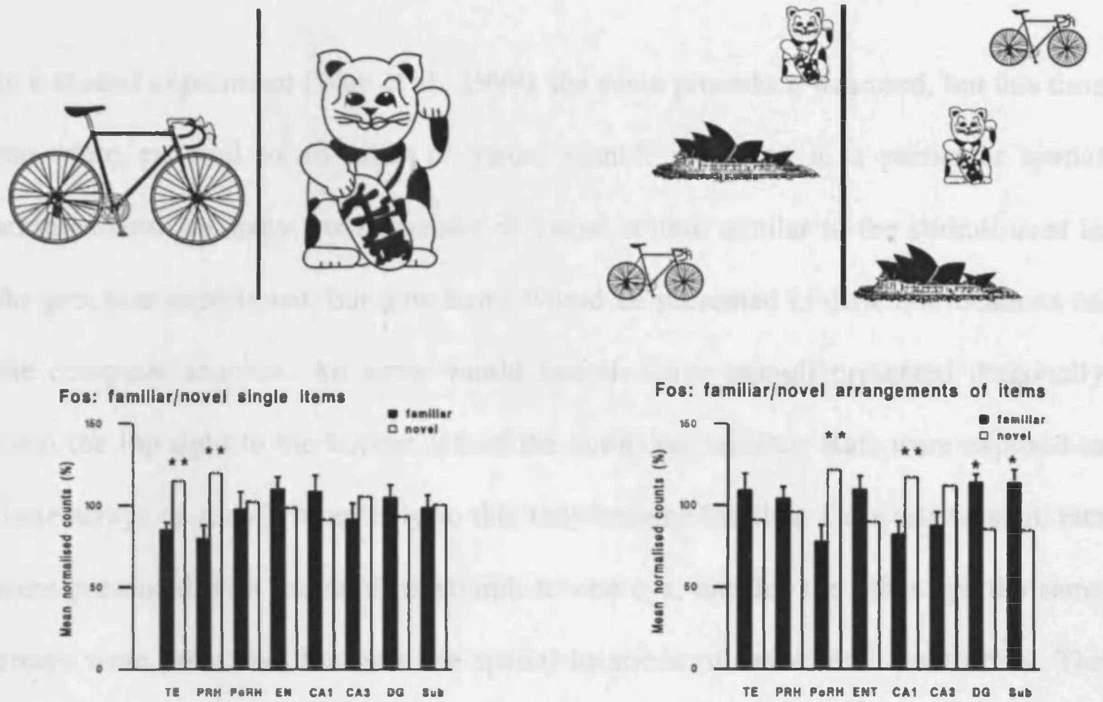

Figure 1.1. Results of Wan et al. (1999). The left hand column depicts an example of stimuli used for Experiment 1. Presentation of novel visual stimuli did not result in an increase of c-*fos* activation in the hippocampus. The right hand column depicts an example of stimuli used for Experiment 2. Presentation of novel arrangements of familiar arrays of visual stimuli resulted in an increase of Fos activation in the hippocampus.

In the first experiment (Wan et al., 1999), rats were presented with a variety of visual stimuli on the computer monitors. Stimuli were shown repeatedly to both eyes, so that stimuli became familiar. In a test session, rats saw stimuli that had previously been presented through one eye, and a novel set of stimuli presented to the other eye. There was not a significant increase in c-*fos* in the hippocampus in the hemisphere contralateral to the eye that had been exposed to the novel stimuli, compared to the

1.3 Configural association theory of the hippocampus

1.3.1 Spatial tasks and non-spatial discrimination learning

The work that has so far been discussed in this chapter provides evidence for the hippocampus being important for spatial learning of allocentric cues, and also for learning of objects and the spatial locations in which they are presented. The 'cognitive map' theory of the hippocampus (O'Keefe and Nadel, 1978) can account for these findings by claiming that the hippocampus encodes the spatial relationships between cues that appear in an environment. However, the theory of O'Keefe and Nadel (1978) cannot account for impairments on non-spatial tasks that are caused by damage to the hippocampus.

Rudy and Sutherland (1989) found that lesions of the hippocampus impaired the ability of rats to solve a negative patterning discrimination (Woodbury, 1943). In the negative patterning task, a light (L) and a tone (T), when presented individually, were paired with food. When both L and T were presented simultaneously on a trial, no food was provided. Therefore, the compound of LT is required to be discriminated from the separate presentation of its features L and T. Sutherland and Rudy (1989) interpreted this result as reflecting an inability to form configural associations. Due to the molecular neuroanatomical structure of the hippocampus, and with the desire for parsimony, Sutherland and Rudy (1989) concluded that the hippocampus is responsible for the unitary function of forming and storing configural associations (see Moser and Moser, 1998; Witter, Nabler, van Haeften, Machielsen, Rombouts, Barkhof, Scheltens, and da Silva, 2000; Bannerman, Yee, Good, Heupel, Iversen, and Rawlins, 1999, for evidence against a unitary function of the hippocampus). Therefore, it is assumed that configural learning underlies the hippocampal dependent spatial learning of allocentric cues (Sutherland and Rudy, 1989). The 'configural compound ABC, consequently there will be greater responding to A than to BC. The finding of Redhead and Pearce (1995) cannot be accounted for by an elemental theory of learning (Rescorla and Wagner, 1972), therefore, supporting a configural theory of learning. However, elemental models of learning can incorporate findings of configural learning if it is assumed that certain stimuli have a different level of influence over learning of other stimuli when learned in compound (Brandon, Vogel and Wagner, 2000).

1.3.4.3 Feature-neutral discrimination

The feature-neutral discrimination (Gallagher and Holland, 1992) is similar to the negative patterning task in that single elements are paired with an outcome, but when presented in compound, the reward contingencies are reversed. Thus, A is reinforced, but when presented with B, the compound, AB, is now non-reinforced. Similarly, C is non-reinforced, but when presented with B, the compound, BC is now reinforced. Therefore, both A and C do not reliably predict an outcome. Also, the neutral feature, B, fails to gain any associative strength due to being equally reinforced and non-reinforced when presented in compound with either A or C.

1.3.4.4 Transverse Patterning

Spence (1952) claimed that the transverse patterning task is an example of a simultaneous discrimination that requires processing of both stimuli as a configuration for the task to be solved. The discrimination requires three simultaneous discriminations to be solved concurrently. When a pair of stimuli is presented, one stimulus is reinforced and the other stimulus is non-reinforced. Consequently, subjects are required to choose between the two stimuli to receive reward. Three stimuli are used to form three pairs of discriminations so that each element is equally reinforced and non-reinforced. Therefore, A is correct when presented with B, B is correct when presented C, and C is correct when presented with A.

1.3.4.5 Biconditional Discrimination

The biconditional discrimination (Saavedra, 1975) is similar to the transverse patterning task in that stimuli are always presented in compound. However, compounds of stimuli are reinforced or non-reinforced, rather than individual elements within a compound. Four stimuli are used to form four compounds. Each stimulus is reinforced when paired with another particular stimulus, but non-reinforced when paired with a different stimulus. The task can only be solved by learning the unique configurations formed by the compounds of the stimuli.

1.3.5 Tests of a configural association theory of the hippocampus

The four discriminations tasks that have been described, all according to the predictions of Sutherland and Rudy (1989) are dependent on a 'configural association' system, and, therefore, should require the integrity of the hippocampus for their solution. The evidence for the hippocampus' involvement in these tasks will now be assessed.

1.3.5.1 Negative patterning

The initial experimental support for the 'configural association' theory of the hippocampus came from evidence that hippocampal lesioned rats were impaired on a configural solution, hippocampal rats failed to acquire the discrimination, and also the level of performance fell on the two previously learned discriminations. This follows the predictions of the 'configural association' theory as proposed by Sutherland and Rudy (1989).

Whereas, Alvarado and Rudy (1995a; 1995b) and Dusek and Eichenbaum (1998) found that hippocampal lesions impaired performance of a transverse patterning task, Bussey, Warburton, Aggleton and Muir (1998) found that fornix lesions did not impair the ability to learn a transverse patterning task. Moreover, it was found that the lesions facilitated the acquisition of the transverse patterning discrimination, compared to controls. The fornix lesioned rats did, however, show impaired performance on a T-maze alternation and Morris water maze task, thereby making a double dissociation between configural learning and spatial learning, which contradicts the claims of Sutherland and Rudy (1989).

Damage to the hippocampus (Saksida, Bussey, Buckmaster and Murray, 2003) and to the hippocampal system by the use of fornix lesions (Brasted, Bussey, Murray and Wise, 2003) in monkeys has failed to show impairments on a transverse patterning task. These results, together with the findings of Bussey et al. (1998) do not support the 'configural association' theory of the hippocampus (Sutherland and Rudy, 1989). In all of these examples of damage, either to the hippocampus or to the hippocampal system, animals were trained progressively to acquire all three discriminations. This is similar to the procedures used by Alvarado and Rudy (1995a, 1995b) and Dusek and Eichenbaum (1998). It does not appear that there are procedural differences which can account for the contradictory findings. Bussey et al. (1998) in a second experiment, presented rats with all three of the discriminations to be solved concurrently from start negative patterning task (Rudy and Sutherland, 1989). Rats received training of instrumental bar pressing to a tone and a light that were both paired with food when presented individually. When both stimuli were presented simultaneously no food was given. It was found that excitotoxic lesions to the hippocampus causing selective damage to CA1, CA3 and the dentate gyrus, impaired acquisition of the discrimination, and also lesions made after acquisition caused the discrimination to no longer be performed. It was claimed that the deficit in performance of the discrimination was due to an inability to form a configural association between the simultaneous presentation of the tone and light and no food, rather than an inability to withhold responding on non-reinforced trials (Davidson and Jarrard, 2004), because the rats showed a normal drop in responding during inter-trial intervals and normal acquisition of an elemental discrimination. This result has been supported by similar findings in which negative patterning has been found to be dependent on the hippocampus (Alvarado and Rudy, 1995a; McDonald, Murphy, Guarraci, Gortler, White and Baker, 1997).

In contrast Davidson, McKernan and Jarrard (1993) found that hippocampal lesioned rats were not impaired on a negative patterning discrimination. The performance of rats with kainic acid and colchicine lesion, as used by Rudy and Sutherland (1989) were compared with rats who received ibotenic acid lesions of the hippocampus. Davidson et al. (1993) suggested that the ibotenic acid lesions of the hippocampus may be more selective than the kainic acid and colchicine lesion used by Rudy and Sutherland (1989). Therefore, deficits on a negative patterning task may be due to extra damage to non-hippocampal areas. However, both lesion groups were not impaired on the task. In contrast, Alvarado and Rudy (1995a) used both lesion types and still found an impairment on a negative patterning task. The contradictory results hippocampal lesions on configural discriminations. McDonald et al. (1997) suggest that deficits may be found on some configural tasks with hippocampal lesions, but not with fornix lesions due to the sparing of retro-hippocampal connections to other brains areas that may mediate performance.

1.3.5.2 Feature-neutral discrimination

Gallagher and Holland (1992) trained rats on a feature-neutral discrimination. Hippocampal rats were not impaired on this task, but in contrast, were impaired on a spatial reference memory task in a Morris water maze. These results contradict the predictions of the Sutherland and Rudy (1989) and also appear to dissociate configural learning from spatial learning. This finding is surprising due to the similarities between this conditional task and the negative patterning used by Sutherland and Rudy (1989). Both tasks require learning the associations of stimuli when they are presented alone compared to their associations when presented in compound with other stimuli. It is possible that the difference between the lack of impairment on a feature-neutral discrimination (Gallagher and Holland, 1992) and negative patterning (Rudy and Sutherland, 1989) may be due to the ibotenic acid lesions used by Gallgher and Holland (1992) than the kainic acid and colchicine lesions used by Rudy and Sutherland (1989). However, Alvarado and Rudy (1995a) found that ibotenic acid lesions still resulted in an impairment on a negative patterning task, whilst sparing performance of a feature-neutral discrimination. This raises the issue of whether different configural tasks may have a different dependency on the hippocampus. This issue will be addressed when the revised 'configural association' theory of Rudy and Sutherland (1995) is considered.

Nonetheless, the result of Gallagher and Holland (1992) can not be accounted for by a 'configural association' view of the hippocampus. Moreover, it was found by Han, Gallagher and Holland (1998) that hippocampal lesions could facilitate performance of a serial feature-neutral discrimination when a short inter-trial interval was used between presentations of the discriminative stimuli. Han et al. (1998) claimed that the increase in performance was due to reduced pro-active interference between the responses required for reinforced and non-reinforced trials. Therefore, not only was there a lack of impairment found, but also the effect of a hippocampal lesions facilitated performance under conditions that were not specific to the nature of the configural discrimination.

1.3.5.3 Transverse Patterning

It has also been found that hippocampal lesions impair acquisition of a transverse patterning task (Alvarado and Rudy, 1995a, 1995b; Dusek and Eichenbaum, 1998). Alvarado and Rudy (1995a; 1995b) trained rats in a water tank on a transverse patterning task in a progressive manner. Training started with the presentation of A+ B-. Once this discrimination was acquired, the B+ C- discrimination was introduced, and when subsequently learned, the final C+ A- discrimination was introduced. To ensure that a configural strategy is used to solve the task, all three discriminations must be solved concurrently. In the task used by Alvarado and Rudy (1995a, 1995b) the discrimination does not require a configural solution until the final discrimination is introduced, because (up until this point) A always signals reward and C reliably signals non-reward. Alvarado and Rudy (1995b) found that, although performance was lower than that of the control rats, hippocampal rats were able to acquire A+ B- discrimination. When the third discrimination was introduced, thus forcing a of Davidson et al. (1993) and Alvarado and Rudy (1995a) could be due to the measures used for responses made in the presence of stimuli. Davidson et al. (1993) claimed that over responding by kainic/colchicine acid lesioned rats could mask the ability to solve a discrimination, and instead, used a discrimination ratio to compare performance between control and experimental rats. This possible answer does not hold true for the findings of McDonald et al. (1997) in which kainic/colchicine acid lesions of the hippocampus produced deficits on a negative patterning task, even when a discrimination ratio was used to calculate performance.

Although the results of Davidson et al. (1993) may appear anomalous against the evidence of the negative patterning task being dependent on the hippocampus, Bussey, Dias, Redhead, Pearce, Muir and Aggleton (2000) found that damage to the hippocampal system caused by lesions of the fornix also fail to impair performance of a negative patterning task. Bussey, Dias, et al. (2000) also used control discriminations to evaluate whether rats were using non-configural strategies to solve the discrimination. It was found that learning could not be due to suppressing responding on the bias of numeriosity. Animals were given trials in which a stimulus C+ was reinforced. When paired with B and with A, it was found that animals responded more to AC and BC than to AB. Therefore, animals had learned to inhibit responding to the configuration formed by AB rather than to withhold responding to compound stimuli in general.

It is important to note that whilst Bussey, Dias et al. (2000) failed to find evidence of fornix lesions impairing a negative patterning discrimination, McDonald et al. (1997) found that hippocampal lesions retarded acquisition of a negative patterning task, but fornix lesions did not. Therefore, it is possible to dissociate the effects of fornix and

The 'configural association' theory of the hippocampus (Sutherland and Rudy, 1989; Rudy and Sutherland, 1995) fails to account for some of the data on configural discrimination learning by hippocampal lesioned animals. Consequently, it is unlikely that spatial tasks that require learning about allocentric cues need tap into the same processes that underlie the solution of configural discriminations. If the conjunction of an object in a particular spatial location is not encoded by the use of configural learning, then this raises the question of whether the featural information provided by an array of spatial cues is sufficient for spatial learning to occur.

1.4 The hippocampus and structural learning

It will now be proposed that a possible function of the hippocampus is to encode the spatial relationships between stimuli. As opposed to the 'configural association' theory (Sutherland and Rudy, 1989; Rudy and Sutherland, 1995) it is assumed that configural learning is not dependent on the hippocampus, but configurations of stimuli that are encoded with regards to their spatial structure do require the integrity of the hippocampus. Some of the previously discussed literature will now be addressed with regards to reflecting structural learning, and the means of testing structural learning will be described.

Save et al. (1992) habituated rats to an array of objects presented in constant spatial locations. When the spatial arrangement of the objects was altered, control rats showed an increase in exploratory behaviour, whereas hippocampal lesioned rats did not show an increase. As the same objects were used throughout the experiment it was the spatial relationship between the cues that was novel (Save et al., 1992). This finding could be interpreted as evidence for the involvement of the hippocampus in revised 'configural association' theory of Rudy and Sutherland (1995), which will be discussed in the next section.

1.3.6 A revised configural association theory of the hippocampus

1.3.6.1 Implications for the involvement of the hippocampus in learning of non-linear discriminations

In response to the evidence against a 'configural association' theory of the hippocampus, Rudy and Sutherland (1995) provided a revised theory that attempted to reconcile the inconsistencies in the data. Rudy and Sutherland (1995) claimed that configural associations are stored in the neocortex, rather than in the hippocampus, and that the hippocampus plays a modulatory role in amplifying the salience of configural representations stored within the cortex. The consequence of this becomes apparent when the non-linear tasks described previously are now categorised by the amount of conflict between the component features' associative strengths and the configurations' associative strengths. In the case of the negative patterning task, both elements A and B have excitatory associative strengths that are in opposition to the inhibitory associative strength of the configuration AB. The hippocampus is assumed to amplify the salience of the configural representation of the AB compound, thereby decreasing the similarity between the representations of the component features, A and B, and the configural representation AB. Therefore, lesions of the hippocampus result in increased similarity between the individual representations of the constituent features of a compound and the configural representation of the compound itself, making the discrimination more difficult to acquire.

Nissen, 1953). If this is the case then learning a transverse patterning task should be similar to learning a biconditional discrimination. Therefore, the theory of Rudy and Sutherland (1995) could be reinterpreted as making the opposite prediction, i.e. that hippocampal lesions will have little effect on a transverse patterning task.

1.3.6.2 Problems for the revised configural association theory of the hippocampus

Although the revised 'configural association' theory of Rudy and Sutherland (1995) can account for some of the previously discussed findings, the spared performance on a negative patterning discrimination (Davidson et al., 1993; Bussey, Dias, et al., 2000) and on a transverse patterning discrimination (Bussey et al., 1998; Brasted et al., 2003; Saksida, et al., 2003) still remains problematic for the theory. What could be drawn from the results that have been discussed, is that the hippocampus may be responsible for learning of some discriminations, but whether the task requires configural learning is not crucial to the involvement of the hippocampus.

A possible answer to the contradictory results on configural learning and the hippocampus has been proposed by O'Reilly and Rudy (2001). O'Reilly and Rudy (2001) claim that both the hippocampus and the neocortex can learn to encode conjunctive representations of stimuli, but whilst the neocortex slowly acquires conjunctive representations and only does so if a task requires configural learning, the hippocampus rapidly acquires configural representations and automatically encodes configurations even when learning is incidental. Therefore, it may be incorrect to assume that the elemental learning and configural learning is dissociable on the basis of the demands on the task.

Rudy and Sutherland (1995) claim that in the case of the feature-neutral discrimination, as used by Gallagher and Holland (1992), there is less conflict between the associative strengths of the compounds and the individual stimuli. This is because in the feature-neutral discrimination, A+, AB-, C- and CB+, each compound consists of an element that has an individual associative strength that is in direct conflict with the compound's associative strength (i.e. A+ and AB-, C- and CB+), whereas the other stimulus that forms the compound has a neutral associative strength that results in less conflict between its associative strength and the compound's associative strength. Therefore, B has a neutral associative strength and has less conflict with the associative strengths of AB and CB than do the stimuli A and C. The increased salience of the configural representations by the hippocampus will have less of an effect in this task, than for the negative patterning, in which the associative strengths of both the individual stimuli are in opposition to the negative associative strength of the compound, thus accounting for the lack of impairment found by Gallagher and Holland (1992) on the feature-neutral task.

For the case of a discrimination such as a biconditional discrimination in which individual elements are never presented alone, the constituent features of the compounds each have a neutral associative strength. Consequently, the hippocampus will have little effect of facilitation on this task due to the conflict of individual feature's associative strengths and configurations associative strengths being small. This accounts to some extent for the findings that hippocampal lesioned rats can acquire biconditional discriminations (Whishaw and Tomie, 1991; McDonald et al., 1997; Good et al., 1998, Coutereau et al., 2002). However, it follows that less of an impairment should be seen on biconditional discriminations compared to feature-neutral discriminations (Rudy and Sutherland, 1995). This is due to the compounds used in the feature-neutral discrimination containing one element that has a value of associative strength that is opposite to the associative strength of the compound (i.e. A is positively rewarded, but the compound of AB is negatively rewarded). Stimulus B in the compounds presented in the feature-neutral discrimination has a neutral value of associative strength, therefore, this stimulus is in less conflict with the associative strength of the compound. For the biconditional discrimination, none of the stimuli are individually reinforced, therefore, each stimulus has a neutral value of associative strength, and does not take on opposing values to associative strengths of the compounds. Thus, Rudy and Sutherland (1995) claim that the feature-neutral discrimination should require the integrity of the hippocampus more than the biconditional discrimination. However, Whishaw and Tomie (1991) and McDonald et al. (1997) reported mild deficits on a biconditional discrimination, whereas there was no impairment on a feature-neutral discrimination (Gallagher and Holland, 1992).

For the case of the transverse patterning task, Rudy and Sutherland (1995) claim that whilst each stimulus is always presented in compound, similar to the biconditional discrimination, within the compound one stimulus is always reinforced differentially to the other component stimulus. It is claimed that the hippocampus is required to decrease the similarity between the representations that are in conflict. This function accounts for the results of Alvarado and Rudy (1995a, 1995b) and Dusek and Eichenbaum (1998). Although, this account is plausible to some extent, it is not clear what associative strengths the configural representations of the compound stimuli will acquire, as each compound contains a reinforced and non-reinforced element. An alternative view is that a transverse patterning discrimination can be achieved by learning about configurations, and the associations they acquire, formed by the perception of one stimulus and the memory trace of another stimulus (Spence, 1952;

of training, and once again found that fornix lesions facilitated acquisition of the transverse patterning task. Thus, the procedure for training the transverse patterning task does not appear to be crucial in determining whether lesion effects are found.

1.3.5.4 Biconditional discrimination

A lack of impairment following damage to the hippocampus has also been found on a biconditional discrimination. Good, de Hoz and Morris (1998) found that hippocampal lesioned rats were able to learn a biconditional discrimination in which two contexts, A and B, were used to govern responding to stimuli, X and Y. Also Coutereau, Killcross, Good, Marshall, Ward-Robinson and Honey (2002) found that hippocampal lesions did not impair acquisition of two concurrently learned biconditional discriminations. Acquired equivalence/distinctiveness manipulations did not reveal any differences in the representations formed of the configurations (Coutereau et al., 2002). Other studies have suggested that whilst able to learn a biconditional discrimination, hippocampal lesioned rats are retarded in acquisition of this task (Whishaw and Tomie, 1991; McDonald et al., 1997). The slight impairments shown by lesioned rats can to some extent be attributed to the selectivity of the lesions, hyperactive behaviour (Whishaw and Tomie, 1991), and possible ceiling levels of performance masking the ability to assess successful discrimination (McDonald et al., 1997). Nevertheless, it remains that the lesioned rats were able to acquire the task and in the experiments of McDonald et al. (1997) the deficit on the biconditional discrimination was far milder than on a negative patterning discrimination. The difference in the performance of a biconditional discrimination and a feature-neutral discrimination is relevant to the theoretical implications of the learning the spatial structure between two or more spatial cues. Thus, the failure of hippocampal lesioned rats to show an increase in exploratory behaviour could be due to impaired structural learning. Consequently, the spatial arrangement of objects used for habituation and for the test was in essence the same for hippocampal lesioned rats.

The role of the hippocampus in encoding structural features can also be inferred from the study of Wan et al. (1999). Presentation of novel two-dimensional visual cues, did not result in neuronal activation in the hippocampus, but when an array of visual stimuli was presented in a novel spatial arrangement, there was significant activation of cells in the hippocampus (Wan et al., 1999). Therefore, the hippocampus is sensitive to changes in the spatial relationships between stimuli, but is not sensitive to novel visual features. The activation of neurons in the hippocampus may underlie learning of the spatial relationships between two or more visual stimuli.

1.4.1 Structural discriminations

If spatial learning of allocentric cues is achieved by encoding the spatial structure between two stimuli, then it can be predicted that it is possible to learn to discriminate between two configurations that have the same features, but differ in their structure. George, Ward-Robinson and Pearce (2001) have demonstrated that rats are capable of learning about configurations when the task requires explicit learning of the structural features of a stimulus compound. In the task used, rats were required to make a simultaneous discrimination between two configurations, AB+ (i.e. A to the left of B) and BA- (i.e. B to the left of A). The configurations consist of the same features, A and B, but differ in their spatial relationships, i.e. A to the left of B or B to the left of A.

If the structural features of a stimulus-compound are learned by increments in the strength of association with an outcome then it is possible for partial generalisation of learning to occur to novel structural arrangements of the elements within the compound. This logically follows from the model of structural learning as proposed by George et al. (2001). However, O'Keefe and Nadel (1978) state that there is little generalisation between items within and between cognitive maps due to the formation of a cognitive map rendering items within a map distinct due to the unique spatial relationships formed with other items within the map. Also, mismatches between features of an environment and the stored representation cause new learning which results in an all or nothing change of the cognitive map. Therefore, if structural learning requires a 'cognitive map' there should be little or no generalisation between representations of the stimuli. This is contradictory to the claim that structural discriminations are difficult to learn due to the high level of generalisation between reinforced and non-reinforced compounds (George et al., 2001). Thus, the definition of the 'locale' system (O'Keefe and Nadel, 1978) leads to predictions that are at odds with a view of configural learning (Pearce, 1994; George et al., 2001) if it is believed that spatial learning of allocentric cues and structural discriminations both require the hippocampus. These issues are addressed in Experiment 10b.

The prediction that the hippocampus plays a role in the learning and memory of structural discriminations has implications for theories of the hippocampus that stress the importance of flexibility (Eichenbaum, 1992) or discriminability (Gluck and Myers, 1993; O'Reilly and Rudy, 2001) of stimulus representations. Whilst these theories suggest that hippocampal damage can spare configural learning, either the underlying representations of the stimuli are assumed to be different from those formed by animals with an intact hippocampus (Eichenbaum, 1992; Gluck and Myers,

Chapter Two

Conditions for Learning Structural and Configural Discriminations

Introduction

It has been reported that rats can learn a structural discrimination using a water tank apparatus with the reinforced and non-reinforced stimuli presented simultaneously so that rats have to make a choice by approaching one of the stimulus-compounds (George et al., 2001). In this task, rats were trained on the discriminations progressively so that once one discrimination was acquired the rat would then be introduced to another discrimination whilst still being presented with the previously acquired discrimination. This procedure continued until all three discriminations were acquired and were solved concurrently. The progressive introduction of discriminations was used because it was claimed from evidence provided by a pilot study (George et al., 2001) that if rats are presented with all three discriminations from the start of training they will not acquire the task. The pilot study was run for 15 sessions, one session per day, and there was no apparent change in the performance of the rats from chance level (George et al., 2001).

The fact that rats were not able to learn when all discriminations were introduced from the start of training but were able to learn when introduced progressively may be due to the initial level of task difficulty that could result in learned helplessness (Jackson, Alexander and Maier, 1980) and thus rats fail to learn the task. The reasons why rats were able to learn the task when trained in a progressive manner could be due to several factors. Firstly, there could be a 'learning to learn' factor (Kehoe, 1988) that enables the visual stimuli used in the task to dictate behaviour rather than any of

In the following chapters, the hypothesis that the hippocampus is involved in the learning and memory of the structural features of a configuration will be tested, using a variety of tasks. In all of the tasks, two-dimensional stimuli are presented in compound, and will either require discrimination of the structural features that are inherent in the compound, or configural processing that does not require the discrimination of structure. It is predicted that hippocampal lesions will impair a rat's performance on a structural discrimination, due to the impaired learning of configurations that consist of the same elements, but differ in their structure. Hippocampal lesions, however, should not impair a configural discrimination in which unique compounds containing elements that are equally reinforced and non-reinforced are differentially reinforced.

These predictions will be tested by examining the effects of hippocampal lesions on a structural discrimination, transverse patterning task and a biconditional discrimination. It is predicted that whilst impaired on a structural discrimination, performance will not be impaired on the two configural tasks: transverse patterning and a biconditional discrimination. Both of these tasks are of a similar difficulty level to that of the structural discrimination, in the amount of compound-reward associations that have to be learned, and the design of the tasks allows for similar stimuli to be used throughout the three tasks. Also, whilst the predictions for the effect of lesion on a biconditional discrimination address the theory of Sutherland and Rudy (1989), the predictions for the effect of lesion on a transverse patterning task are relevant to the revised 'configural association' theory of Rudy and Sutherland (1995). In one experiment, the effect of hippocampal lesions on a transfer of learning is also examined. In a biconditional discrimination, it is assumed that the presence of structural features will have little or no influence on learning, and will not lead to

1993), or that the factors leading to successful configural learning are subject to the explicit versus incidental demands of the task (O'Reilly and Rudy, 2001). Therefore, if a structural discrimination is interpreted as a non-linear task in which neither the features nor the spatial locations of the stimuli reliably predict an outcome, then the theories of Eichenbam (1992), Gluck and Myers (1993) and O'Reilly and Rudy (2001) would suggest that the effects of hippocampal lesions on structural tasks should be no different than for non-structural discrimination tasks. However, if this is found to not be the case, this will demonstrate a novel role of the hippocampus in learning the conjunctions of stimuli that form structural relationships rather than simply learning configural associations. The ability of these theories to account for the results of the present experiments will be discussed in Chapter Five.

It is possible for this discrimination to be solved elementally if attention is restricted to one area of the compound, so that A on the left is associated with reward and B on the left is associated with non-reward. Therefore, in the design employed by George et al. (2001) two other simultaneous discriminations were required to be solved to provide evidence of the learning of structure of the compound stimuli. As well as learning the AB+ BA- discrimination, rats were required to learn a BC+ CB- and a CA+ AC- discrimination (for the full design of the structural discrimination used by George et al. (2001) see Table 1.1). This does not permit an elemental solution as each stimulus in each location is equally rewarded as non-rewarded. For example, A to the left is reinforced when presented with B on the right, but when A is on the left with C on the right, A is no longer rewarded. None of the elements or any of the configurations of the elements reliably predicts the reinforcement contingency. Only the unique structural relationships between the stimuli within a configuration predict when reinforcement occurs.

Table 1.1. The design of a structural discrimination (George et al., 2001). Stimuli on the left are reinforced, whilst stimuli on the right are non-reinforced

+	-
AB	BA
BC	CB
CA	AC

Whilst is it presumed that a structural discrimination is of a high level of difficulty due to the amount of generalization between the features of reinforced and non-reinforced patterns, it could be argued that such visual scenes could be encoded as a whole representation and that consequent learning requires template matching of the visual scene with the mental representation of the scene. Rather than the component features of a visual array being required to activate configural representations of the various compounds, each compound is learned individually. An experiment by George and Pearce (2003) demonstrates that this is not the case. Pigeons were trained on a discrimination in which combinations of features, colour and orientation of a rectangular bar, were counterbalanced in a similar manner to the task used by George et al. (2001), and either predicted reinforcement or non-reinforcement. On test trials patterns were presented in a 90° rotation. The template matching account would predict that responding to the test patterns would be the same as when presented in their original state, since the pattern, even though rotated, would match the mental representation. In contrast, if the structure of the combination of the features is encoded then the rotation would alter the structural features (e.g. horizontal green bars to the left of vertical red bars rotated clockwise 90° becomes vertical green bars above horizontal red bars). According to this account, the rotation should cause a change in conditioned responding to the pattern, since it no longer consists of the same features with which it was trained. A reinforced pattern consisting of horizontal green bars to the left of vertical red bars rotated clockwise 90° contains the same conjunction of features of a non-reinforced pattern that consists of vertical green bars and horizontal red bars, but presented in a novel arrangement (i.e. above or below, rather than to the left or to the right). Therefore, there should be a reversal of learning.

The probe tests demonstrated that pigeons showed a change in conditioned responding as a result of the rotation, and it appeared that the rotation caused a complete reversal of performance, consequently not providing support for a template matching account of learning visual discriminations (George and Pearce, 2003). In increased exploration. However, once a feature of an environment has been encoded subsequent experience has no influence over the representation of the feature within the map (O'Keefe and Nadel, 1978).

Learning of structure may simply be the mechanism with which cognitive maps are formed. To be able to discriminate two spatial locations within an environment by the use of the distal and geometric relationships between cues is similar to the demands of the structural discrimination in as much as the presence of two cues may have dissociable associations depending on their spatial arrangement. Therefore, it is plausible to assume that the solution to a structural discrimination requires a cognitive map of the stimulus representations. However, whereas the 'cognitive map' theory of the hippocampus makes the distinction between 'taxon' and 'locale' learning systems, it is not necessary to make these distinctions when considering the role of the hippocampus in structural discriminations. The reasons for rejecting the distinction between 'taxon' and 'locale' learning will now be briefly discussed.

Simple, configural and structural discriminations can be achieved by incremental and decremental changes in strength of the association between the representations of the stimuli and an outcome of motivational significance. O'Keefe and Nadel (1978) state that learning of stimulus-reward associations that are motivated by biological necessity are dependent on the 'taxon' system and therefore, should not require the hippocampus. Following the definition of the 'taxon' system as offered by O'Keefe and Nadel (1978) there is no *a priori* reason to believe that simple, configural and structural discriminations should be dissociable due to the effects of hippocampal lesions.

impaired performance by hippocampal lesioned rats. However, when tested on a new biconditional discrimination in which the same compounds are presented, but the structural information within the compounds is reversed, it is predicted that this will result in a generalization decrement in normal animals, but this will be reduced for animals that have received lesions of the hippocampus. This tests the prediction that structural learning is only critical when required for the solution of a task, and thus impairments seen by hippocampal lesioned rats will only be apparent in such cases.

These predictions make the claim that configural learning about the features of compound stimuli does not underlie spatial learning of allocentric cues, therefore, contradicting the prediction of the 'configural association' theory (Sutherland and Rudy, 1989; Rudy and Sutherland, 1995). However, it is believed that the spatial structure of cues is dependent on the hippocampus for learning and memory. From this assumption, the prediction can be made that hippocampal lesions will impair performance on a configural task that requires the discrimination of the structure of the elements contained within a compound stimulus.

It is possible that the ability to encode the spatial structure of configurations of visual stimuli underlies the formation of a 'cognitive map' (O'Keefe and Nadel, 1978). It was claimed that the hippocampus maps the locations of landmarks within an environment which is independent from an animal's specific orientation within the environment (O'Keefe and Nadel, 1978). Learning about a place is not dependent on any one particular cue, but is reliant on the presence of at least two or more cues and knowledge of unique distal and angular relations to one another. The formation of a map is exploratory driven and does not require explicit training. Mismatches between the perception of landmarks and the formed map are updated, thus novelty leads to the factors that may be present during training of the task. Learning one of the discriminations enables the visual stimuli to enter into excitatory and inhibitory associations with the unconditioned stimulus (US). Therefore, because attention is increased to the factors that reliably predict reinforcement (Mackintosh, 1975), this facilitates learning of the subsequent discriminations. It is possible that at the start of training other factors may initially accrue some associative strength due to spurious correlations with the US (e.g. approach towards either the left or right goal location areas), and if the salience of the visual stimuli is not strong enough, performance on the task will not increase above chance performance. One point that could be made is that if all discriminations are presented in initial training, stimuli may accrue associative strength within a trial, but will then lose associative strength across other trials.

Another possibility is that training the discriminations in a progressive manner until all discriminations are learned may allow for the individual stimuli to become easier to discriminate. The failure to learn when all discriminations are initially presented could be due to a failure to appreciate the perceptual differences between the stimuli that are used to form the structural configurations. In the progressive training of discriminations, it is not until all discriminations are learned that stimulus compounds must be appropriately responded to on the basis of their structure. Therefore, in the first stage, the BW+ WB- discrimination may be learned in an elemental manner. One of the stimuli of a compound in a particular location (i.e. to the left, or to the right) may be associated with reward, whilst when the other stimulus is presented in the same location this may come to predict the absence of the US, i.e. B(left) predicts reinforcement, but W(left) predicts non-reinforcement. Due to the formation of excitatory and inhibitory associations with the black and white stimuli, the stimuli light of this, a configural model of learning (Pearce, 1994) can be adapted so that combinations of physical features can activate structural units. The incorporation of structural units, allows for configurational representations that consist of the same elemental features to acquire differential levels of excitatory and inhibitory associative strength.

1.5 Predictions

It is possible that hippocampal lesioned rats are impaired on object-in-place tasks since normal rats encode the structural features created by the conjunction of stimuli in different spatial locations. The hippocampus may not be necessary for encoding of configural associations based on the conjunction of the component elements, but may be responsible for encoding the structural relationship between the stimuli. If this distinction is made between structural learning and configural learning, it may aid in understanding how spatial learning can be impaired whilst sparing configural learning (Gallagher and Holland, 1992). In keeping with the original notion of Sutherland and Rudy (1989) that spatial learning can be accounted for by an underlying learning mechanism, it can now be hypothesised that spatial learning is dependent on the same learning mechanism that is responsible for learning the structural relationships between stimuli. This notion assumes that configural learning is spared by hippocampal damage, but discrimination learning that requires learning about structural features is impaired by hippocampal lesions. Thus, it would be predicted that hippocampal lesions would impair an animal's ability to solve a structural discrimination, but would not impair the ability to solve configural discriminations in which the structural features created by compound stimuli are not crucial to the solution of the task.

association between a stimulus in a location and the outcome, as described earlier. Therefore, if naïve animals with hippocampal lesions were trained using this procedure and there were impairments evident before all three discrimination had been introduced, it would not be clear whether they were impaired due to an impairment on structural learning or because of an impairment in forming simple associations.

In an experiment by Alvarado and Rudy (1995b) animals were trained on a transverse patterning task, which was composed of three component discriminations (A+ B-, B+ C- and C+ A-). Rats were trained in a water tank using a progressive method similar to the one described for the structural discrimination (George et al., 2001). It was found that hippocampal lesioned rats were impaired on the transverse patterning task once trained on all three of the component discriminations. However, the hippocampal lesioned rats also showed an impairment on the first discrimination (A+ B-) that only requires an elemental solution, therefore raising the issue of whether the transverse patterning task impairment was due to elemental rather than configural learning. Alvarado and Rudy (1995b) concluded that the impairment shown on the transverse patterning task was not due to an inability to learn about elemental associations due to the normal performance of the hippocampal lesioned rats on a control task (A+ B-, C+ D-, E+ F-). Thus they claimed that the initial impairment was due to non-specific effects caused by the lesion. Therefore, by using a similar method to Alvarado and Rudy (1995b) of running an appropriate control task, it may be possible to rule out non-specific effects of the lesions on the structural discrimination in the stages of training before performance demands a structural solution. However, to ensure that a deficit was due to impaired structural learning, an effect of hippocampal lesion needs to be dissociated from the effect of hippocampal lesions on become more perceptually distinct. This is possible because the black stimulus contains unique features, whilst the white stimulus contains other unique features, but both stimuli may share common elements. Therefore, the discrimination can be described as taking the form of B*C*+ W*C*- if the black stimulus comes to be associated with reward (B and W refer to the features that are unique to the particular stimuli and *C* refers to the features that are common to both stimuli). If the discrimination takes this form, B will enter into an excitatory association and W will enter an inhibitory association. C will not come to gain any associative strength, and according to theory proposed by Mackintosh (1975) attention will increase to the unique features of the stimuli and attention will decrease to the common elements. The simple process of learning about the stimuli in an elemental manner may enable the subsequent discriminations to be learned because the stimuli have become more perceptually distinct due to diminishing attention to the common features of the stimuli. Once all the discriminations are learned, all the stimulus compounds share many common features, and therefore attention increases to the unique structural features of a compound that reliably predict the outcome of either reward or non-reward.

Due to animals only being able to learn structural discriminations under certain conditions, this places limitations on how to test the effects of hippocampal lesions on such a task. To test the role of the hippocampus as a learning mechanism, it is necessary to find a way of training animals on a structural discrimination in which acquisition could only be due to structural learning. When animals are trained on the structural discrimination in a progressive manner, learning is not described as reflecting structural learning until all three discriminations are acquired and solved concurrently. This is because until all three discriminations are acquired it is possible that animals may be learning by some other means, such as learning of a simple a configural discrimination. This raises the question of what would be an appropriate configural discrimination to use as a control task for testing the effects of hippocampal lesions on the acquisition of a structural discrimination.

A solution to the problem of ensuring that a deficit on a structural discrimination specifically reflects impaired structural learning is to find a method of training rats on a structural discrimination with all discriminations presented concurrently from the start of training, so that learning can only be due to processing of the structural features of the stimuli. If hippocampal lesioned rats were impaired on a structural discrimination presented in this manner, but not impaired on a configural discrimination of similar difficulty, this would reflect the necessity of the hippocampus for learning structural information. George et al. (2001) reported that pigeons are capable of learning a structural discrimination with all three discriminations being presented concurrently from the start of training. Pigeons were trained with reinforced and non-reinforced patterns being presented in a successive manner. Therefore, there is evidence to show that birds are capable of learning the task in this manner, so it may be possible, under the right conditions, for rats to solve the task presented in a similar manner. In this chapter two experiments will be described that attempt to find a possible means of training rats on all three component discriminations of the structural discrimination.

If it is not possible to train rats on all three discriminations from the start of training, then it would be more appropriate to train normal animals on the structural discrimination in a similar manner to the procedure that was used by George et al. (2001) and then to examine post-operative performance after receiving lesions of the hippocampus. This approach would have the advantage of gauging the level of performance by individual rats on the task before surgery so that lesion and sham groups could be matched for their performance. This would reduce the chances of there being differences between the groups that are not specific to the ability to solve the structural discrimination after damage to the hippocampus, which could increase the likelihood of type one error. Also, it is possible that due to demands of the task, some animals may not acquire the discrimination. It would, therefore, be possible to remove any such animals.

The effects of hippocampal lesions on a structural discrimination can be tested in acquisition of the task and also on retention of the task. Whilst testing acquisition and retention would both provide information about the necessity of the hippocampus for the structural discrimination, they would have different theoretical implications. If animals are trained on a structural discrimination after receiving lesions of the hippocampus, then it is possible to test role of the hippocampus in learning, but not of storage of the task. It is possible that the hippocampus does not store memories of structural features, and is only required for learning. Therefore, this approach is limited in the conclusions that can be made. If animals are tested on their retention of the discrimination after lesions of the hippocampus then it is possible to not only examine whether lesions affect performance of a task that has been previously acquired but also whether the task can be reacquired. The latter measure is based on an increase in performance over periods of training. Testing in this manner would not necessarily answer whether hippocampal lesions affect storage of a structural discrimination, as this would require testing responses made to individual patterns in extinction without providing the opportunity for new learning. This would remove the possibility of testing the reacquisition of the task through subsequent training.

In four experiments, various conditions for training structural discriminations are tested. It is also examined whether these procedures can be adapted for training on configural discriminations that can be used as control tasks. In the first two experiments, normal rats were trained on a structural discrimination in automated conditioning chambers. In Experiments 3 and 4 the methodology of George et al. (2001) is replicated, but a novel probe test was used to uncover more about the nature of the underlying learning.

Experiment 1

To try and find a possible method for training rats on all three components of the structural discrimination from the start of training, rats were trained in an operant conditioning chamber, chain pulling for reward. Operant training of chain pulling for reward was used due to rats being unable to learn a structural discrimination by Pavlovian conditioning (Ward-Robinson and Pearce, unpublished data). Stimuli were presented on a computer monitor. Groups of rats were subjected to different training procedures to test the effectiveness of these procedures for learning structural discriminations.

For two groups, patterns were presented successively. Rats were required to chain pull for reward during a reinforced pattern, but were required to inhibit chain pulling during a non-reinforced pattern to demonstrate acquisition of the discrimination. For these groups, there were six trial types: BW+, WB-, WH+, HW-, HB+ and BH-. The trial types are depicted in Figure 2.1. One group of four rats (Successive-Mixed) were presented with the reinforced and non reinforced patterns of all three discriminations in a random order, so that they were required to solve all three discriminations

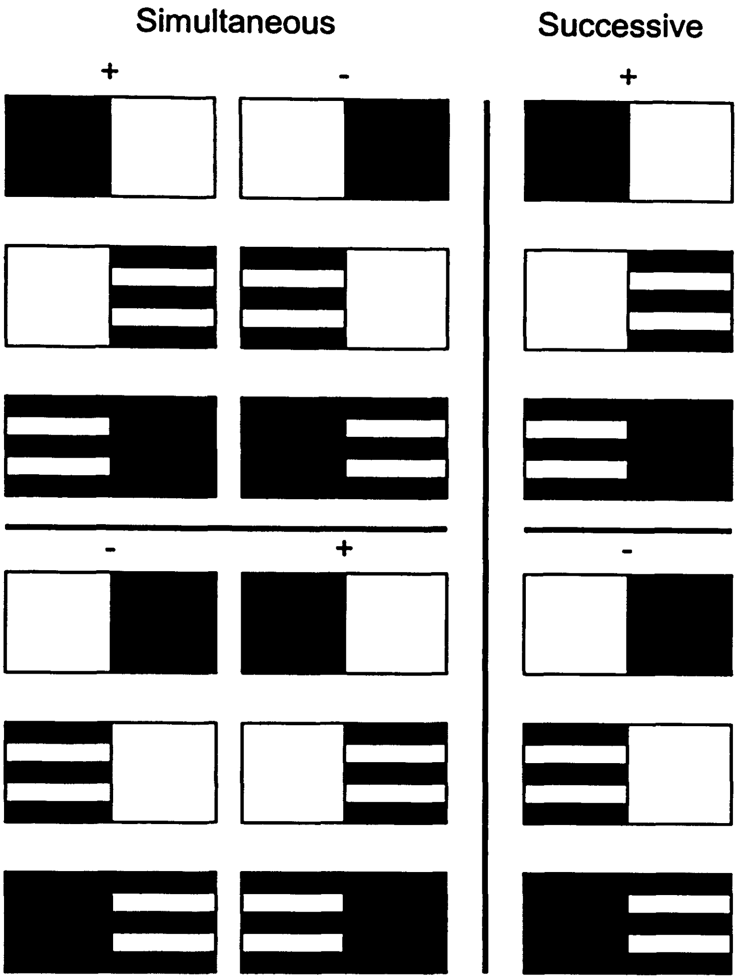

Figure 2.1. The trial types for groups trained either on a simultaneous or successive discrimination. For a simultaneous discrimination both the reinforced and non-reinforced patterns were presented on a trial. For the location of a reinforced pattern to be counterbalanced, in one trial the correct pattern would be located on the left, and in another trial the correct would be located on the right. For a successive discrimination, one pattern would be presented on a trial. Therefore, there were three trial types in which reinforcement was provided, and another three trials in which no reinforcement was provided.

Method

Subjects. The subjects were 12 male Dark Agouti rats (Harlan, UK). They were housed in pairs in a room that was illuminated for 14.5 hours per day. All testing was carried out during the period of light at the same time each day. Before the start of the experiment the rats weighed approximately 250g (with a range of 230-265g). Subjects

Several theories have emphasised the role of the hippocampus in learning associations, but claim the hippocampus is not necessary for subsequent performance after acquisition (Gluck and Myers, 1993; O'Reilly and Rudy, 2001). However, Reidel, Micheau, Lam, Roloff, Martin, Bridge, de Hoz, Poeschel, McCulloch and Morris (1999) have shown that the hippocampus is required for normal performance during acquisition and retrieval of spatial learning in the Morris water maze. Due to the logical possibility that learning about spatial arrays may be subject to encoding of the structural relationships between cues, it can be predicted that hippocampal lesions will impair structural learning in a similar manner to allocentric spatial learning. Therefore, there are no *a priori* reasons to believe that hippocampal lesions will impair acquisition of a structural discrimination but spare retrieval (or vice versa).

If it is found that hippocampal lesions impair processing of structural information, such a result could be explained by Sutherland and Rudy's 'configural association' theory of the hippocampus (1989). The impairment would not necessarily be due to processing of structural information, but could be explained in terms of learning about unique configurations of stimuli that contain elements that by themselves can not be associated with a reward outcome. For this reason it also needs to be demonstrated that hippocampal lesions spare configural tasks of a similar complexity to the structural discrimination for it to be claimed that a deficit on a structural task is only due to structural processing. For configural tasks to be used as an appropriate comparison with the performance of a structural task, the tasks must be learned in a similar manner as the structural discrimination. Therefore, the stimuli and procedures that are used for the structural discrimination and for the control configural discrimination must be as similar as possible.

concurrently. Another group of four rats (Successive-Blocked) received sequential presentation of blocks of trials of the three discriminations. The order of the presentation of the discriminations was the same every session.

A third group (Simultaneous-Mixed) received similar training to the first two groups, but pairs of reinforced and non reinforced stimuli were presented simultaneously, in contrast to the go/no go procedure used for the first two groups. Two chains were hung from the top of the conditioning chamber, one was positioned in front of the pattern presented on the left and the other positioned in front of the pattern presented on the right. Reward was contingent on pulling the chain that was in the same spatial location as the reinforced pattern (i.e. if the correct pattern was positioned on the left, then pulling the left chain would lead to reinforcement, but pulling the right hand chain in front of incorrect pattern would not lead to reinforcement). Consequently, there were three trial types in which pulling the left chain was reinforced (BW-WB, WH-HW and HB-BH) and three trial types in which pulling the right chain was reinforced (WB-BW, HW-WH and BH-HB). The trial types are depicted in Figure 2.1.

All experiments reported within this thesis were in accordance with United Kingdom Animals (Scientific Procedures) Act, 1986.

were food deprived to 85% of their free feeding weight and were maintained at this weight, by restrictive feeding, during all experimental procedures. Rats were allowed free access to water whilst in their home cage.

Apparatus. Four conditioning chambers made from Perspex were used. The chambers were 26cm wide, 22cm in length and 28cm high. The front wall and the side wall that could be opened were both transparent, whilst the two remaining walls were painted black. The floor was made from wire mesh and fixed into the walls, 7cm from the base of the chamber. In the centre of the front wall was a circular hole (3cm in diameter) 1cm above the wire mesh floor. On the outside of the front wall, immediately below the hole was a circular food well (3cm in diameter and 0.5cm deep) made from Perspex. From this well a 25% sucrose solution could be dispensed via a peristaltic pump that was positioned 5cm behind the black side wall. A pair of photodiode sensors were positioned either side of the hole that gave access to the food well. Therefore, a horizontal infra-red beam was positioned across the centre of the hole. The chamber was illuminated by a house light that was in the centre of the ceiling of the chamber. In the ceiling, 4.5cm from the front of the chamber were three holes through which chains (18cm long) could be suspended. One hole was positioned in the centre of the width of the ceiling. The other holes were positioned 5.5cm from the edge of the ceiling, one on the left and the other on the right.

For groups Successive-Mixed and Successive-Blocked, one chain was suspended from the centre hole. For the group Simultaneous-Mixed, chains were suspended through the left and right holes. The chains were connected to a switch that when activated would cause sucrose solution to be dispensed.

Chain pulling and breaks of the infra-red beam across the food well were recorded via the appropriate circuitry by an Acorn Risk PC (Acorn Computers Ltd., Cambridge, England), which was programmed in Arachnid (Paul Fray Ltd., Cambridge, England) to control and record all experimental events.

Procedure. *Pre-training*. All rats received one session of magazine training. During the 1hour session, 1ml of a 25% sucrose solution was dispensed at regular 1-min intervals. For the next five (1-hour) sessions rats were trained to chain pull for reward. For the first three sessions chain pulling was on a continuous reinforcement schedule. On the first session a lab chow pellet was attached to the top of a chain near to the ceiling of the chamber. On the second session, half a pellet was attached. On the third session no food was attached to the chains. On the fourth and fifth session chain pulling was rewarded on a variable interval schedule (VI) of 15s and VI 30s schedule respectively. Pre-training procedures were the same for all three groups, except that the Simultaneous-Mixed group were trained to pull two chains. The two chains for the Simultaneous-Mixed group were equally rewarded.

Structural Discrimination. The three groups were trained, using different methods, on the structural discrimination. The groups differed in that two of the groups were trained on a successive discrimination, and one group was trained on a simultaneous discrimination. One of the groups that was trained on the successive discrimination received pseudo-random presentations of the reinforced and non-reinforced patterns of the three component discriminations of the structural discrimination (Successive-Mixed). The other group that was trained on a successive discrimination received blocks of trials of each of the component discriminations of the structural

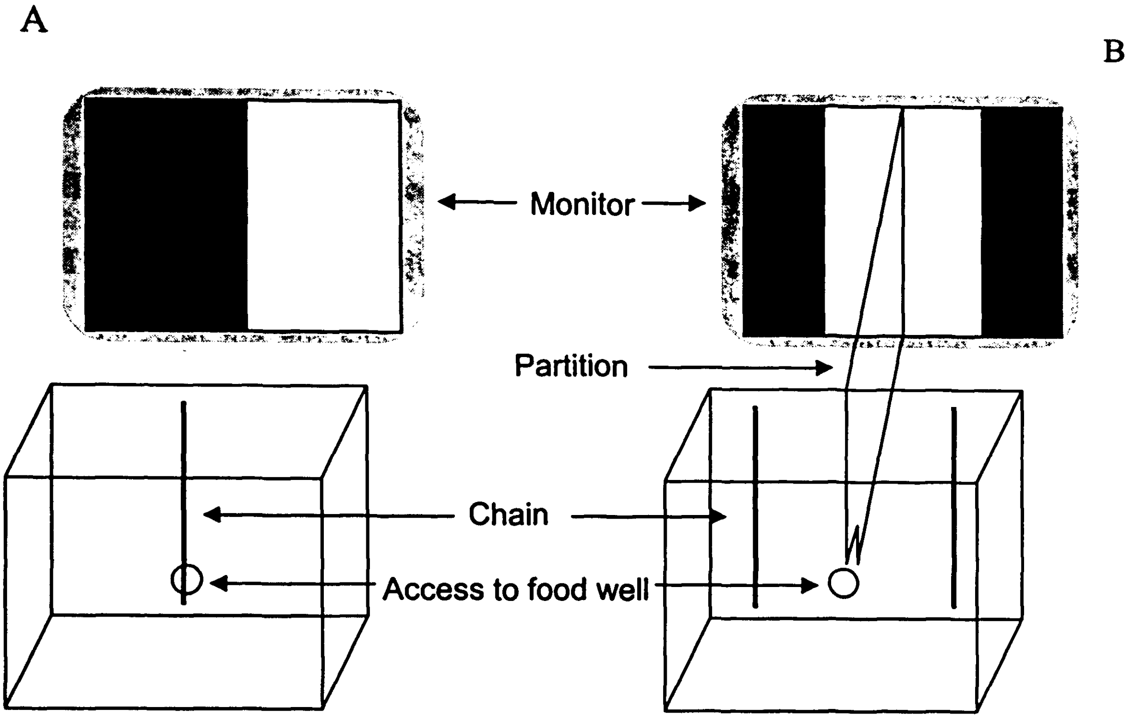

Figure 2.2. Apparatus used for Experiment 1. Section A shows the apparatus used for training of the structural task as a successive discrimination (Successive-Mixed, Successive-Blocked). Patterns were presented on a monitor. Reinforcement was contingent on chain pulling during the presentation of a S+. Section B shows the apparatus used for training of the structural discrimination as a simultaneous discrimination. Reinforced and non-reinforced patterns were presented simultaneously on a monitor. A partition wall intersected the two patterns so that whilst responding in the presence of one pattern, the other pattern could not be viewed. Reinforcement was contingent on pulling the chain that was in front of the S+.

The arrangements of the apparatus for the Successive (Mixed, Blocked) and Simultaneous are depicted in Figure 2.2. A monitor screen was positioned facing the front wall of the chamber, separated by a distance of 10cm. The monitor was 36cm by 22cm, whilst the screen was 28.5cm by 21.5cm. The monitor was positioned on a circular base that elevated the monitor by 10cm. Stimuli were displayed on the monitor. For groups Successive-Mixed and Successive-Blocked stimuli were a black rectangle (B), a white rectangle (W) and a rectangle that contained black and white horizontal stripes (H). The horizontal stripes were 2cm high. The rectangles were discrimination (Successive-Blocked). A block of trials of the reinforced and non-reinforced patterns of a component discrimination would be followed by subsequent blocks of the remaining component discriminations. The order of the presentations of each discrimination, was the same for each session. After training of the discrimination in blocks of trials of each discrimination, the trial order was pseudo-randomised to test whether the Successive-Blocked group were solving the task by discriminating the structural features of the patterns.

The remaining group was trained on a simultaneous discrimination (Simultaneous-Mixed). On each trial a reinforced pattern and its corresponding non-reinforced version was presented (i.e. BW+ WB-, WH+ HW- or HB+ BH-). Reward was given for pulling the chain that was in front of the correct pattern. Discriminations were presented in a pseudo-random order.

The following procedures were the same for the three groups. The duration of a session was 59.5 minutes. A session began with a one minute period in which no stimuli were presented. The duration of a conditioned stimulus (CS) was 60s, and there was a mean inter-trial interval (ITI) of 90s (range=60-120s). Responding to a reinforced stimulus pattern (S+) was rewarded by the presentation of 1ml of a 25% sucrose solution. Reinforcement was provided for responding to an S+ on a variable interval (VI) schedule of 30s. However, no reinforcement was provided during the first 10s of an S+. Therefore, responding during this period reflects conditioned responding that is not confounded by the presentation of reward. The amount of responding to reinforced and non-reinforced stimuli during the first 10s of the CS duration was recorded. In each group, half of the rats were reinforced for responding

12cm wide and 20cm high. Stimuli were presented in pairs to form six patterns: BW, WB, WH, HW, HB and BH (see Figure 2.3). Pairs of stimuli were displayed in the centre of the screen with stimuli directly adjacent to each other. Stimuli could be presented on both the left and right half of the screen. The remaining screen was coloured grey.

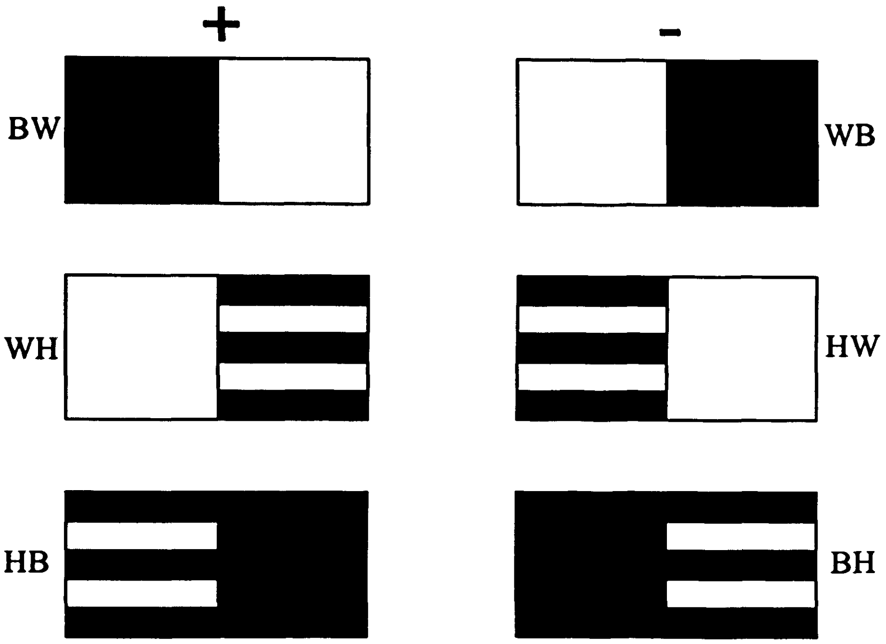

Figure 2.3. Structural discrimination stimuli. Patterns depicted on the left were reinforced and patterns depicted on the right were non-reinforced.

For the Simultaneous-Mixed group the same stimuli were used as for the other two groups, but the stimuli were half the width so that the rectangles were now 6cm wide and 20cm high (see Figure 2.2). Two pairs of stimuli were presented on the screen simultaneously adjacent to each other. Therefore, stimuli could be presented in four locations on the screen: the left or right half of the left half of the screen, and the left and right half of the right half of the screen. The reinforced and non-reinforced stimulus compounds were separated vertically in the centre by the partition wall.

to the BW, WH and HB patterns. The remaining rats were reinforced for responding to the WB, HW and BH patterns.

Successive-Mixed. The Successive-Mixed group received 40 sessions, one per day, of training on the structural discrimination. Each session consisted of four trials of each of the six stimulus compound combinations: BW+, WB-, WH+, HW-, HB+ and BH-. Trial types were presented in a random order with the constraint that no more than three trials of same reinforcement contingency could be presented in a consecutive order. Also, no more than three trials of same component discrimination (i.e. BW+ WB-, WH+ HW-, HB+ BH- could be presented in consecutive order.

Successive-Blocked. Simultaneous-Blocked received 30 sessions, one per day, of training on the structural discrimination. Each session consisted of 8 trials the BW+ WB- discrimination, followed by 8 trials of the WH+ HW- discrimination, and, finally, by 8 trials of the HB+ BH- discrimination. Within each block of 8 trials there were four S+ trials and four S- trials. The order of S+ and S- trials were random with the constraint that no more than three trials of same reinforcement contingency could be presented on consecutive trials.

For a further 10 sessions of training, trials were presented in a pseudo-random order. Therefore, the procedures for these sessions were the same as for the Successive-Mixed group.

Simultaneous-Mixed. The Simultaneous-Mixed group received 30 sessions, one per day, of training on the structural discrimination. As opposed to Successive-Mixed and Successive-Blocked, which both received 40 sessions, Simultaneous-Blocked only received 30 sessions due to not showing evidence of learning by this stage. Each session consisted of 8 trials of each discrimination: BW+ WB-, WH+ HW- and HB+ BH-. On a trial the S+ and S- of one of the component discriminations was presented simultaneously. The patterns were presented adjacent to each other (i.e. on the left or on the right). The presentation of each of the patterns, either on the left or on the right, was counterbalanced within a session. Trials were presented in a random order with the constraint that the three trials of the same reinforcement contingency or of the same discrimination type could not be presented in consecutive order.

Results

Successive-Mixed. The performance on the structural discrimination is shown, in two session blocks, in Figure 2.4. The ability to solve the discrimination is expressed as a discrimination ratio defined as follows: number of responses to reinforced stimuli divided by the total number of responses to reinforced and non-reinforced stimuli. This ratio was based on the number of responses during the first 10s of each trial, during which no food reinforcement was provided. Performance increased over training with rats making a proportionally greater amount of responses to reinforced stimuli than would be expected from chance. An analysis of variance showed that there was a significant effect of block, $F(19,57)=3.28$, $p<0.001$, demonstrating that performance improved over the course of training. A one-sample t-test performed on the mean performance of the last five blocks of training revealed that rats were performing above chance (0.5), $t(3)=5.55$, $p<0.05$. Even though rats were making proportionally more responses to the reinforced stimuli than to the non-reinforced stimuli actual, rates of responding were rather low, with only a mean response of 0.66 (±0.17SEM) to the reinforced stimulus compounds on the last block of training.

pseudo-random order, rats only made 48% of the responses to the reinforced stimuli. Both stages of training are analysed independently of each other.

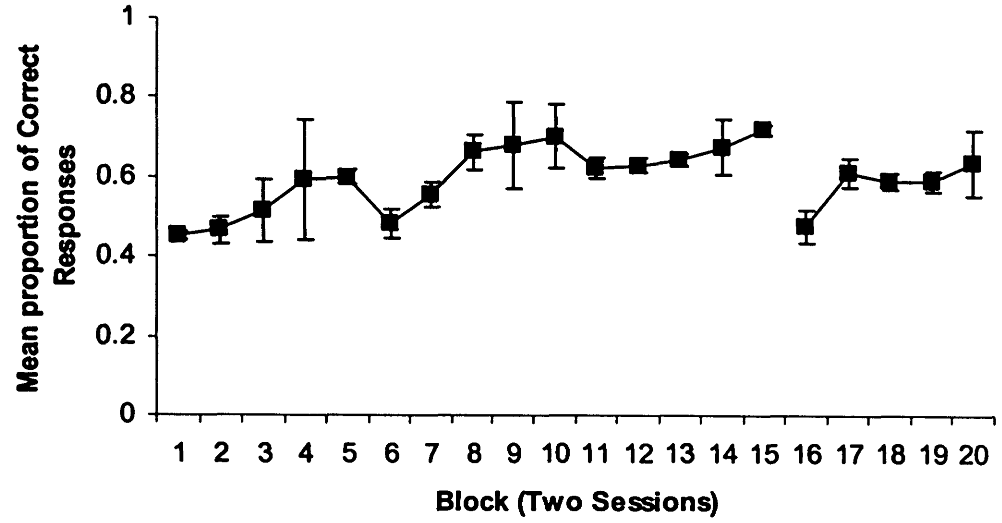

Figure 2.5. Performance on the structural discrimination for the Successive-Blocked group. Scores reflect the amount of responding to correct stimuli divided by the total amount of responding to all stimuli. For the first 15 sessions, discriminations were presented in blocks of trials. For the last five sessions, discriminations were presented in a pseudo-random order. Error bars indicate ±SEM.

An analysis of variance on the data for the first 15 blocks of training, in which discriminations were presented in blocks of trials, showed that there was a significant effect of block, F(14,42)=2.56, $p<0.01$. An analysis of variance of the last five blocks of training, in which discriminations were presented in a pseudo-random order, did not show an effect of block, F(4,12)=1.54, implying that the drop in performance was inconsistent. A one-sample t-test on the data from the last five blocks of training revealed that rats were performing above chance on the discrimination, t(3)=4.61, The procedures were the same as for Successive-Mixed group in Experiment 1 with regards to the CS duration, inter-trial interval, the number of trials per session and the amount of reward given for correct responding. However, in this experiment rats were required to nose-poke rather than chain pull for reinforcement. Rats were reinforced for nose-poking during a CS+ trial on VI 30s schedule. For the first 11 sessions reward could be given at any time point within the duration of the CS+. For the next 12 sessions, half the CS+ trials, were treated as probe trials. Reinforcement could only be obtained on the VI 30s schedule for the last 30s of these probe trials. Therefore, responding during the first 30s of a CS reflects learning about the structural discrimination, whereas responding in the last 30s will be subject to the influence of the presentation of food. The other half of the CS+ trials were reinforced in the manner that was used in the previous sessions of training. For the first 11 sessions all responding during both CS+ and CS- trials was recorded. In the last 12 sessions responding during the first 30s of probe trials, and the first 30s of all CS- trials was recorded. Probe trials and normal CS+ trials were intermixed in a pseudo-random order in the same manner as used in Experiment 1.

Results

The performance on the structural discrimination during the first 11 sessions of training is shown in Figure 2.7. Responding is shown as a ratio of responses to reinforced patterns divided by the total amount of responses made to all patterns. Rats made proportionately more responses to reinforced stimuli than to non-reinforced stimuli. This is reflected in the increase of the discrimination ratio. An analysis of variance showed that there was a significant effect of session over the first 11 sessions of training, $F(10,150)=7.16$, $p<0.001$.

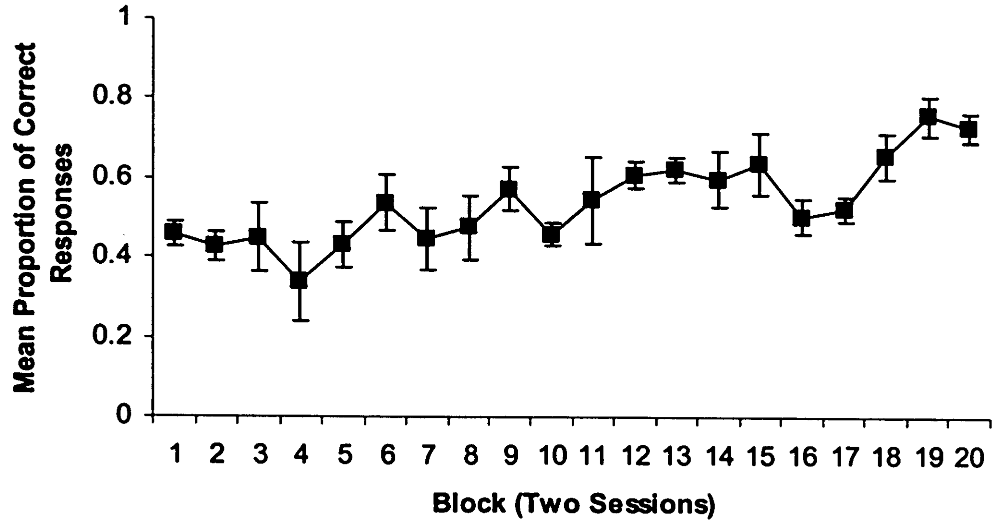

Figure 2.4. Performance on the structural discrimination for the Successive-Mixed group. Scores reflect the amount of responding to correct stimuli divided by the total amount of responding to all stimuli. Error bars indicate ±SEM.

Successive-Blocked. The performance on the structural discrimination is shown, in two session blocks, in Figure 2.5. The ability to solve the discrimination is expressed as a ratio of the responding to the reinforced stimuli (during the first 10s in which no food was provided) divided by the amount total amount of responding to the non-reinforced stimuli (during the first 10s of a trial) and reinforced stimuli. Performance increased over training with animals making a proportionally greater amount of responses to reinforced stimuli than would be expected from chance. In the final stages of training, when presentation changed from blocked trials of each discrimination, to a pseudo-random trial order, performance dropped, but was quickly regained. Rats made 72% of their responses to the reinforced stimuli on the session prior to the trial order changing. For the session when the trial order changed to a

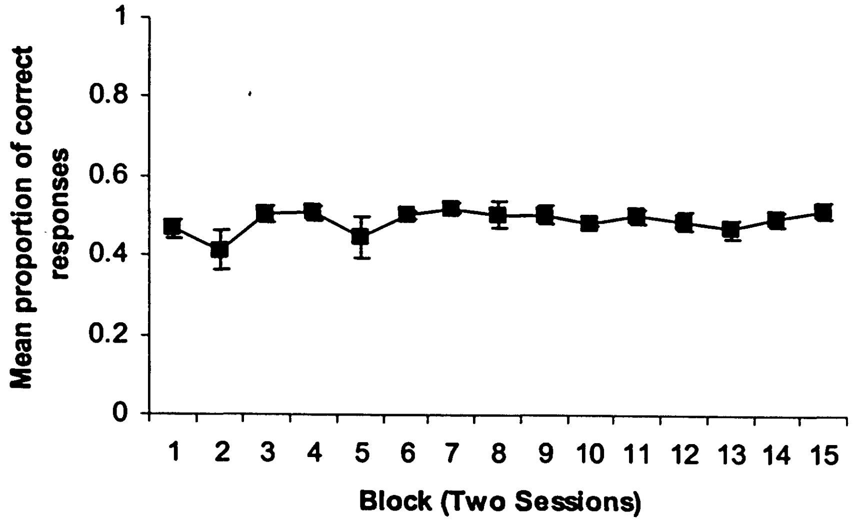

Figure 2.6. Performance on the structural discrimination for the Simultaneous-Mixed group. Scores reflect the amount of responding to correct stimuli divided by the total amount of responding to all stimuli. Error bars indicate ±SEM.

Discussion

Rats in the Successive-Mixed and the Successive-Blocked groups acquired the discrimination over the course of training. In contrast, rats in the Simultaneous-Mixed group did not acquire the discrimination. Rats in this group did not show any improvement over the course of training. Therefore, presenting the discrimination in a successive manner facilitated the acquisition of the discrimination. There did not appear to be any advantages of presenting the discrimination in blocks of trials, for successive presentation. Although the Successive-Blocked group showed a level of performance that was above chance at the end of training, the initial drop in performance from blocked exposure to pseudo-random exposure of discrimination type reflects how rats were affected by the order of discrimination type. It is possible that rats were adopting a win-shift strategy by responding to one stimulus, and then,

$p<0.05$. To test whether the drop in performance when the trials were presented in a pseudo-random order was significant, a t-test was performed on the data for block 15 (last block of blocked training) and 16 (first block of mixed training). It was found that performance on block 16 was significantly lower than on block 15, $t(3)=4.81$, $p<0.05$, and also rats did not perform above chance on block 16, $t(3)=-0.46$.

Similar to the Successive-Mixed group, responding was rather low. Rats only made a mean response of 1.51(±0.46SEM) to the reinforced stimulus compounds during the last five blocks of training.

Simultaneous-Mixed Group. The performance on the structural discrimination is shown in Figure 2.6. The ability to solve the discrimination is expressed as a ratio of the responding to the reinforced stimuli (during the first 10s in which no food was provided) divided by the amount of total responding to the non-reinforced stimuli (during the first 10s of a trial) and the reinforced stimuli. Performance did not appear to improve over the course of training. This was reflected in an analysis of variance that did not reveal a significant effect of block, $F(14,42)=1.27$. Performance during the blocks of training was close to chance levels of performance, showing a similar level of responding to reinforced and non-reinforced stimulus-compounds. It was found, averaged across the 15 blocks of training, that rats were not performing above chance, $t(3)=-1$. The mean level of responding during the last block of training was 2.05(±0.44SEM) to reinforced stimulus compounds and 1.84(±0.3SEM) to non-reinforced stimulus compounds. The responding to the reinforced and non-reinforced compounds did not significantly differ, $t(3)=1.18$.

once that stimulus was no longer reinforced, the rat changed responding to another stimulus. Performance can not be totally explained by this hypothesis, as performance was quickly regained, but it is possible that over the course of sessions the structural features of the stimuli were acquiring associative strength, whilst within blocks of trials individual stimuli regardless of their structure acquired associative strength (only to lose associative strength in the next block of trials). Therefore, there might be a dual effect of learning structural information across sessions, and learning of elemental features within blocks of trials, and the drop in performance can be credited to the loss of within block elemental learning.

Even though successive presentation was more effective than simultaneous presentation of the structural discrimination, there may be other differences than nature of the presentation. It is possible that the stimuli were less salient for the Simultaneous-Mixed group due to the stimuli being smaller than for the successive presentation groups. Another reason for the failure to learn can be explained in terms of a model proposed by Wagner model (1981). It is proposed that for effective learning of a stimulus, the stimulus has to receive full attention. When a stimulus is attended to, the representation of the stimulus is in an active state (A1). When the stimulus represented is no longer the focus of attention, but is not inactive, it decays to a second active state (A2). Wagner (1981) claims that if a representation of a stimulus is in the A2 state it can not enter into associations with an outcome. Due to the stimulus compounds used in a structural discrimination sharing common features, it can be assumed that to some extent learning of the excitatory associations of the reinforced stimulus compounds will generalise to the non-reinforced compounds. This will occur until the unique structural features of the compounds gain sufficient associative strength for the discrimination to be achieved. Therefore, if elements of a reinforced pattern have decayed to the A2 state, according to Wagner (1981), the elements will not undergo new learning if presented again in a non-reinforced compound. For the Simultaneous-Mixed group, due to reinforced and non-reinforced stimuli being simultaneously presented, elements of one pattern may be active in the A2 state when perceived in the alternative pattern. Consequently, this would retard learning.

Even through the groups trained on a successive structural discrimination learned the task, responding to the reinforced stimuli was very low. For the Successive-Mixed group, in the last block of training, even though 73% of their responses were to reinforced stimulus-compounds, rats only made on average a mean response of 0.64 chain pulls during the first 10s of a S+. This may make it difficult to find significant differences between the ability of different groups to solve a structural discrimination[1]. Due to the low level of responding, a null result between groups may reflect floor or ceiling effects, which may hide differences between groups. Therefore, the low level of responding may contribute to the likelihood of Type 2 errors in the statistical analysis of between group designs.

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[1] In a pilot study performed using rats from Experiment 1, rats that subsequently received hippocampal lesions had a much greater baseline level of responding compared to a control group. Therefore, due to the low level of responding of the control group, it was inappropriate to make comparisons between the two groups on performance of the structural discrimination.

acquired, reinforcement only occurred in the last 30s of the stimulus for half of the reinforced trials. The amount of nose-poking during the first 30s of the CS was recorded and compared to the amount of responding during the first 30s of the non-reinforced trials.

Method

Subjects. The subjects were 16 male Dark Agouti rats (Harlan, UK). They were housed in pairs in a room that was illuminated for 14.5 hours per day. All testing was carried out during the period of light at the same time each day. Before the start of the experimental procedures the rats weighed approximately 250g (with a range of 237-270g). Subjects were food deprived to 85% of their free feeding weight and were maintained at this weight, by restrictive feeding, during the experiment. Rats were allowed free access to water.

Apparatus. The apparatus was the same as that used for Experiment 1, except that all chains were removed from the chambers, and no dividing wall was present. The number of times the infra-red photo beam, that was across the hole that provided access to the food well, was broken, was recorded during all procedures.

Procedure. All rats received one session of magazine training. During the 1hour session 1ml of a 25% sucrose solution was dispensed at regular 1-min intervals. Subsequently, rats received two 1-hour sessions in which they were trained to nose-poke for reinforcement. For the first of these sessions nose-pokes were reinforced on a VI 15s schedule. On the second session nose-pokes were reinforced on a VI 30s schedule.

Experiment 2

In Experiment 1 it was found that presenting the stimuli in a successive manner did result in the acquisition of a structural discrimination, but the levels of responding shown by rats to the reinforced stimuli were not particularly high. Even though the method provides a means of testing naïve lesioned rats on their ability to acquire a structural discrimination, due to the levels of responding it may be hard to find statistical differences between the groups' performances. It is possible that the low level of responding could be attributed to the muscular demands of chain pulling. Therefore, in this experiment the instrumental response for gaining reward was nose-poking in the magazine.

Nose-poking may be an easier behaviour to demonstrate due to it being a response that is likely to become conditioned as a consequence of Pavlovian conditioning. Nose-poking in the magazine chamber will be one of the unconditioned responses that animals will demonstrate when a stimulus is paired with food. As a consequence of training, in Pavlovian conditioning, nose-poking will become a conditioned response, so that the behaviour will be demonstrated during the presentation of the stimulus before the food is presented. Therefore, it is plausible that nose-poking in the magazine will be more readily learned as an instrumental response than chain pulling for reward.

The procedures were similar to those used for the training of the Successive-Mixed group in Experiment 1. All rats received presentations of the reinforced and non-reinforced in a successive manner in a random trial order. Rats were reinforced for nose-poking during reinforced stimuli on VI 30s schedule, with a stimulus duration of 60s. After a period of training, to assess whether the discrimination had been

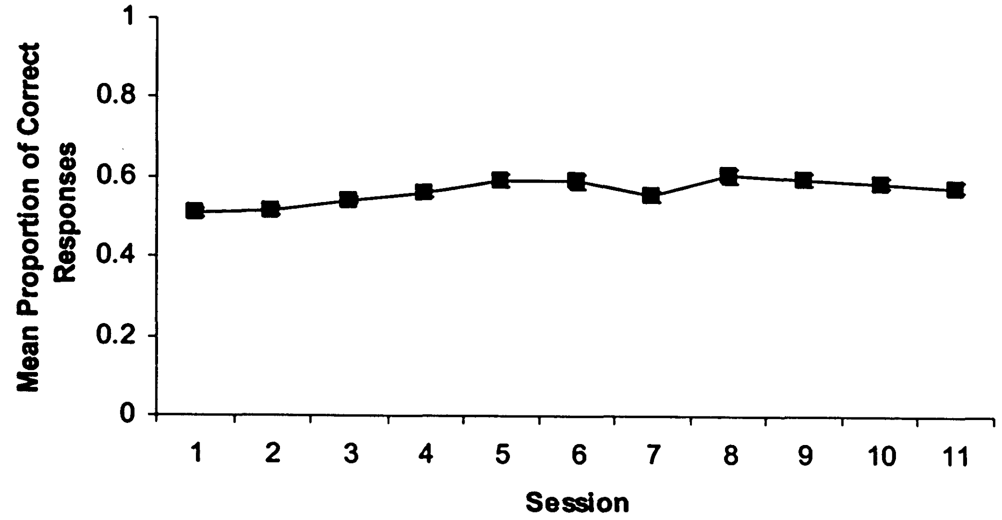

Figure 2.7. The performance of the structural discrimination over the first eleven sessions of training. Scores reflect the amount of responding to correct stimuli divided by the total amount of responding to all stimuli. Error bars indicate ±SEM.

The performance for the last 12 sessions of training is shown in Figure 2.8. Data are shown as a ratio of the responding during the first 30s of probe reinforced trials (in which no reward was presented) divided by the total amount of responding to probe and non-reinforced trials during the first 30s. Therefore, in this stage of training, data reflect responding to stimulus compounds before the presentation of reward, demonstrating whether rats have learnt the discrimination. Performance was at a level above chance, but decreased over training. This was reflected by an analysis of variance that revealed that there was a significant effect of session, $F(11,165)=4.25$, $p<0.001$. Performance was significantly above chance on the first session of probe trials, $t(15)=4.69$, $p<0.001$, but not by the last session of testing, $t(15)=1.04$.

duration. This could have led to an inhibition of delay in which animals learn that a US is less likely to occur early in the onset of CS+. However, this would not explain the decline in performance on the discrimination as the occurrence of the US is still more like to occur for the reinforced stimulus compounds than for the non-reinforced stimulus compounds during the first half of the duration of a CS. The fact that the ability to solve the discrimination was not evident by the end of training may indicate that the level of performance at the start of the second stage was due to chance, and therefore may reflect Type 1 error.

Another possibility is that the discrimination had been acquired, but now was not sustainable with the amount of reward that was provided. Even though rats were able to receive reinforcement on every trial, the decrease in frequency of reward being provided during the probe trials may have caused a drop in responding, masking evidence of ability to solve the discrimination. To rule out this possibility evidence would be needed to show that the structural discrimination could be acquired with probe trials being present at the commencement of training.

Experiment 3 and 4

Rats were not able to learn a structural discrimination by nose poking for reward whilst stimuli were presented in a successive manner in an operant chamber. In Experiments 3 and 4 the procedures used by George et al. (2001) were replicated. Animals were trained on a structural discrimination in a water tank, making a simultaneous discrimination between reinforced and non-reinforced patterns. Rats were trained in a progressive manner on the discriminations, starting with one placed in the water at the entrance of one of the goal areas and was allowed to swim to the platform. For stage 4 a platform was placed at the end of both goal areas. The rat was placed in the water at the end wall opposite the goal areas, facing away from the goal areas. The rat was allowed to swim to either platform.

During all training, rats were released into the tank facing away from the goal areas. The procedure for drying and storing the rat between trials and at the end of sessions was maintained throughout all training.

Structural discrimination training. The stages of training are listed in Table 1. Stage 1 consisted of five sessions of the BW+ WB- discrimination (see Figure 2.10). On each trial a pattern consisting of a black rectangle to the left of a white rectangle (BW), was placed in one of the goal areas. A pattern consisting of a white rectangle to the left of a black rectangle (WB), was placed on the other goal area. Each pattern was presented in both the left and the right goal area an equal amount of times over a session. For half the rats, the platform was positioned underneath the BW pattern and never underneath the WH pattern, and for the other half the platform was always underneath the WH pattern. For the first session there were 20 trials, and 30 trials for the four subsequent sessions. The sequence of trials was randomised with the constraint that no more than three trials, in consecutive order, could take place with the same pattern in the same goal area. On each trial a rat was released from the start point and was allowed to swim into either goal area. If the rat swam to the correct goal area, it was allowed to remain on the platform for 10s, before being removed. If the rat swam to the incorrect goal area it was allowed to carry on swimming until it successfully found the platform, where it would remain for 10s. If the rat had failed to find the platform within 120s it was lifted from the water and placed on the platform for 10s. A were housed in pairs in a room that was illuminated for 14.5 hours per day. Rats were tested in groups of nine on alternating days, six days a week, at the same time during the period of light in the holding room.

Apparatus. An illustration of the apparatus is shown in Figure 2.9. A grey fibreglass tank was used. The tank was 100cm long, 62cm wide and 62cm deep. The tank was filled with water to a depth of 32cm. The water was made opaque by adding 35cl of opacifier liquid, and was maintained at a temperature of 25°C (±2°C). The water was changed daily.

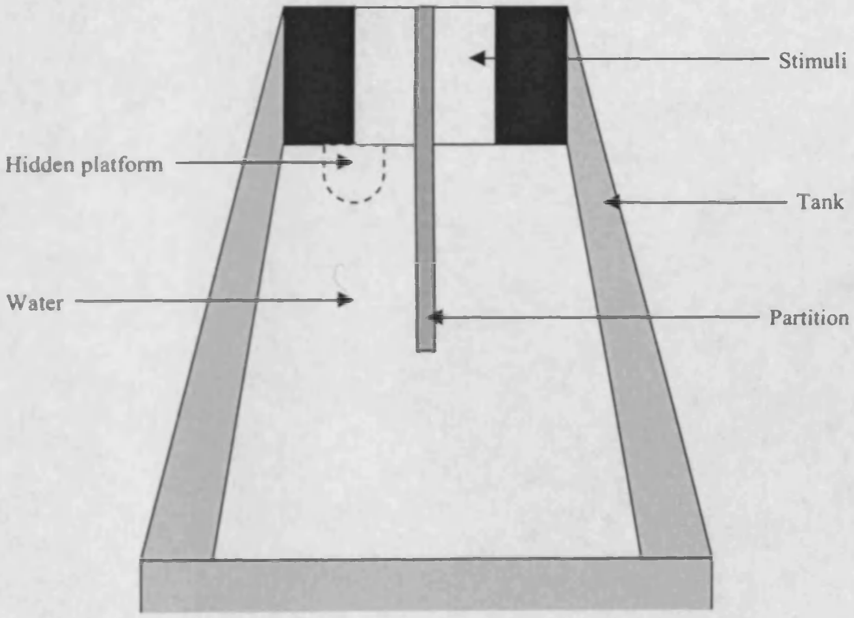

Figure 2.9. The water tank apparatus used for testing of the structural discrimination. Rats were placed in the water facing the south wall of the tank. Stimuli were presented at the north end of the tank, and a partition wall separated the reinforced pattern from the non-reinforced pattern. A hidden platform was always present underneath the reinforced pattern.

A partition wall (62cm high and 46cm long) made from grey Perspex, was attached vertically at a right angle to the midpoint of one of the end walls. This created two lanes in the tank with either side of the end wall being the goal areas. An escape platform could be attached to either side of the end wall. The escape platform was made from transparent Perspex, 0.4cm thick, 11cm long and 9cm wide. The front was curved with a radius of 4.5cm. The platform was 2cm below the surface of the water and was not visible. The tank was placed on a table 70cm above the floor. The room containing the tank was 3m by 3m with white walls and ceiling, one door, and no windows.

Stimuli. The stimuli used for the structural discrimination are illustrated in Figure 2.10. The three stimuli used were a black rectangle, a white rectangle and a rectangle contained black and white horizontal stripes.

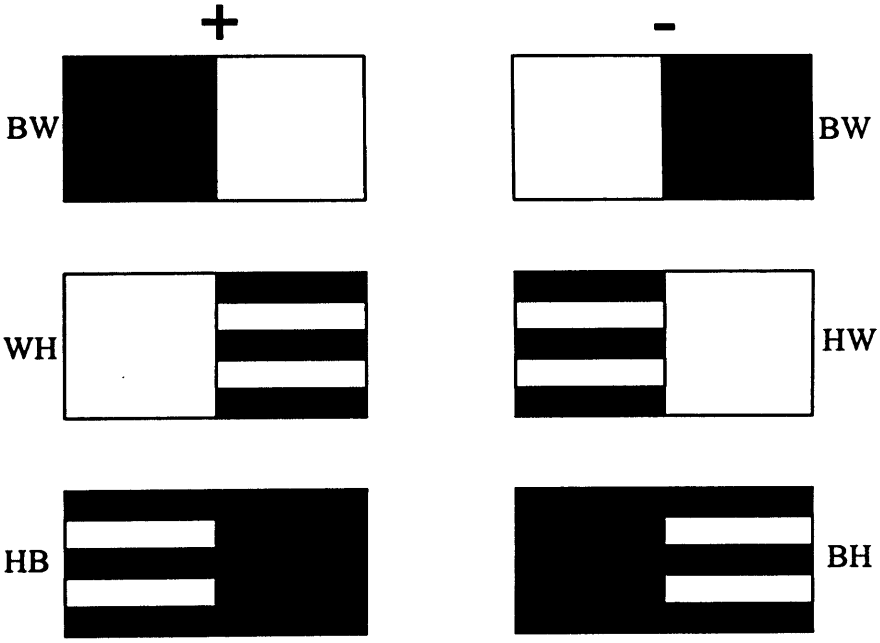

Figure 2.10. The structural discrimination stimuli. Patterns are formed from the stimuli B, W and H presented in pairs. Reinforced patterns are presented in the left column, and non-reinforced compounds are presented in the right column.

The horizontal stripes were 2.5cm. All rectangles were 28cm high and 14cm wide. Three patterns formed by the three stimuli (i.e. BW, WH, HB, WB, HW and BH) were printed and laminated. The patterns were suspended 1cm above the surface of the water on the end wall in one of the goal areas. The centre of the pattern was aligned with the centre of the goal area.

Procedure. *Pre-training.* All pre-training and experimental training procedures on the acquisition of the structural discrimination followed similar design as that used by George et al., (2001).

Rats were carried to the test room in the home cages, one pair at a time. During testing the cage partner remained in its cage positioned on the floor in one of the corners of the room. All rats received one session of pre-training in the tank, without any of the experimental stimuli present. Pre-training consisted of four stages, each containing six trials. For each stage of pre-training the animal was allowed access to the platform which appeared in the left and the right goal area, alternating trial by trial. In all stages rats were allowed to sit on the platform for 20s, before being removed and briefly dried and placed in the holding cage which was located in a corner of the room on the floor. An interval of 30s passed before the next trial commenced. At the end of pre-training, the rat was thoroughly dried and returned to its home cage. Once both cage partners had completed the session, the rats were returned to the holding room.

Stage 1 of pre-training trials consisted of the rat being placed on the platform. Stage 2 consisted of trials in which the rat was placed in the water in front of the platform and was allowed to swim to the platform. Stage 3 consisted of trials in which the rat was discrimination, and with new discriminations being introduced once the previous discrimination had been acquired. The experiment was repeated in Experiment 4.

It was found that this procedure was successful in training rats to learn the structural discrimination. Therefore, the rats from both Experiment 3 and 4 subsequently either received lesions of the hippocampus or control procedures and their post-operative performance of the structural discrimination was tested (Experiment 7 and 8, Chapter Three). Due to differences in the length of training, and in some of the procedures used, the methods and results are presented separately for Experiment 3 and 4. The results of the two experiments are discussed collectively.

To assess the nature of the structural discrimination, rats in the Experiment 3 also received probe trials once the discrimination had been acquired. It is possible that when simultaneously presented with reinforced and non-reinforced stimuli, that are presented adjacent to each other, the stimuli may be encoded as forming one visual scene. However, if the stimuli are treated as forming one compound stimulus then approach to one part of the compound will result in reward whilst approach to another part of the compound will result in non-reward. Therefore, the compound can not enter into an association due to being equally reinforced and non-reinforced, and the task is not soluble. It is, however, possible that instead of approach and avoidance response being elicited by the compound, that conditional responses may be formed so that a compound may require a 'go left' response, whilst another may require a 'go right' response. Consequently the discrimination can now be solved in terms of if ABBA-go left, if BAAB-go right. It has been shown that learning of conditional responses is possible, but it is unclear whether animals might automatically adopt this strategy, as it would involve a more difficult type of learning than simple approach

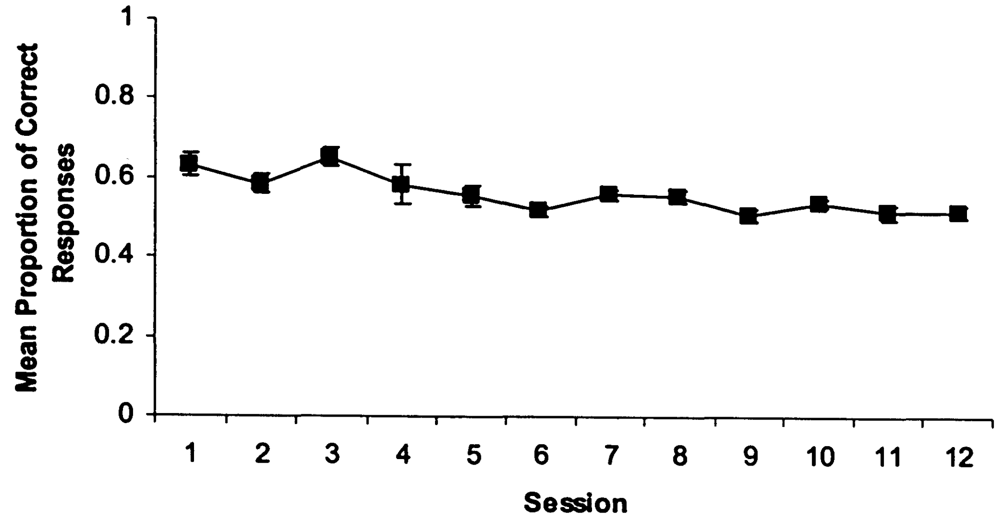

Figure 2.8. Performance of the structural discrimination during the final twelve sessions of training in which scores reflect responding to conditioned stimuli prior to the presentation of the US. Scores reflect the amount of responding to correct stimuli divided by the total amount of responding to all stimuli. Error bars indicate ±SEM.

Discussion

Rats trained to nose-poke for reward showed an increase in responding to the reinforced stimuli during the first stage of training when all responding to stimuli was recorded. During the last stage of training when responding to reinforced stimuli was not cued by the presence of the reward stimulus, responding declined to the reinforced stimuli until there was no apparent discrimination between reinforced compounds and the non-reinforced compounds. The discrimination between the reinforced and non-reinforced compounds during the first 11 sessions can be attributed to an increase in nose-poking whilst consuming the reward. However, at the start of the second stage of training rats did appear to be solving the discrimination, but as training progressed performance declined. It is conceivable that overall responding should decline in the second stage due to only being partially reinforced during the first half of CS+

and avoidance learning (Nissen, 1950; Bitterman, 1952; Spence, 1952; Woodinsky and Bitterman, 1952).

It is possible, therefore, that a simultaneous structural discrimination can either be learned by approach and avoidance of patterns, or by learning of conditional responses. The nature of how the discrimination is learnt is of importance for appreciating a possible lesion deficit on the task. Both the strategies of approach and avoidance and conditional responses require learning about the structural nature of the compound stimuli: it is only possible to learn to discriminate AB from BA, or ABBA from BAAB by appreciating the compounds' structure. However, it is possible that a deficit may reflect impaired learning of conditional responses rather than reflecting impaired structural learning. This factor needs to be accounted for when considering appropriate control tasks to confirm the role of the hippocampus in structural discrimination learning.

To test whether rats learned the structural discrimination by the use of a conditional response, probe trials consisted of a reinforced pattern being simultaneously presented with a non-reinforced pattern that it has not previously been paired with (e.g. AB vs. CB or AC). If rats learn by encoding conditional response to the scene formed by both the reinforced and non-reinforced patterns, then the discrimination will now no longer be solved on the probe trials, due to these scenes being novel to the rat.

Experiment 3

Method

Subjects. The subjects were 18 male rats (DA strain: Harlan, UK). Prior to and during the experimental procedures they were allowed free access to food and water. They trials of the WH+ HW- discrimination, followed 20 trials of the new HB+ BH- discrimination.

Stage 4 consisted of six sessions. For each session, each discrimination was presented in blocks of five trials, in the order of BW+ WB-, then WH+ HW- and lastly HB+ BH-. This order of presentation was repeated so that they received 30 trials of two blocks of five trials of each of the three discriminations.

Table 2.1. Stages of training of the structural discrimination used for Experiment 3. The stimuli were counterbalanced. Half the rats were trained to approach BW, WH and HB. The other half of rats were trained to approach WB, HW and BH.

Stage	***Discrimination***	**Presentation**
1	BW+ WB-	Consecutive blocks of trials of each discrimination.
2	BW+ WB-; WH+ HW-	
3	BW+ WB-; WH+ HW-; HB+ BH-	
4	BW+ WB-; WH+ HW-; HB+ BH-	Blocks of five trials (two per session) of each discrimination in consecutive order.
5	BW+ WB-; WH+ HW-; HB+ BH-	Blocks of five trials (two per session) of each discrimination in a pseudo-randomised order.
6	BW+ WB-; WH+ HW-; HB+ BH- Probe	Trials of each discrimination in a pseudo-randomised order.

response was deemed correct or incorrect once the rat's snout crossed over line drawn on the side walls that was 20cm from the end wall containing the goal areas.

Stage 2 consisted of nine sessions of continued training of the BW+ WB- discrimination and training with a new WH+ HW- discrimination. For the new discrimination the S+ consisted of a white rectangle to the left of a rectangle containing black and white horizontal stripes (WH), and for the S- a rectangle containing horizontal stripes was to the left of the white rectangle (HW) (see Figure 2.10). Once again, the reinforcement contingency of the patterns was counterbalanced across the group of rats, so that half the rats were reinforced for approaching BW and WH and the other half of rats were reinforced for approaching WB and HW. For the first two sessions rats received five trials of the BW+ WB- discrimination, and then 25 trials of the WH+ HW- discrimination. For the last seven sessions rats received ten trials of the BW+ WB- discrimination followed by 20 trials of the WH+ HW discrimination.

Stage 3 consisted of seven sessions of continued training on the BW+ WB- discrimination and the WH+ HW- discrimination, and also training on a new HB+ BH- discrimination (see Figure 2.10). For the new discrimination the S+ was a rectangle containing horizontal stripes to the left of a black rectangle (HB), and the S- was a black rectangle to the left of a rectangle containing horizontal stripes (BH). The reinforcement contingency of the patterns was counterbalanced across the group of rats. Therefore, half of the rats were reinforced for approaching BW, WH and HB, whilst the other half was reinforced for approaching WB, HW and BH. For each session, rats received five trials of the BW+ WB- discrimination followed by five

Stage 5 consisted of three sessions. The same procedure as Stage 4 was used, but the presentation of each discrimination was randomised within the first three blocks of five trials, so that each discrimination would have been presented in a block of five trials within the first 15 trials of the session. The order in which the discriminations were presented was then repeated for the last 15 trials of the session.

Stage 6 consisted of seven sessions. For the first session rats received randomised presentations of the discriminations with the constraint that the same discrimination could not be presented twice in consecutive order. Rats received ten presentations of each of the three discriminations. For the second and third session, rats were tested on the three discriminations as in the first session, but only received eight presentations of each discrimination. A probe test was presented at every fifth trial for a total of six times. Therefore, the rats still received a total of 30 trials. The probe trials consisted of presentations of the S+ patterns presented simultaneously with S- patterns which did not belong to the same structural discrimination pair of patterns, e.g. BW+ vs. HW-. Figure 2.11 depicts the new S+ and S- pairings that were presented in the probe trials. For probe trials the platform remained underneath the reinforced pattern. The reinforced and non-reinforced patterns appeared an equal amount of times in either goal area.

The last four sessions of Stage 6 consisted of 12 trials each. Rats received three trials of each discrimination in a random order with the constraint that the same discrimination could not be presented on consecutive trials. The amount of times that the S+ and S- of a discrimination appeared in either the left or right goal locations was counterbalanced over blocks of two sessions. For each session three probe trials were presented. Probe trials were presented every fourth trial of a session. The combination of S+ and S- pairings for the probe trials were counterbalanced over blocks of two sessions.

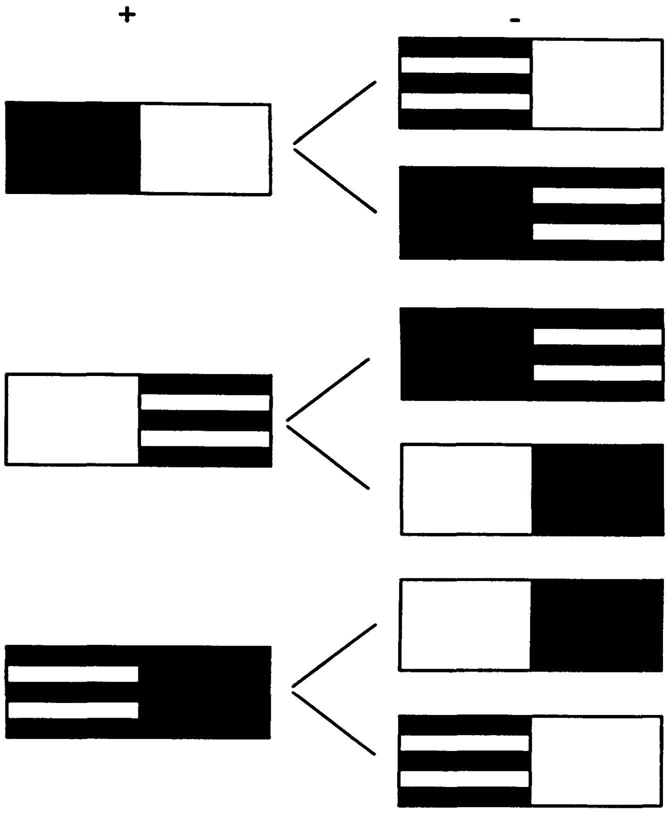

Figure 2.11. The novel S+ and S- pairings used for the probe trials. Reinforced patterns presented (left-hand column) are presented simultaneously with a non-reinforced pattern (right-hand column) which have not previously been paired together, e.g. BW (top left hand corner) must now be discriminated from the HW and BH patterns.

Experiment 4

Subjects. The subjects were 16 male rats (DA strain: Harlan, UK). Prior to and during the experimental procedures they were allowed free access to food and water. They were housed in pairs in a room that was illuminated for 14.5 hours per day. Rats were tested at the same time every day during the period of light in the holding room

Apparatus and Stimuli. The apparatus and stimuli were the same as used for Experiment 3.

Procedure. The stages of training are listed in Table 2. All procedures were the same as for Experiment 3, except for the following differences.

In Stage 2 rats received six sessions of continued training on the BW+ WB- discrimination and also the WH+ HW- discrimination was introduced. For each session rats received ten trials of the BW+ WB- discrimination followed by 20 trials of the WH+ HW- discrimination.

Table 2.2 Stages of training of the structural discrimination used for Experiment 4. The stimuli were counterbalanced. Half of the rats were reinforced for approaching BW, WH and HB. The other half of rats were reinforced for approaching WB, HW and BH.

Stage	***Discrimination***	***Presentation***
1	BW+ WB-	Consecutive blocks of trials of each discrimination.
2	BW+ WB-; WH+ HW-	
3	BW+ WB-; WH+ HW-; HB+ BH-	
4	BW+ WB-; WH+ HW-; HB+ BH-	Blocks of five trials (two per session) of each discrimination in a pseudo-randomised order.
5	BW+ WB-; WH+ HW-; HB+ BH-	Trials of each discrimination in a pseudo-randomised order.

In Stage 3 rats received six sessions of training on the BW+ WB-, WH+ HW- and the HB+ BH- discrimination.

Performance on the probe test was at a similar level to that of the structural discrimination. The overall mean score for the six sessions of testing was 79.9% for the probe test and 78.1% for the normal structural discrimination, and these scores did not significantly differ, F<1. A one sample t-test performed on the data from the last session of testing revealed that the rats were performing significantly above chance on the probe test, t(17)=3.25, p<.05. Therefore, rats were solving the task in a structural method rather than encoding the pattern formed by the S+ and S- as one scene and learning a conditional rule.

Experiment 4

Results

The performance for the first three stages of training is shown in Figure 2.15. Acquisition of the structural discrimination was similar to the performance of rats in Experiment 3. Each component of the discrimination was acquired over training, with performance starting off poor and eventually improving. When new discriminations were introduced, performance of previously learnt discriminations initially decreased, but eventually improved over the sessions of training.

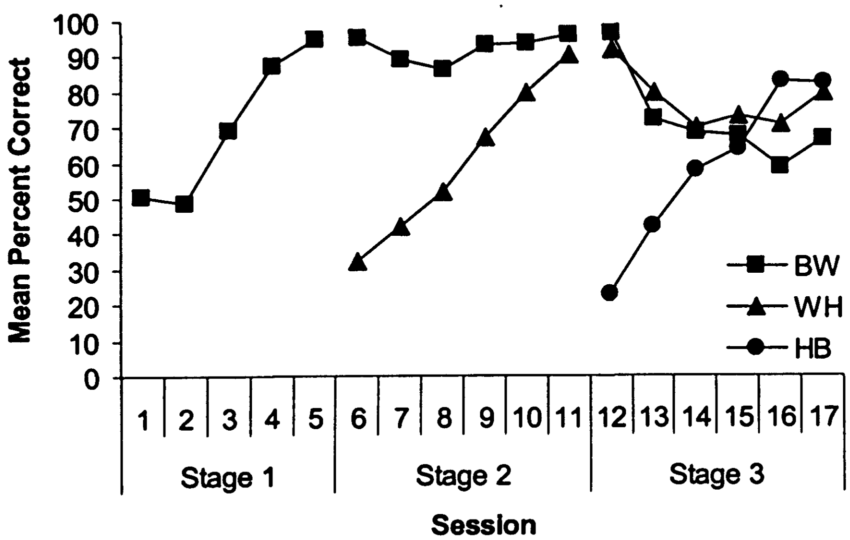

Figure 2.15. The performance of the structural discrimination for the Stages 1-3 of training.

For stage 5, in which all discrimination trial types were presented in blocks, but the order of the blocks was pseudo-randomised, performance was initially lowered but improved over sessions. For the last stage of testing when all trial types were presented in a pseudo-random order, performance did not increase.

A one sample t-test was performed on the data for the overall percentage correct for all three structural discriminations, for the last day of training, when the group mean was 73.5% correct. It was found that the group performed significantly above chance (50%), t(17)=5.97, p<.05. Each discrimination was also performed significantly above chance: BW, t(17)=3.7, p<.05; WH, t(17)=5.2, p<.05; HB, t(17)=2.8, p<.05. Performance on the three discriminations did not significantly differ from each other, F(2,34)=1.04.

Performance on the probe test, in which S+ patterns were presented with S- patterns with which they had not been previously been paired, is shown in Figure 2.14.

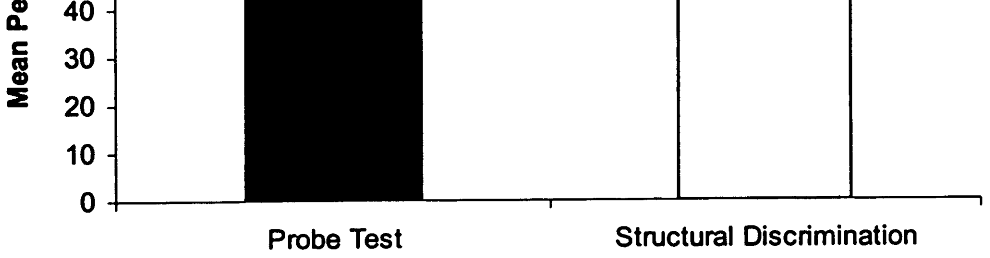

Figure 2.14. Performance of the probe test and the structural discrimination for the last six sessions of training. Error bars indicate ±SEM.

In stage 4 rats received four sessions of training on all three discriminations. For each session, the discriminations were presented two blocks of five trials. The blocks of trials were presented in a random order with the constraint that two blocks of the same discrimination could not appear consecutively.

Stage 5 consisted of five sessions. For the first two sessions each of the three discriminations were presented ten times in a pseudo-random order identical to the procedure used in Experiment 3. For the last three sessions rats received 12 trials (four trials of each discrimination). Rats were not presented with probe trials at any stage of training.

Experiment 3

Results

Statistical analyses of the data are only provided for the Test Stage, because only this stage must reflect structural learning of the discrimination, whereas other stages need not. The performance of the first three stages of training is shown in Figure 2.12.

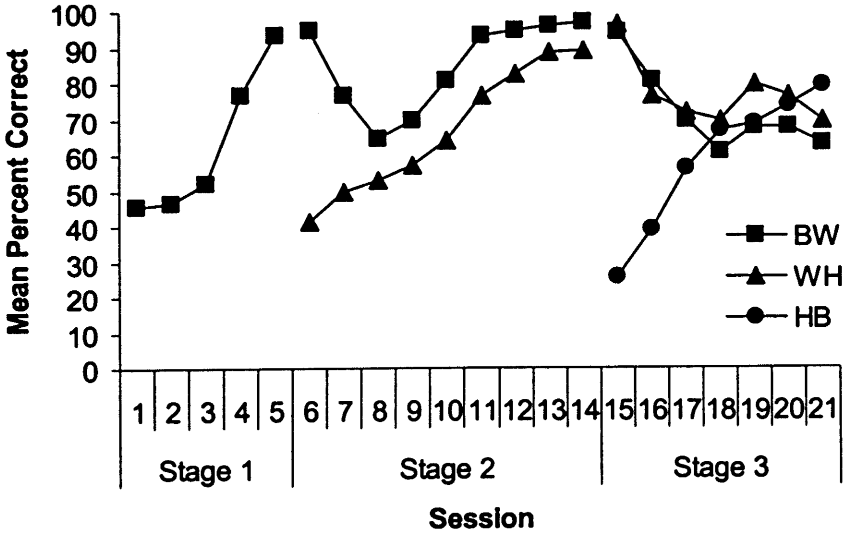

Figure 2.12. The performance of the structural discrimination for Stages 1-3 of training.

Each discrimination was acquired over training, with performance starting off poor and eventually improving. In stage 2 and stage 3, in which new discriminations were introduced, performance on the previously learned discriminations decreased at the beginning of these stages. Eventually performance for all the discriminations in stages 2 and 3 increased over sessions.

Performance on the last three stages of training is shown in Figure 2.13. For stage 4, in which the discriminations were presented in blocks of trials presented in consecutive order (BW+ WB-, then WH+ HW- and finally HB+ BH-), performance of the overall ability on the three components of the discrimination improved over sessions.

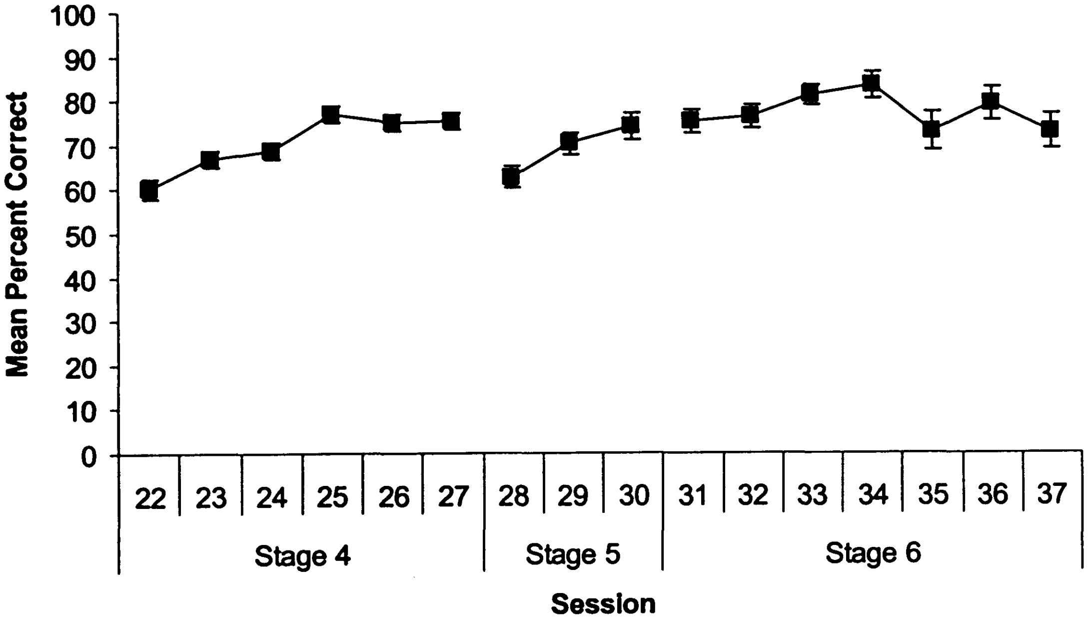

Figure 2.13. The performance of the structural discrimination collapsed over the three discriminations, Stages 4-6 of training. The last stage of training reflects performance that can only be achieved by appreciating the structural features of the compound stimuli. Error bars indicate ±SEM.

discriminations were performed significantly above chance level: BW+ WB-, t(15)=15.7, $p<0.05$; WH+ HW-, t(15)=11.6, $p<0.05$; HB+ BH-, t(15)=4.9, $p<0.05$.

Discussion

Rats were able to learn a structural discrimination in a water tank. The procedure for training rats followed a similar method to that used by George et al. (2001). Rats were initially trained on one discrimination (BW+ WB-) and once acquired they were required to maintain performance on that discrimination whilst acquiring a new discrimination. This procedure continued until all three discriminations were being performed at a similar level. It was found that rats could acquire the discrimination to a high level, with the rats in Experiment 3 performing at 73% correct and rats in Experiment 4 performing at 86% correct by the end of training.

It was found during the course of training that once the first discrimination had been achieved there was generalisation to the new discriminations. Performance on the second and the third discrimination started at a level somewhat below chance. As performance on these discriminations increased over the course of training, performance on previously acquired discriminations decreased, indicating that there was a reversal of learning. This implies that rats were initially solving the discriminations in an elemental manner. This is evident in Stage 3 when the final discrimination is introduced. All the elements that form the stimulus compound have been learnt to predict the opposite outcome. Previously HL(left) had been paired with W to signal the absence of the platform (HW-), also BR(right) had been paired with W to signal the absence of the platform (WB-). Consequently when presented with the

The performance for the last two stages of training of the structural discrimination is shown in Figure 2.16. For Stage 4 in which discriminations were presented in blocks of five trials, in a pseudo random order, performance was maintained at a level similar to performance in Stage 3. In the Test stage, in which trials of each discrimination were presented in a pseudo-random order, performance was maintained at a level similar to the previous stage, with an average performance of 83.8% correct.

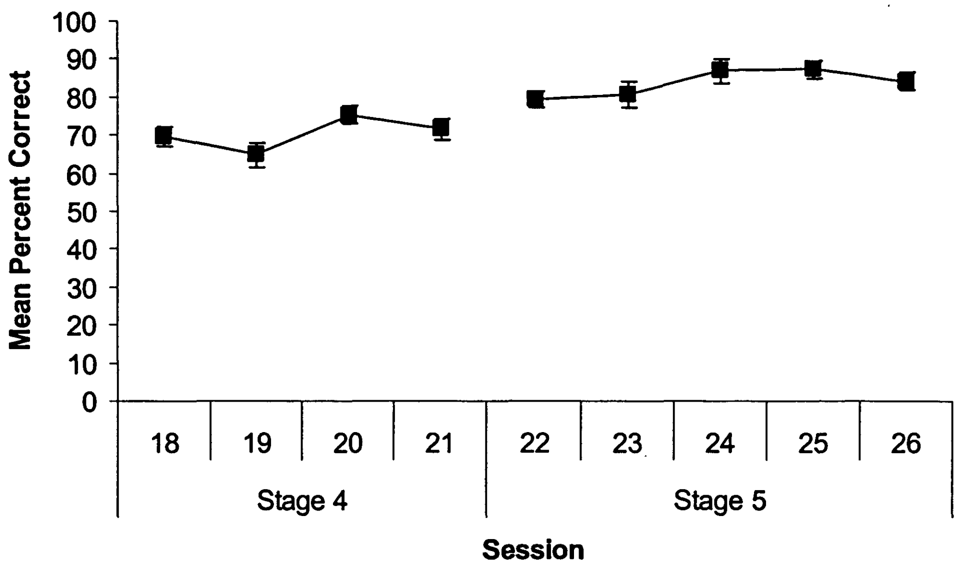

Figure 2.16. The performance of the structural discrimination collapsed over the three discriminations, for Stages 4-5 of training. The last stage of training reflects performance that can only be achieved by appreciating the structural features of the compound stimuli. Error bars indicate ±SEM.

Performance on the structural discrimination on the last session of training was significantly above chance, $t(16)=15.2$, $p<0.05$. Performance on the three discriminations did significantly differ, $F(2,30)=11.04$, $p<0.05$, but all three

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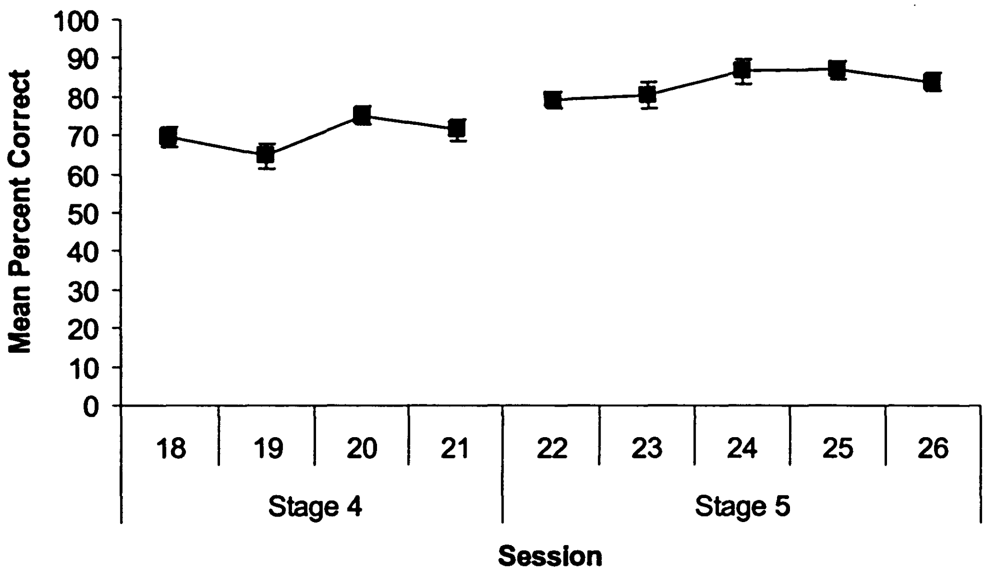

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HB and BH compounds, HB elicits an avoidance response and BH elicits an approach response due to its component stimuli being previously paired with reward.

According to Alvarado and Rudy (1992) when confronted with a stimulus that has ambiguous associations, rats will use a configural solution for discrimination learning. Alvarado and Rudy (1992) found that when rats were trained on an A+ B- discrimination and then received training on B+ C-, when transferred onto a C+ A- discrimination, performance was greater than for another group that had received A+ B- training followed by D+ C- training prior to testing on the C+ A- discrimination. Rats that had not been trained with the ambiguous element (B) showed a reversal of learning in the final stage, implying that elemental associations of A+ and C- had previously been learnt. Alvarado and Rudy (1991) concluded that training with the ambiguous element (B) encouraged rats to adopt a configural rather than an elemental solution to the task.

In the present experiments, rats receive training on a BW+ WB- discrimination followed by WH+ HW- discrimination. Within a discrimination elements have ambiguous associations due to being reinforced in differing structural relationships, but by the second stage the stimulus W should have no associative strength as it is equally reinforced and non-reinforced when presented both on the left and the right of another stimulus. According to Alvarado and Rudy (1992) this should encourage the use of a configural solution that should facilitate learning of new configural stimulus compounds, instead of elemental learning of the configurations' elements. Whilst no controls were provided for the structural discrimination, it can be inferred that this did not happen due to performance on the third discrimination being below chance. It is possible that there is generalisation between configurations that could produce the negative transfer of learning to the final discrimination, but according to Alvarado and Rudy (1992) configural training by the presentation of an ambiguous element should reduce the amount of negative transfer so that novel configurations of previously learnt elements are treated as having neutral associative strength. This was shown by the transfer of a configural solution to a novel discrimination that contained no ambiguous features.

The probe test did not provide evidence that rats make conditional responses to visual scenes created by the simultaneous presentation of the reinforced and non-reinforced stimuli. When rats were presented with a reinforced stimulus presented adjacent to a non-reinforced stimulus with which it had not previously been paired, performance was maintained. If rats had associated a conditional response of 'go left' or 'go right' to visual scenes, then performance should have been worse on probe trials in which novel visual scenes were presented, compared to normal trials. Bitterman (1952) reported that rats make conditional responses towards compound visual stimuli. Rats were presented on successive trials with two visual stimulus compounds. Each stimulus compound consisted of two visual patterns that were placed adjacent to each other, contiguous in space. Rats were required to make a left response when presented with stimulus compound AB so that responding was direct to the A stimulus, and to make a right response to stimulus compound CD so that responses were directed to D (Bitterman, 1952). On a transfer test rats were presented with the same configurations, but the spatial relationship between the elements were reversed. It was found that rather than making approach/avoidance response towards the elements of the compounds, rats continued to go left when presented with BA and go right when presented with CD (Bitterman, 1952). Therefore, under certain conditions it appears that rats automatically initiate conditional response towards stimuli, but in the present experiment there is no convincing evidence to suggest that rats were forming responses in this manner.

It is possible that compounds may be associated with conditional responses to receive reward when they are presented in different locations. If BW is to the left (of WB) the response to be learnt would be 'go left', and in the other instance if BW is to the right (of WB) the response to be learnt would be 'go right'. Learning of this manner would not be contingent on the features of the other compound that is present on a trial. Consequently, forming new pairs of reinforced and non-reinforced compounds would not have any impact on a rat's ability to perform a conditional response. However, if performance was based on forming conditional responses in this manner the discrimination now becomes extremely complex. Compounds would have to be encoded as to their relative location in space. Therefore to learn BW(left)-go left, BW(left) has to be discrimination from BW(right), and BW(left)-go left has to be discriminated from BW(left)-go right. This has to occur in parallel to encoding the structural features of the compounds. Instead of having to discriminate between six configurations that have differing structural features, the discrimination now requires the ability to discriminate between 12 configurations with two conditional responses, creating 24 stimulus-response associations to be learned. Although such learning may be possible, the more parsimonious interpretation of the present experiment is that rats learn to solve a structural discrimination by approach and avoidance of compounds of stimuli.

Experiment 5

Alvarado and Rudy (1992) trained rats on a transverse patterning task (Spence, 1952) using a water tank apparatus similar to the apparatus in used in Experiment 3 and 4. The present experiment attempts to replicate the findings of Alvarado and Rudy (1992) by training rats on a transverse patterning task using the water tank apparatus and the same stimuli that was used for experiments 3 and 4.

The transverse patterning discrimination is an appropriate control task for testing whether a lesion can selectively impair learning of a structural discrimination, due to the two tasks sharing many similarities, but differing in that the transverse patterning task does not require structural learning. Both tasks use three stimuli that are differentially reinforced when presented in different compounds. Also, the tasks cannot be solved by elemental learning and both require non-linear solutions. The tasks may also be matched for their difficulty to the extent that they both consist of three discriminations that must be solved concurrently. Therefore, if hippocampal lesions selectively impair structural learning, it should follow that it is possible to dissociate the effects of hippocampal lesions on a structural discrimination from a transverse patterning discrimination.

In the transverse patterning task subjects are required to solve three concurrent discriminations: A+ B-, B+ C- and C+ A-. Each stimulus is equally reinforced and non-reinforced over the three discriminations. Therefore, subjects have to learn the reward contingencies of each stimulus with regards to the stimulus with which it is paired within a given discrimination. The apparatus was adjusted so that the partition wall, that divided the left and right goal locations, was now transparent, so that both

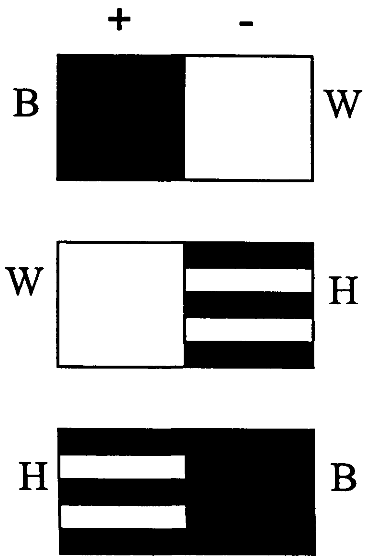

Figure 2.17. Transverse patterning stimuli. The stimuli are identical to the component stimuli used for Experiments 3 and 4. Individual stimuli within a compound were differentially reinforced, in contrast to the structural discrimination in which compounds formed by the stimuli were differentially reinforced.

Procedure. In a similar procedure to that of Alvarado and Rudy (1992), rats received training in which the three discriminations were progressively introduced before rats were presented with all three discriminations presented in pseudo-random order.

All procedures for pre-training in the water tank were the same as used for Experiments 3 and 4.

Animals were trained on the discriminations in a progressive manner starting with one discrimination, followed successively by the others until animals were solving all three discriminations concurrently. Rats received one session of training per day.

The stages for training of the transverse patterning discrimination are listed in Table 2.3.

stimulus and sit on the platform for 10s. A response was deemed correct if the rat mounted the platform, but was deemed incorrect if the rat's snout came within 20cms of the incorrect goal location. These procedures were used for all training.

Stage 2 consisted of six sessions of continued training on the B+ W- discrimination and the introduction of training on the W+ H- discrimination. Each session consisted of 10 trials of the B+ W- discrimination, followed by 20 trials of the W+ H- discrimination.

Stage 3 consisted of six sessions of continued training on the B+ W- and W+ H- discriminations with the introduction of training on the H+ B- discrimination. Each session consisted of five trials of B+ W- followed by five trials of W+ H-. Within these ten trials the amount of times a reinforced stimulus appeared in a given goal location was counterbalanced, and within each discrimination the goal location was counterbalanced over blocks of two sessions. After the ten trials of the previously learnt discriminations, rats received 20 trials of the H+ B- discrimination.

Stage 4 consisted of six sessions of training on all three discriminations. Each session consisted of two blocks of five trials of each discrimination, presented randomly, with the constraint that two blocks of the same discrimination could not be presented consecutively. Across the two blocks of trials, for each discrimination, the number of times a correct stimulus appeared in a given goal location was counterbalanced.

Stage 5 consisted of 17 sessions of training on all three discriminations. The first 14 sessions consisted of ten trials of each discrimination presented in a random order, with the constraint that the same discrimination could not be presented on two consecutive trials. The final three sessions consisted of four trials of each discrimination presented in the same manner as in the previous 14 sessions.

Results

The mean percent correct for each session of the first three stages of training is shown in Figure 2.18.

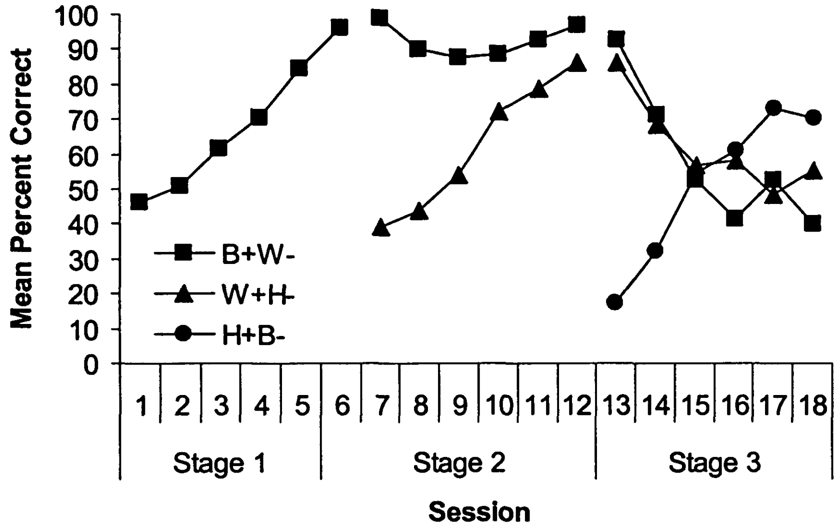

Figure 2.18. Mean performance of the transverse patterning task on Stages 1-3 of training.

Over the first six sessions, performance on the B+ W- discrimination increased from chance level until animals were performing at ceiling. Performance of the W+ H- discrimination started below chance level, but quickly increased over sessions. The performance of the B+ W- discrimination fell slightly with the initial acquisition of the W+ H- discrimination, but then increased to its previous level of performance. Performance of the H+ B- discrimination started below chance, but increased over days. During acquisition of the H+ B- discrimination, performance of both the B+ W-the reinforced and non-reinforced stimuli could be seen when a rat had made a choice and was approaching a goal location.

It is claimed by Alvarado and Rudy (1992) that by training rats first on an A+ B- discrimination followed by a B+ C- discrimination, a configural solution to the task is encouraged, due to stimulus B having ambiguous associations. This is inferred from the higher rate of acquisition of the C+ A- discrimination compared to rats that have had the same training in stages one and three, but receive training on a D+ C- discrimination for the second stage. Alvarado and Rudy (1992) argue that in the second stage, because B no longer consistently predicts an outcome, rats adopt a configural rather than elemental solution to the task. In Experiment 3 and 4 it was found that once animals had acquired the AB+ BA- discrimination and were introduced to the BC+ CB- discrimination performance of the new discrimination started below chance, and in the final stage when the CA+ AC- discrimination was introduced performance was again below chance, inferring that there was a reversal of learning. It can be argued that this reflects elemental learning of each stimulus in each location in which it is presented. From the hypothesis of Alvarado and Rudy (1992) it could be claimed that the structural training should encourage a non-elemental (or non-linear) solution to the task due to neither stimuli consistently predicting an outcome. Therefore, from the evidence of Experiments 3 and 4 it appears that rats do not treat the stimuli as configurations until explicitly required to do so. This is contrary to the predictions of Alvarado and Rudy (1992). These predictions will be tested further in the present experiment.

In the present experiment rats were trained on a transverse patterning task. Rats were trained progressively on the three discriminations that form the transverse patterning

Table 2.3. Stages of training of the transverse patterning discrimination, Experiment 5. Stimuli were counterbalanced, so that half of the rats were trained on B+ W-, W+ H- and H+ B-. The other half of rats were trained on W+ B-, H+ W- and B+ H-.

Stage	***Discrimination***	***Presentation***
1	B+ W-	Consecutive blocks of trials of each discrimination.
2	B+ W-; W+ B-	
3	B+ W-; W+ H-; H+ B-	
4	B+ W-; W+ H-; H+ B-	Blocks of five trials (two per session) of each discrimination in a pseudo-randomised order.
5	B+ W-; W+ H-; H+ B-	Trials of each discrimination in a pseudo-randomised order.

Stage 1 of training consisted of six sessions of 30 trials of training on the B versus W discrimination. Half of the rats received training on a B+ W- discrimination, and the other half received training on a W+ B- discrimination. All discriminations were counterbalanced in the same manner. Therefore by the end of training half of the rats had been trained on B+ W-, W+ H-, and H+ B-, and the other half of the rats were trained on W+ B-, H+ W-, and B+ H-.

Each stimulus appeared equally often in the right and left goal location. The trial order of reward in the two goal locations was random with the constraint that animals could not receive reward in the same goal location on more than three consecutive trials. If a rat approached the correct stimulus it was allowed to sit on the platform for 10s before being removed and the next trial commencing. If the rat swam to the incorrect stimulus it was allowed to swim back around the partition wall to the correct task, in a similar manner to the training on the structural discrimination in Experiments 3 and 4. If rats are able to acquire a transverse patterning task using the same apparatus and stimuli as previously used for the structural discrimination, then it will be possible to compare performance of hippocampal lesioned rats on a structural and an appropriate configural discrimination.

Method

Subjects. The subjects were 14 male Dark Agouti rats (Harlan, UK). Prior to and during the experimental procedures animals were allowed free access to food and water. They were housed in pairs in a room that was illuminated for 14.5 hours per day. All testing was carried out during the period of light at the same time each day.

Apparatus. The apparatus was the same as used for Experiments 3 and 4, with the exception that the partition wall that separated the left and right goal areas was made of transparent Perspex. Therefore, both stimuli could be viewed after a rat had made a choice and was approaching a goal area.

Stimuli. Figure 2.17 shows the stimuli used and the design of the discrimination. The stimuli used were the same as described for Experiments 3 and 4 (B, W and H). Whereas, previously in Experiments 3 and 4, two patterns, consisting of pairs of the stimuli B, W and H, were presented either side of the partition wall, now only one stimulus was presented on either side of the partition wall. For example, if the BW pattern was presented, stimulus B would be to the left of the partition wall and stimulus W to the right of the partition wall.

and W+ H- discrimination dropped considerably to a level close to chance. In the fourth stage of training, when discriminations were presented in blocks of trials in a pseudo-random order, performance on all three discriminations stayed close to chance level.

Performance on Stage 4 and 5 is shown in Figure 2.19. In Stage 4 of training when discriminations were presented in blocks of trials in a pseudo-random order, performance on all three discriminations stayed close to chance level. In Stage 5 of training, in which the order of discrimination presentation was pseudo-randomised, the performance of the three discriminations increased over sessions.

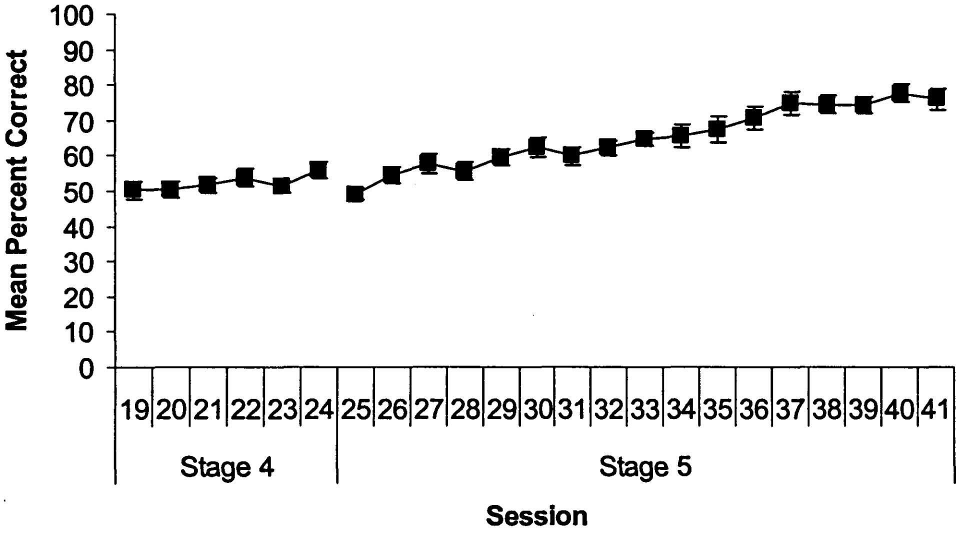

Figure 2.19. Performance of the transverse patterning discrimination on Stages 4-5 of training. Error bars indicate ±SEM.

Analysis of the last session of training revealed that rats were performing the discrimination significantly above chance, $t(13)=13.5$, $p<0.05$. Performance on the three discriminations did not significantly differ, $F(2,26)=0.83$, and separate analyses of each discrimination revealed that all three discriminations were performed significantly above chance: B+ W-, $t(13)=4.7$, $p<0.05$; W+ H-, $t(13)=4.9$, $p<0.05$; H+ B-, $t(13)=3.7$, $p<0.05$.

Discussion

Rats were able to learn a transverse patterning discrimination using the same stimuli that were used for the structural discrimination. Instead of two pairs of stimuli presented simultaneously, only one pair of stimuli was presented and only one of these stimuli was reinforced. Rats were trained on the transverse patterning task using the same procedure as used for the structural discrimination. Rats were trained on one discrimination (B+ W-) until it had been acquired, and then the next discrimination was introduced. This continued until all three discriminations had been acquired and were being performed at a similar level. Performance did not readily increase until all three discriminations were presented in a pseudo-random trial order.

Similar to the findings of Experiment 3 and 4, rats showed a negative transfer of learning to the third discrimination, which implies a reversal of learning. This does not support the results of Alvarado and Rudy (1992) who concluded that when presented with an ambiguous feature rats will use a configural solution for the performance of discrimination tasks. As previously stated, it is possible that generalisation from configurations could result in negative transfer occurring when the third discrimination is presented. This view is formally expressed in a theory proposed by Pearce (1994), which claims that stimuli that are presented simultaneously will be represented as a configuration unique from the individual representations of its component features. Discriminations are achieved by dissociating the similarity between configurations. Configural representations that share features will both be activated partially by the presentation of the common feature, but a configural representation will only be fully activated when all the features of a configuration are present. According to the similarity rule used by Pearce (1994) (no. of common elements/no. of elements × no. of common elements/no of elements) the configuration BW will generalise to HB to the extent of 0.25, similarly WH will generalise to HB to the same value. Therefore, if this view is taken, there will be negative transfer, but similar to the view of Alvarado and Rudy (1992) there will not be 100% transfer of learning due to the previously learnt configurations ability to only partially activate the HB configuration.

According to an elemental theory of learning (Rescorla and Wagner, 1972), stimuli acquire associative strength individually and when presented in compound stimuli compete for associative strength. Therefore, if animals had learned the B+ W- and W+ H- discriminations in an elemental fashion, B should have positive associative strength, H should have negative associate strength and W should have no associative strength due to being equally reinforced as non-reinforced. Consequently when presented with H+ B-, there should negative transfer of learning because the discrimination requires a complete reversal of previously learnt associations. Performance on the H+ B- discrimination should reflect the previous learning in which B was positively reinforced and H was negatively reinforced, therefore there should 100% negative transfer of learning. If the view of Pearce (1994) is taken, when the third discrimination is introduced the average number of correct responses to B+ W- and W+H will be initially greater than the amount of incorrect responses on the H+ B- discrimination, due to previously learnt configurations only being able to partially activate a HB configural representation. Analysis of the first session in which the H+ B- discrimination was introduced showed that incorrect (i.e. previously

Spence (1952)[2] claimed that a transverse patterning discrimination could be solved by encoding the memory trace of one stimulus paired with the perception of another stimulus, and consequently this configuration would be associated with an outcome. Learning of the B+ W- discrimination would take the form of the configuration of B plus the memory trace of W being paired with reward and W plus the memory trace of B being paired with non-reward, and consequently approach and avoidance responses to the configurations can be initiated. If this description of the transverse patterning task is correct, the task should be similar to the structural discrimination except that the structure of the elements forming the configuration does not need to be discriminated. If, however, the configurations of stimuli are associated with approach towards a component stimulus of the compound, then the configuration of BW needs to form an excitatory association with B and an inhibitory association with W. Therefore, the transverse patterning task becomes more complex than the structural discrimination, because now compounds of stimuli activate configural representations that activate the representation of a component stimulus that elicits either an approach or avoidance response. Whilst, the nature of how animals solve a transverse patterning is questionable, the task shares similarities with a structural discrimination, and the ability to dissociate learning of a structural discrimination from a transverse patterning task by the use of lesions could provide important insights into the role of learning by the hippocampus.

Experiment 6

In Experiment 5 it was found that rats could learn a transverse patterning task using a similar training procedure and the same stimuli that was used for the structural

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[2] This interpretation of a transverse patterning task is described in further detail by Nissen (1953).

discrimination. Although there can be no direct comparisons, it can be noted that acquisition of the transverse patterning task took longer than the structural discrimination. It is possible that even though the transverse patterning task and the structural discrimination used the same stimuli, the demands of the two tasks may differ more than just whether compounds have to be learned with regards to the structural features. It may not be entirely appropriate to compare performance of lesioned rats on the two tasks, as the task difficulty may reflect possible non-structural demands of the task. So, in order to look at another class of configural discrimination, this experiment used a biconditional discrimination.

The demands of the biconditional discrimination are more similar to the demands of the structural discrimination, in as much as reinforcement is given for approach or avoidance of whole compounds, rather than having to make responses to components of a compound as in the transverse patterning task. In a biconditional discrimination, stimuli are presented in compounds of two stimuli, with each stimulus being reinforced in one compound and being non-reinforced when in compound with a different stimulus. Therefore, no one stimulus predicts an outcome, only the unique configurations formed by the stimuli can predict an outcome. The design takes the form of AB+, CD+, AD-, and CB-. Whereas in the structural discrimination, stimuli presented in a certain location in relation to another stimulus predicted the reward outcome, in the biconditional discrimination stimuli always appear in a certain location within a compound, therefore the features of the stimuli are only required for the solution of the task. Rats were trained on a biconditional discrimination in the water tank in a similar manner to the training of the structural discrimination. Rats were required to make a simultaneous choice between a reinforced compound and a non-reinforced compound.

correct) responses to H+ B- were not significantly less than the correct responses to B+ W-, W+ H-, t(13)=1.76. Therefore, it can argued that following the Rescorla-Wagner (1972) theory of elemental learning, there was a near 100% transfer of learning reflecting elemental encoding of the associations within the discrimination. From this evidence, it appears that rats only use a configural strategy for the solution of the discrimination when forced by the demands of the task. When there is an elemental solution to the discrimination rats appear to use the elemental solution rather than using a configural solution.

Although, animals acquired the discrimination, the rate of learning was notably slower than acquisition of the structural discrimination. This would imply that the transverse patterning task is more difficult to solve than the structural discrimination. The difference between the rates of acquisition of the two tasks is surprising since both tasks require stimuli to enter into multiple associations when encoded with regards to the configurations that the stimuli form. It is possible that there are procedural differences between the tasks that cause the transverse patterning task to be harder to acquire. In the structural discrimination rats are required to approach and avoid stimulus compounds that require discrimination of their structural features. In the transverse patterning task, the configurations formed by the compound stimuli have to be discriminated, but to receive reward animals are required to respond to a component of the compound. Therefore, the requirements of the transverse patterning task may be qualitatively different from the structural discrimination, due to the nature of initiating a response.

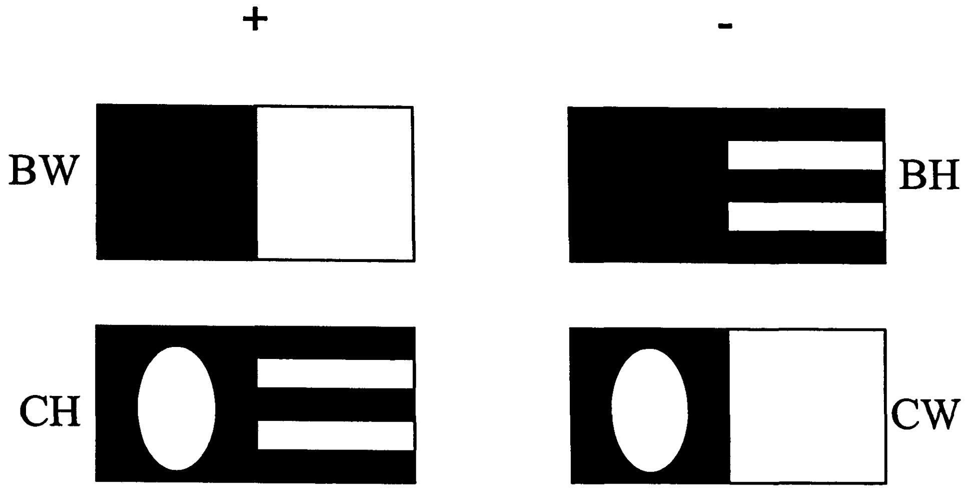

Figure 2.20. Biconditional discrimination stimuli. Stimuli B and C are only ever presented on the left, and W and H are always presented on the right. Each stimulus is reinforced when presented in compound with a specific stimulus, and reinforced when presented with another stimulus.

Procedure. All procedures for pre-training in the water tank apparatus were the same as for Experiments 3-5.

Subjects were trained on the biconditional discrimination in a progressive manner, starting with one discrimination (BW+ BH-) and once acquired, a new discrimination (CH+ CW+) was introduced. In the final stage rats received training of the four possible combinations of reinforced and non-reinforced patterns; BW+ BH-, BW+ CW-, CH+ BH-, CH+ CW-, which were required to be solved concurrently.

The stages of training of the biconditional discrimination are listed in Table 2.4.

Stage 1 consisted of five sessions of training on the BW+ BH- discrimination. Each session consisted of 30 trials. Each pattern appeared equally often in the right and left goal location. A reinforced stimulus could not appear in the same goal location on

Method

Subjects. The subjects were 14 male Dark Agouti rats (Harlan, UK). Prior to and during the experimental procedures animals were allowed free access to food and water. They were housed in pairs in a room that was illuminated for 14.5 hours per day. All testing was carried out during the period of light at the same time each day.

Apparatus. The apparatus was the same as used for Experiment 3 and 4.

Stimuli. The stimuli used were a black rectangle (B), a white rectangle (W), a rectangle containing horizontal black and white stripes (H), and a white oval on a black rectangular background (C). The stimuli are depicted in Figure 2.20. All rectangles were 28cm in height and 14cm wide. The rectangle containing black and white horizontal stripes (H), consisted of four white and three black stripes that were each 4cm wide. The white oval used for stimulus C, was 10cm at its widest, and 24cm at its longest. Four patterns containing combinations of two of the stimuli were made. These patterns were made by printing stimuli adjacent to other stimuli. They were then laminated and suspended from the wall of the two goal areas in the water tank. The patterns consisted of B to the left of W (BW), B to the left of H (BH), C to the left of W (CW) and C to the left of H (CH). For counterbalancing purposes some subjects were presented with the same patterns placed upside down. Therefore, the structural-spatial relationships between the stimuli were now reversed, and four new patterns were formed; WB, HB, WC and HC. All stimuli were symmetrical along all axes. Consequently, turning a pattern upside down did not change any of the physical properties of the individual stimuli, but it did change the structural relationship between them.

more than three consecutive trials. If a rat approached the correct stimulus it was allowed to sit on the platform for 10s before being removed and the next trial commencing. If the rat swam to the incorrect stimulus it was allowed to swim back around the partition wall to the correct stimulus and sit on the platform for 10s. A response was deemed correct if the rat mounted the platform, but was deemed incorrect if the rat's snout came within 20cms of the incorrect goal location. These procedures were used for all training.

Table 2.4. Stages of training of the biconditional discrimination, Experiment 6.

Stage	*Discrimination*	*Presentation*
1	BW+ BH-	Consecutive blocks of trials of each discrimination.
2	BW+ BH-; CH+ CW-	
3	BW+ BH-; CH+ CW- BW+ CW-; CH+ BH-	Blocks of seven trials of each discrimination in a pseudo-randomised order.
4	BW+ BH-; CH+ CW- BW+ CW-; CH+ BH-	Trials of each discrimination in a pseudo-randomised order.

Rats were divided into four counterbalanced groups (see Table 2.5). Two groups were trained on the BW+ BH- discrimination, with one group reinforced for approaching BW and non-reinforced for approaching BH, the other group received the opposite contingencies. The other two groups were trained on the same discrimination, but with the structural relationships between the stimuli in the patterns reversed. One group was reinforced to approach WB and non-reinforced for approaching HB, the other group received the opposite contingencies. Therefore, reinforcement of patterns and the structural relationship between the stimuli contained within the patterns was counterbalanced.

Table 2.5. The counterbalancing of groups for Experiment 6. Compounds of stimuli were counterbalanced for their reward contingencies and also the structural arrangements of compound stimuli were also counterbalanced.

Group	+	-
1	BW CH	BH CW
2	BH CW	BW CH
3	WB HC	HB WC
4	HB WC	WB HC

Stage 2 consisted of five sessions of continued training on the BW+ BH discrimination, and the introduction of training on the CH+ CW- discrimination. Each session consisted of ten trials of the BW+ BH- discrimination followed by 20 trials of the CH+ CW- discrimination.

Stage 3 consisted of four sessions in which all four simultaneous discriminations were presented (i.e. BW+ BH-, BW+ CW, CH+ BH- and CH+ CW-). The mean percent correct for each reinforced pattern was calculated averaging across the score for the two discriminations in which a pattern appeared. Each discrimination was presented in blocks of seven trials, therefore, rats received in total 28 trials per session. Blocks of each discrimination were presented in a random order, and changed session by session. The amount of times a pattern appeared in each goal location was counterbalanced over the two blocks of seven trials in which it appeared. The amount of times a pattern in a particular discrimination appeared in the two goal locations was counterbalanced over blocks of two sessions.

Stage 4 consisted of nine sessions. For the first six sessions, seven trials of each discrimination were presented. Discriminations were presented in a random order, with the constraint that a pattern could appear on more than three consecutive trials. The same counterbalancing procedures for the presentation of patterns in goal locations were used as in stage three. For the final three sessions, training continued the same as in the previous sessions, but rats only received three trials of each discrimination.

Results

The mean percent correct for each discrimination, for the first two stages, is shown in Figure 2.21.

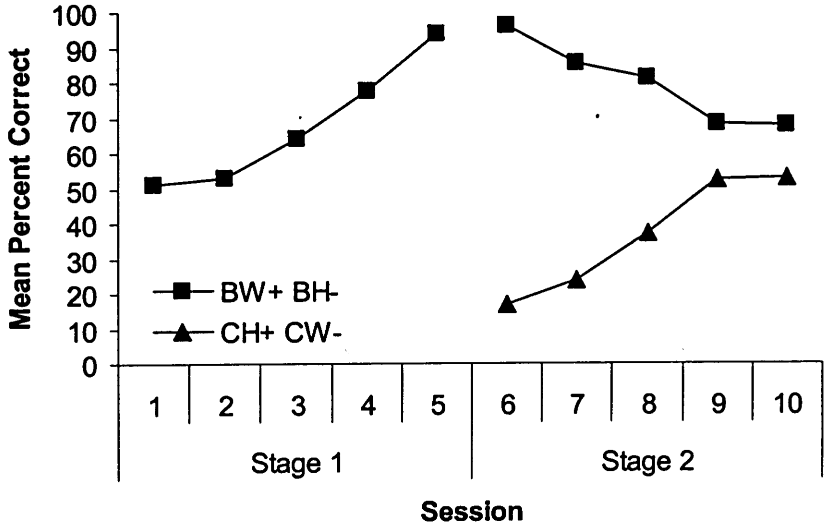

Figure 2.21. Performance of the biconditional discrimination on the first two stages of training.

Performance on the BW+ BH- discrimination started close to chance (50% correct), but increased over sessions until it approached ceiling level. When the CH+ CW- discrimination was introduced, performance began below chance, but rapidly improved with training. Whilst the CH+ CW- discrimination improved over time, performance on the previously acquired BW+ BH discrimination rapidly fell. Eventually performance on both discriminations met at a level that was similar to chance performance.

The performance of the biconditional discrimination in the last two stages of training is shown in Figure 2.22.

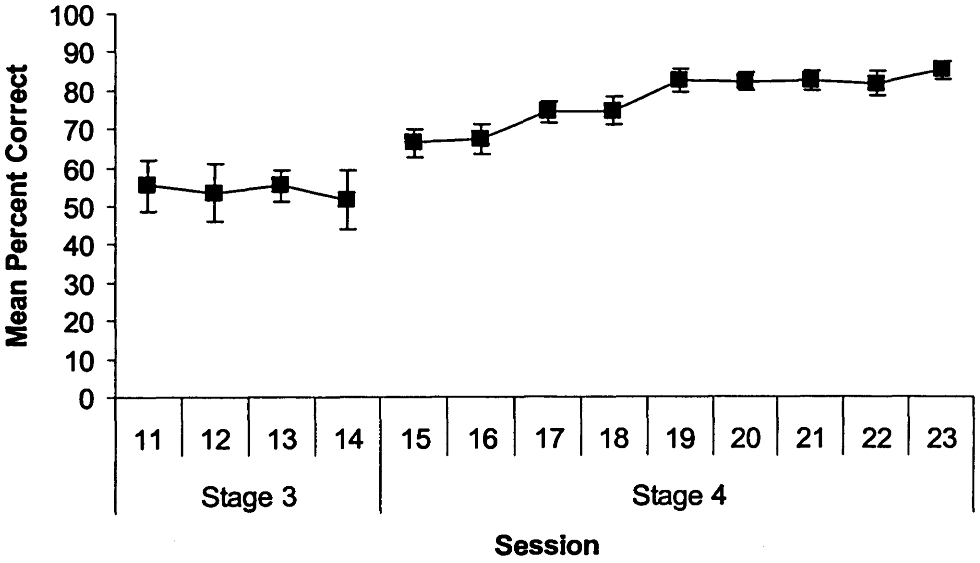

Figure 2.22. Performance of the biconditional discrimination on Stages 3 and 4 of training. Error bars indicate ±SEM.

In Stage three of training in which discriminations were presented in blocks of seven trials, performance remained at a level close to chance. For the final stage of training in which all discriminations were presented in a pseudo-random order, performance to both reinforced patterns increased over sessions. Analyses of the last session of training revealed that rats were performing significantly above chance, $t(13)=15$, $p<0.05$. Performance of BW+ compared to CH+ trials did not significantly differ, $t(13)=1.75$, and performance was above chance for both reinforced compounds: BW+, $t(13)=12.03$, $p<0.05$; CH+, $t(13)=8.04$, $p<0.05$.

Discussion

It was found that rats were able to acquire a biconditional discrimination using the same apparatus and similar stimuli used for the training of a structural discrimination. Rats were initially trained on a BW+ BH- discrimination and then received continued training of the BW+ BH- with the introduction of a CH+ CW- discrimination. As was found for the structural discrimination and the transverse patterning task, learning of one discrimination transferred to performance of the new discrimination. Therefore, when the CH+ CW- discrimination was introduced performance was below chance. Also, acquisition of this discrimination caused performance of the previously learnt discrimination to decrease. As with the transverse patterning discrimination, performance did not readily increase until discriminations were presented in a pseudo-random order. Again, this can be attributed to the elimination of within-block learning of elemental associations. The pseudo-random trial order can be viewed as encouraging discrimination learning of configural associations.

The discrimination was acquired to a level of 86% correct on the final session of training. This level of performance is similar to the level of performance achieved by rats on the structural discrimination in Experiment 4. Therefore, performance on the biconditional discrimination is comparable to the performance on a structural discrimination, providing an appropriate control task for testing the effects of hippocampal lesions on a structural discrimination.

General Discussion

In Experiment 1 it was found that rats could be trained on a structural discrimination if the stimulus compounds were presented in a successive manner. Presenting the compounds simultaneously did not result in acquisition of the task. Although rats were able to acquire the automated task, responding, by chain-pulling, was at a very low rate, with less than one response being made on average during the first 10s of a CS.

In Experiment 2 responding was by nose-pokes made in the magazine chamber where food was presented. Higher levels of responding were recorded compared to the amount of responding by chain-pulling. However rats failed to acquire the discrimination to an adequate level. Therefore, training of a structural discrimination in an operant chamber did not provide an adequate method in which to test the performance of lesioned rats.

In Experiments 3 and 4 it was found that rats could acquire a structural discrimination when trained in a water tank apparatus, using a similar method to that used by George et al. (2001). Rats were required to make a simultaneous discrimination between reinforced and non-reinforced patterns and to swim towards a pattern underneath which there would either be a hidden platform or no platform. A self correction procedure was used that allowed rats to swim back round a partition wall to locate the platform if an incorrect response was made. Therefore, reinforcement was available on every trial.

There was a lack of evidence to suggest that rats encoded configurations of stimuli when acquiring the component discriminations within the task that permitted an elemental solution. Also, rats did not appear to make conditional responses based on the unique visual scenes formed by the reinforced and non-reinforced stimulus compounds. It can be concluded that once all three discriminations were acquired, rats were only able to solve the task by discriminating the structural features of the configurations formed by the compound stimuli.

In experiments 5 and 6 rats were trained on configural tasks that can be viewed as being of a similar difficulty as the structural discrimination. Rats were trained on the tasks in the same water tank apparatus. The stimuli used in Experiment 5, for training of a transverse patterning task were the same as used for the structural discrimination, but in this instance only one compound was presented on a trial and rats were required to make a response directed towards a component element of the compound. In Experiment 6, in which rats were trained on a biconditional discrimination, rats were presented with reinforced and non-reinforced compounds on a trial, so consequently had to make a simultaneous discrimination similar to the demands of the structural discrimination task.

Even though the transverse patterning task and the biconditional discrimination are similar in their complexity to that of a structural discrimination, it could be argued that the structural discrimination is an inherently more difficult task as it requires structural learning of configural stimuli. Reinforced stimuli and non-reinforced stimuli share more common features than compared to the similarity between the also be noted that in stage 3 of training of the biconditional discrimination, in which discriminations were presented in blocks of trials, the discrimination did not appear to improve over session. The biconditional discrimination was only acquired when all discriminations were presented in a pseudo-random order. When the same procedure of presenting discriminations in blocks of trials was used for training of a structural discrimination, performance did improve over sessions. Therefore, blocked-trial training facilitated learning of a structural discrimination, but not of a biconditional discrimination. The fact that blocked trial training did not facilitate learning of a biconditional discrimination is contrary to the predictions of McClelland, McNaughton and O'Reilly (1995) who suggest that that the gradual interleaving of conflicting associations facilitates learning. The biconditional discrimination required all component discriminations to be interleaved in a pseudo-random order for the task to be acquired. From the predictions of McClelland et al. (1995) it could be concluded that the structural discrimination was easier to acquire than the biconditional discrimination.

Although a structural discrimination requires configurations that contain the same elements to be discriminated from each other, whereas configural tasks require the discrimination of unique combinations of ambiguous elements, it does not appear that this results in a structural discrimination being harder than configural discriminations to acquire. It is possible that the structural features of compound stimuli are highly salient, and thus structural discriminations are learned at a rate that is not noticeably slower that a configural discrimination. If it is found that hippocampal lesions impair performance of a structural discrimination, but spare performance of a configural discrimination, this would suggest that the difference between configural discriminations and structural discrimination is qualitative rather than quantitative.

in that both stimuli presented in the transverse patterning task are relevant for receiving reinforcement. In contrast, the structural discrimination can be solved by approaching one configuration or simply avoiding another configuration. This is evident from the results of the probe test in Experiment 3. Therefore, there are differences between the tasks that may account for why a transverse patterning discrimination is harder to acquire than a structural discrimination. However, it appears that structural discriminations are not harder to acquire than all non-linear discriminations that are believed to require configural learning.

The biconditional discrimination differs from the transverse patterning in the same manner as the structural discrimination. Responses are made to configurations of stimuli rather than to elements within the configuration. The biconditional discrimination was acquired at a faster rate than the transverse patterning discrimination. Therefore, the difference in the requirement of responses appears to distinguish between a biconditional and structural discrimination from the transverse patterning discrimination. If the biconditional discrimination and the transverse patterning task both require configural learning, the differences in the two tasks lie in the procedures for initiating responses.

Even though the biconditional discrimination required two component discriminations to be learned, whereas the structural discrimination requires the acquisition of three component discriminations, it can be noted that there were not noticeable differences in the rates of acquisition of the two tasks. At the end of 23 sessions, rats trained on a biconditional discrimination were performing at 86% correct, whereas rats trained on a structural discrimination (Experiment 4) were performing at 84% correct after 26 sessions. There is not a large difference in the acquisition of these two tasks. It can

Therefore, the structural discrimination was learned faster than the transverse patterning task, which requires a non-linear solution.

As previously discussed, until the final component discrimination of each task was introduced, it appears that learning of the other component discriminations of the structural, biconditional and transverse patterning tasks had been learned by elemental encoding of the stimuli. These discriminations were acquired at a rate that is not noticeably different between the three discriminations. It is of interest to note that the acquisition of the first two discriminations of the transverse patterning were not appreciably faster than for the structural or biconditional discrimination, even though a more obvious elemental solution to these discriminations was available. Therefore, until the final component discrimination of task was introduced, it can be concluded that these tasks were taxing learning in a similar manner. However, the third discrimination of the transverse patterning task was acquired at a much slower rate than for the structural discrimination. Thus, it appears that the transverse patterning task is much harder to acquire than the structural discrimination. This contradicts the prediction that a structural discrimination is more complex than a configural discrimination due to the level of similarity between reinforced and non-reinforced compounds.

The transverse patterning task and the structural discrimination differ in how responses are required to be made towards the stimuli. In the transverse patterning task rats are required to learn to choose one stimulus over another depending on which stimulus it is paired with on a given trial. It is possible that because one element of a configuration is reinforced, whilst the other is not, that an elemental strategy persists for longer than for the structural discrimination. Also, the tasks differ reinforced and non-reinforced stimuli in the biconditional discrimination. In the biconditional discrimination, even though each element is equally reinforced and non-reinforced, each configuration has a unique combination of elements. In the structural discrimination, reinforced configurations are comprised of the same combination of elements as the non-reinforced configurations, and only the structure of the elements differs. It could be predicted that a structural discrimination should be harder to learn than a configural discrimination. If this prediction is correct it would be problematic to test whether hippocampal lesions selectively impair learning and memory of a structural discrimination, because it has been found that hippocampal lesions result in greater stimulus generalisation (Solomon and Moore, 1975).

In the present set of experiments, it may not be appropriate to compare acquisition of a biconditional discrimination to that of a structural discrimination, due to the use of a progressive training procedure. As a consequence of progressively introducing the component discriminations, the training procedure was longer for the structural discrimination, in which rats learned three component discriminations, than for the biconditional discrimination, in which rats learned two component discriminations. However, the design of the transverse patterning discrimination is more closely matched to that of the structural discrimination. Both discriminations have three component discriminations that were progressively introduced into training.

The transverse patterning discrimination took considerably longer for rats to learn than for the structural discrimination. When all three component discriminations were presented in a pseudo-random order, rats performed at a level of 79% correct on the first session for the structural discrimination (Experiment 4), whereas rats only reached a level of 76% correct on the transverse patterning task after 17 sessions.

Chapter Three

The Effects of Hippocampal Lesions on the Performance of a Structural Discrimination

Introduction

The 'configural association' theory of Sutherland and Rudy (1989) claims that the hippocampus plays an important role in the acquisition and storage of certain types of discrimination learning. Sutherland and Rudy (1989) claimed that learning can result in elemental or configural associations being formed, and that these two types of processes can be dissociated from each other through the use of different discrimination tasks. In a task in which a stimulus is paired with a single outcome, the stimulus enters into a direct linear relationship with the unconditioned stimulus (US) so that, as a consequence of training, the stimulus can elicit a mental representation of the stimulus, and thus produce a conditioned response. In other discrimination tasks in which a stimulus may be paired with different outcomes (i.e. reinforcement and non-reinforcement) when paired in compound with other stimuli, the stimulus can not form a linear relationship with the outcome, e.g. negative patterning (Woodbury, 1943), A+, B+, and AB-. In this instance, according to Sutherland and Rudy (1989) learning can only occur due to the unique configurations formed by the compound stimuli entering into a relationship with the US. Therefore, an elemental association system that can only encode linear elemental associations would not allow for individual stimuli to enter into multiple associations and would fail to learn a non-linear discrimination. In contrast, a 'configural association system' would allow for unique configurations of stimuli to enter into associations even though the net sum of the associative strength of the individual stimuli may sum to zero.

Sutherland and Rudy (1989) claimed that elemental learning and configural learning are underpinned by different neural mechanisms. Therefore, it would be possible, by causing damage to certain neuroanatomical areas to dissociate these two types of learning. Sutherland and Rudy (1989) claimed that configural associations are learned and stored in the hippocampus, and consequently causing damage to the hippocampus would impair an animal's ability to solve discrimination tasks that require a configural solution. Testing of this prediction has revealed contradictory results, but there is sufficient evidence to suggest that the causes of impairments on certain discrimination tasks are not due to whether the formation of configural associations is required (Whishaw and Tomie, 1991; Gallagher and Holland, 1992; Davidson et al., 1993; Mcdonald et al., 1997; Bussey et al., 1998; Bussey, Dias et al., 2000, Coutereau et al., 2002).

Recent evidence from immediate early gene studies has suggested that the hippocampus plays a role in the detection of novel spatial arrangements of familiar stimuli (Wan et al., 1999; Jenkins et al., 2004). In the experiments by Wan et al. (1999) it was found that presentation of a familiar array of visual items in a novel spatial rearrangement resulted in neuronal activation in the hippocampus. In comparison the presentation of individual novel visual items did not result in activation in the hippocampus. This finding was repeated by Jenkins et al. (2004) who found that rats trained on a radial arm maze task, using controlled visual cues, showed activation in the hippocampus when presented with the same visual cues in a novel spatial arrangement.

If it is assumed, from the findings of Wan et al (1999) and Jenkins et al. (2004), that the activation of neurons in the hippocampus is necessary for the detection of novel spatial arrangements of visual arrays, then damaging the hippocampus would result in a behavioural impairment on tasks that reflect this process. Bussey, Dias, et al. (2000) have shown that rats with fornix lesions do not show a preference for objects in novel locations in their exploratory behaviour, compared to the preference shown by control rats, whilst still being able to solve elemental visual discriminations. This implies that the hippocampus is not necessary for learning of visual stimuli, but for learning of features that occur when a stimulus is placed in conjunction with other features that enter into associations that control behaviour. Due to the lack of consistent evidence that damage to the hippocampus impairs all configural discriminations (Gallagher and Holland, 1992; Good et al., 1998, Bussey et al., 1998), it is possible that hippocampal dependent allocentric spatial learning is dependent on a mnemonic function that can not be accounted for by non-linear association learning. One possibility is that learning the spatial structure of two or more visual cues is dependent on the hippocampus. Therefore, damage to the hippocampus would impair an animal's ability to solve a task in which discrimination of the spatial structure between two cues was essential to its solution. This leads to the prediction that configural processing will be impaired when the encoding of the structural features of a configuration are crucial to the solution of a discrimination.

As discussed in Chapter Two, George et al., (2001) demonstrated that animals are capable of discriminating between configurations of stimuli that contain the same elements but differ in their spatial relationship (see Figure 3.1 for a depiction of the design used). The solution of the task is reliant on learning the structural features of the compounds. It is possible that learning of this discrimination is dependent on the hippocampus, as reflected by the hippocampal activation as a result of exposure to novel spatial arrangements of familiar visual cues, seen in the studies by Wan et al. (1999) and Jenkins et al. (2004).

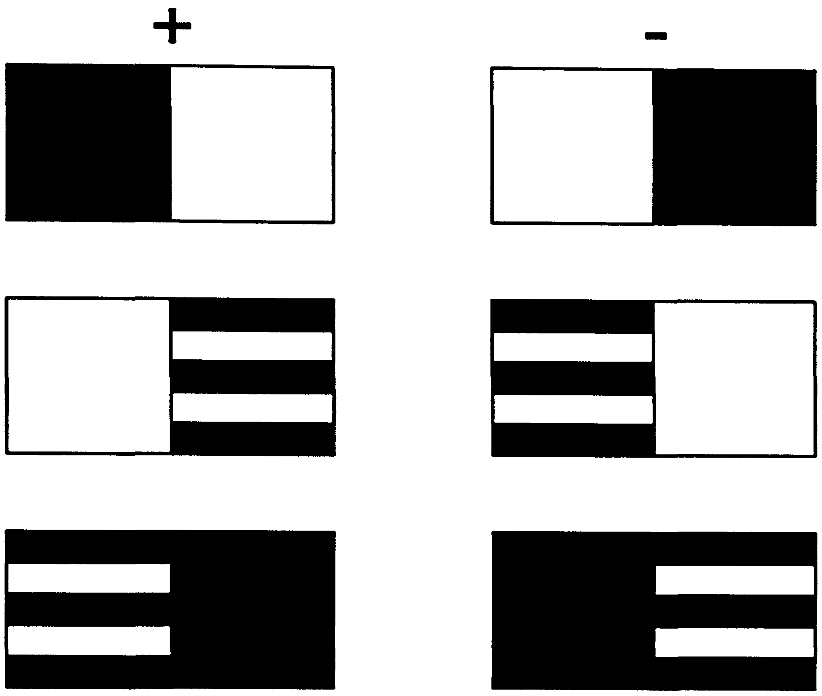

Figure 3.1. Design of the Experiment 2 by George et al. (2001). Patterns on the left were reinforced and patterns on the right were non-reinforced. A pattern on the left would be presented simultaneously adjacent to its mirror image (patterns on the right).

The prediction that the hippocampus is necessary for performance of a structural discrimination was tested in two experiments. In both experiments rats with hippocampal lesions were tested on their ability to perform a structural discrimination that had been acquired previous to receiving surgery (see Experiments 3 and 4, Chapter Two). Training of the task prior to surgery ensures that all rats are able to learn a structural discrimination and performance can be matched between the experimental and control groups. It is predicted that damage to the hippocampus will impair performance of a structural discrimination.

In both experiments rats were also trained before surgery on a simultaneous simple discrimination in which a visual stimulus is consistently rewarded, whilst another visual stimulus is consistently non-rewarded. Post-operative behavioural testing commenced with training on this same simple discrimination. Successful performance on the simple discrimination ensures that the groups are able to learn the procedural demands of the task, i.e. rats are attending to the visual stimuli and are approaching the stimuli in the appropriate manner to receive reward. In addition, successful performance demonstrates that rats are able to make correct choices to either the left or right goal areas in a flexible manner.

The first experiment was run in two stages. In the first stage the effect of hippocampal lesions on performance of a structural discrimination was examined in comparison to performance by a control group that received anaesthesia. In the second stage of the experiment, the control rats received either lesions of the hippocampus or lesions of cortex overlying the hippocampus.

Experiment 7a

In this experiment, the effects of excitotoxic lesions made by injections of *N*-methyl-D-asparate (NMDA) in the hippocampus were tested on the performance of a structural discrimination. Rats that had previously acquired a structural discrimination (see Experiment 3, Chapter 2) were divided into two groups that were matched for their pre-operative performance on the structural discrimination. One group received bilateral lesions of the hippocampus (Hippocampal), the other group only underwent anaesthesia (Sham). Before testing on the structural discrimination began, rats were retrained on a simple discrimination. Groups were tested on their performance on the structural discrimination using a similar procedure as that used in the pre-operative training of the discrimination. Thus, rats were initially tested on the first discrimination (BW+ WB-), and subsequently the second discrimination (WH+ HW-), and finally the third discrimination (HB+ BH-) was introduced. Rats then received testing on all three discriminations in a pseudo-random order, which requires processing of the structural features of the compounds of stimuli for the solution of the task.

Method

Subjects. The subjects were 18 male rats (DA strain: Harlan, UK). The rats were trained on a structural discrimination (see Experiment 3, Chapter Two). Prior to and during the experimental procedures they were allowed free access to food and water. They were housed in pairs in a room that was illuminated for 14.5 hours per day. Rats were tested in groups of nine on alternating days, six days a week, at the same time during the period of light in the holding room. All procedures used were in accordance with the United Kingdom Animals (Scientific Procedures) Act, 1986.

Surgery. Surgical procedures began three days after the end of behavioural testing. During surgery all animals were maintained under anaesthesia by the inhalation of isoflurane gas (apart from one rat that was deeply anaesthetized by intraperitoneal injection (60mg/kg) of pentobarbitone sodium). Animals were placed in a stereotaxic headholder (David Kopf Instruments, Tujung, CA) and the scalp was cut and retracted occupied by the white rectangle with the black circles, no pattern was presented. Therefore, the other stimulus was the uniform grey tank wall (Y).

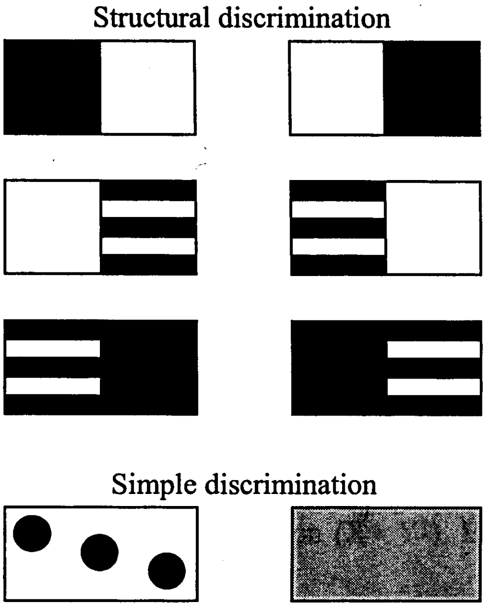

Figure 3.2. The stimuli used for behavioural training of the structural and the simple discrimination. Patterns on the left were reinforced, whilst patterns on the right were non-reinforced. The reinforced and the non-reinforced stimuli were counterbalanced within groups. Pairs of reinforced and non-reinforced patterns were presented simultaneously adjacent to each other.

Post-operative behavioural testing. The rats were assigned to two groups. Two animals died during surgery, therefore, the animals were split into groups of five hippocampal lesioned animals and 11 anaesthetic controls.

Post-operative testing began two weeks after surgery. Testing consisted of six stages. Initial testing began with the simple discrimination, and the structural discrimination was not introduced until both groups were performing at a high level on the simple discrimination.

All coordinates were calculated from bregma and ear-bar zero. Each injection was made gradually over a period of two minutes and the needle was left *in situ* for three minutes. When all injections had been made the skin was sutured and antibiotic powder was applied (Acramide, Dales Pharmaceuticals, Skipton, UK). All animals then received 5ml of glucose saline injected subcutaneously. All control animals were deeply anaesthetised, but no surgical procedures were performed.

Histology. Once all behavioural procedures had been completed all animals were deeply anaesthetised with an intraperitoneal injection of pentobarbitone (Euthatal, Rhone Merieux) and were perfused transcardially with saline followed by 10% formol-saline. The brain was removed and post-fixed in formol-saline for at least 12 hours before being immersed in 25% sucrose solution for at least 24 hours. The brain was then cut coronally on a freezing microtome into 40μm sections and stained with cresyl violet, a Nissl stain.

Apparatus. The apparatus was the same as that used for Experiment 3, Chapter Two.

Structural discrimination stimuli. The stimuli were the same as those used for Experiment 2, Chapter Two. Figure 3.2 depicts the stimuli that were used for the pre-operative and post-operative testing.

Simple discrimination stimuli. Two stimuli were used. One of the stimuli was a white rectangle containing three black circles (X). The rectangle was 28cm high and 14cm wide. Each circle had a radius of 2.5cm and the circles were presented descending diagonally from left to right in a row, an equal distance from each other on two opposite corners of the rectangle (see Figure 3.2). In the goal area that was not

Behavioural procedure. *Pre-operative training of the simple discrimination.* Rats received four sessions of training on the simple discrimination. Sessions consisted of 18 trials of training on a simple discrimination (X+ Y-) in which patterns were presented simultaneously, an equal number of times in each of the goal areas. The platform was always positioned underneath the X pattern, and never under the Y pattern. Sessions of training on the simple discrimination were run on the same days as the last four sessions of training on the structural discrimination. Each session commenced immediately after a session of training on the structural discrimination.

Post-operative testing. The first stage consisted of four sessions, during which rats only received trials of the simple discrimination (X+ Y-). Each session contained 30 trials. In the second stage rats received eight sessions with both the first structural discrimination (BW+ WB-) and the simple discrimination (X+ Y-). A session consisted of 20 trials on the first structural discrimination (BW+ WB-) and 10 trials on the simple discrimination (X+ Y-). The trial types were presented in a pseudo-random order with the constraint that the simple discrimination was never presented twice in succession, and that that no more than four BW+ WB- trials were presented in succession. The third stage consisted of 12 sessions that contained trials of first (BW+ WB-) and second (WH+ HW-) structural discriminations, and the simple discrimination (X+ Y-). Each session contained 10 trials of the BW+ WB- discrimination followed by 15 trials of WH+ HW- discrimination. Every sixth trial the simple discrimination (X+ Y-) was presented, making a total of five trials per session. In the fourth stage, which consisted of six sessions, the third discrimination (HB+ BH-) was introduced. As in the previous stage, on every sixth trial the simple discrimination (X+ Y-) was presented. The first five trials consisted of the BW+ WB- discrimination followed by five trials of the WH+ HW- discrimination and then 15 to expose the skull, and a craniotomy was performed. Lesions were made by injecting NMDA dissolved in a phosphate buffer, pH 7.2, through a 1μl Hamilton syringe into 32 sites (see Table 3.1).

Table 3.1. Lesion coordinates for the hippocampus. All co-ordinates were taken from Bregma and ear-bar zero.

AP	LAT	DV	Volume of NMDA (microlitres)
-2.4	±1.0	-3.5	.1
-2.7	±.05	-3.7	.1
	±1.0	-3.7	.1
	±2.5	-3.6	.1
-3.0	±1.2	-3.4	.1
	±2.5	-3.5	.1
-4.0	±1.5	-3.2	.1
	±2.5	-3.0	.1
	±4.0	-3.2	.1
	±5.5	-4.0	.1
-4.5	±2.5	-3.4	.15
	±4.5	-4.0	.15
-5.2	±4.6	-4.2	.15
-5.6	±4.8	-5.0	.15
-5.8	±4.8	-6.5	.15
-6.0	±4.8	-6.5	.15

trials of the HB+ BH- discrimination. In the fifth stage, which consisted of four sessions, rats received presentations of all the structural discrimination trials presented in a pseudo-random order, with the constraint that the same discrimination (i.e. BW+ WB-, WH+ HW- and HB+ BH-) could not be presented on consecutive trials. On every fifth trial the simple discrimination (X+ Y-) was presented. The rest of the trials consisted of eight presentations of each of the structural discriminations. In the final stage, testing continued for four more sessions using the same procedure as the previous stage, but only the hippocampal lesioned rats were tested.

Results

Histology. The extent of the lesions are depicted in Figure 3.3. All of the rats (n=5) had large dorsal lesions of the hippocampus, including near complete removal of the CA1, CA2 and CA3 regions. Three rats had slight sparing of parts of the dentate gyrus, and one rat had a large amount of sparing of the ventral hippocampus. Typically, the lesions included the vast majority of the dorsal subiculum, and part of the ventral subiculum. Two rats had sparing of the caudal hippocampus, and one of these rats had sparing of the retrohippocampal areas. Two rats had slight damage to the anterior cingulate cortex, and one of these rats also had slight damage to the cingulum bundle. As a consequence of surgery all rats sustained partial damage to the cortex overlying the hippocampus. The cortical damage was most noticeable in three cases in which there was a substantial amount of bilateral damage. For the majority of rats damage was limited to the parietal cortex, but one rat also sustained damage to the somatosensory cortex and the anterior retrosplenial cortex. The performance by this animal was not noticeably different from the other lesioned animals on the simple and structural discrimination. Therefore, this animal was included in all analyses.

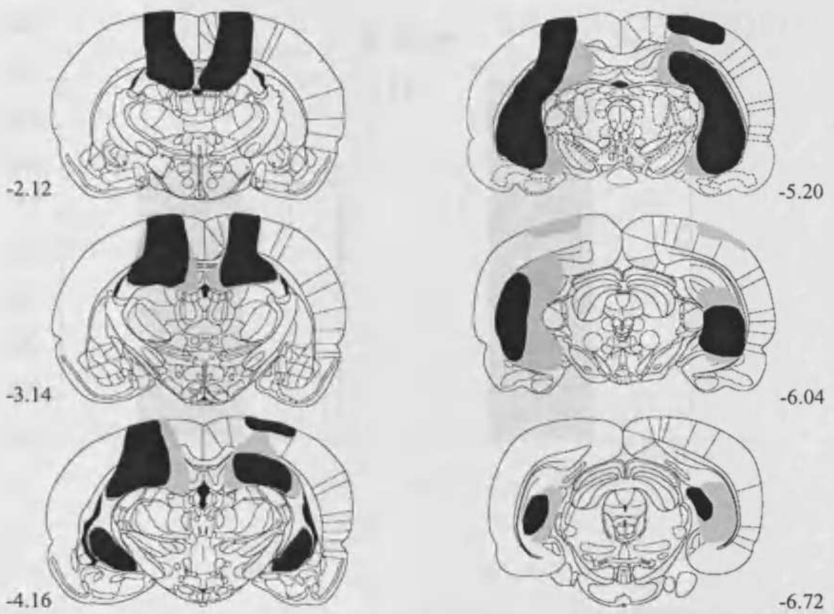

Figure 3.3. Coronal sections illustrating the extent of the largest (grey) and the smallest (black) lesions of the hippocampus. Distances are posterior to bregma (Paxinos and Watson, 1997).

Behavioural Testing. *Simple discrimination.* The pre-operative performance for the last four sessions of training on the structural discrimination and the simple discrimination is shown in Figure 3.4. The groups were matched for their pre-operative performance on the two tasks, F<1.

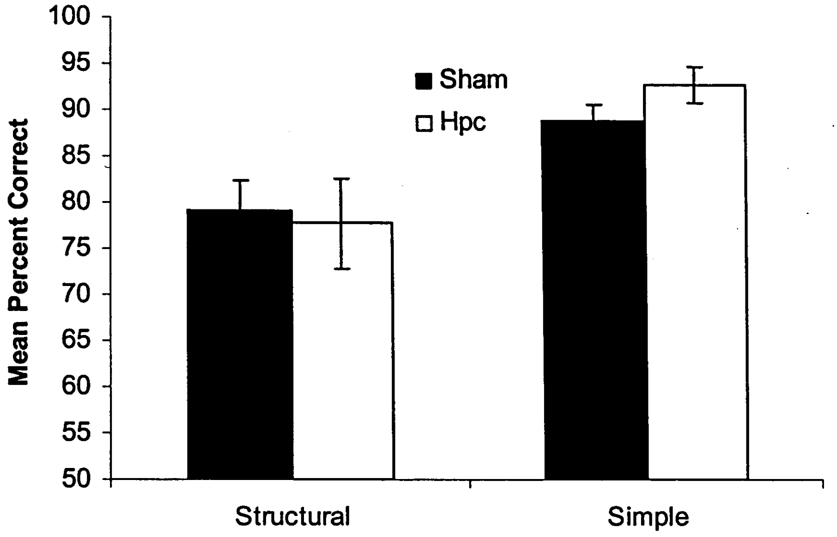

Figure 3.4. The pre-operative performance of the Sham and the Hippocampal (Hpc) group on a structural and simple discrimination. Error bars indicate ±standard error of the mean.

The post-operative performance of both groups on the simple discrimination is shown in Figure 3.5. Each block represents two sessions. The Sham group performed at a consistently high level over the course of training. The Hippocampal group initially showed a low level of performance compared to the control group, but by the third block of training performance levels converged. Performance after the third block of training remained at a level that was close to 100% correct for both groups. An analysis of variance on the 17 blocks of training revealed that there was a significant effect of block, F(16,224)=37.52, $p<0.001$, a significant effect of group, F(1,14)=14.57, $p<0.001$ and a significant interaction of these factors, F(16,224)=31.76, $p<0.001$. Simple main effects analysis of the significant interaction revealed that there were significant effects of group for the first three blocks of training, F(1,144)=440.04, $p<0.05$, F(1,144)=11.27, $p<0.05$, and F(1,144)=7.49, $p<0.05$, respectively. For the remaining blocks of training the two groups did not block interaction, F(3,42)=4.24, $p<0.05$, reflecting the different rates of acquisition on the task. Simple main effects analysis of the interaction revealed that there were significant effects of group for the first three blocks of training, F(1,31)=16.77, $p<0.05$, F(1,31)=13.18, $p<0.05$ and F(1,31)=4.54, $p<0.05$, respectively, but there was no significant effect of group for the last block of training, F(1,31)=0.9.

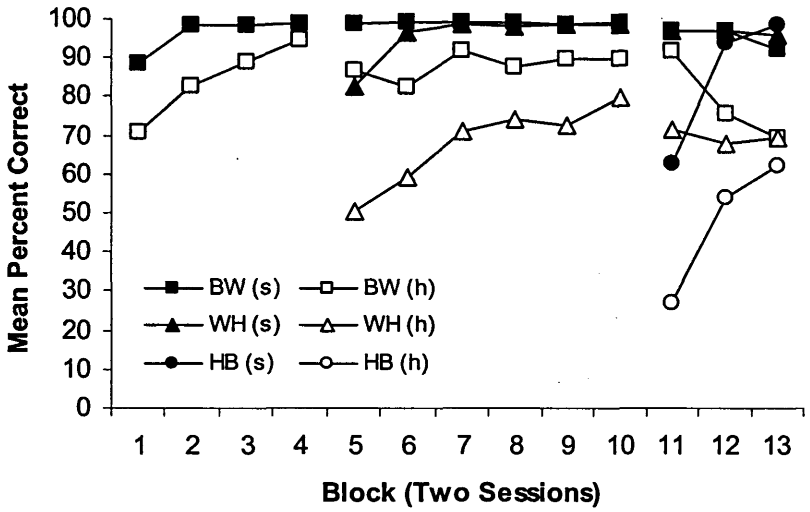

Figure 3.6. The performance on the first three stages of training of the structural discrimination by the Sham (s) and Hippocampal (h) group.

In the second stage of training, in which rats were trained on both the first (BW+ WB-) and second (WH+ HW-) discrimination, the significant difference between groups was reinstated, F(1,14)=33.48, $p<0.05$ and there was a significant effect of block, F(5,70)=19.13, $p<0.05$. The slower rate of learning of the Hippocampal group compared to the Sham group was reflected in a significant group by block interaction, F(5,70)=20.86, $p<0.05$. There was a significant effect of discrimination, F(1,14)=30.13, $p<0.05$, and this factor significantly interacted with the effect of group, F(1,14)=14.56, $p<0.05$. Simple main effects analysis of the group by significantly differ. There was a significant effect of block for the Hippocampal group, F(16,224)=50.14, $p<0.05$, but not for the Sham group, F(16,224)=0.52.

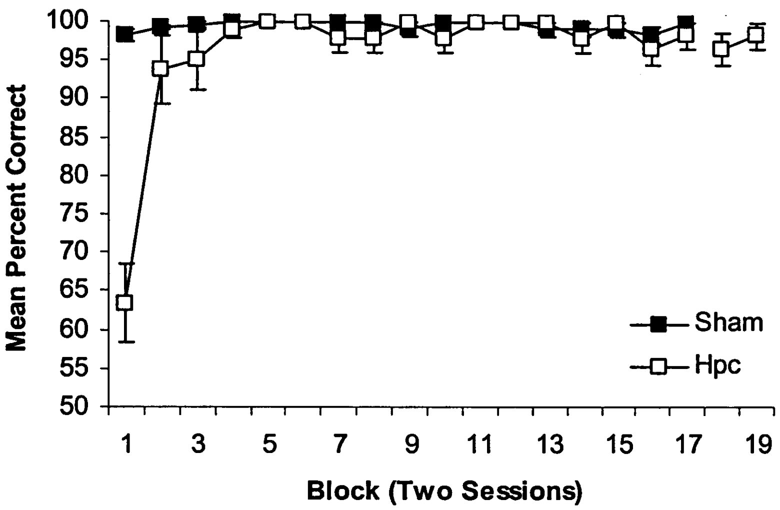

Figure 3.5. Performance of the simple discrimination by the Sham and the Hippocampal (Hpc) group. Error bars indicate ±standard error of the mean.

Structural Discrimination. The results for the first 13 blocks (each of two sessions) of testing on the structural discrimination are shown in Figure 3.6. The Hippocampal group were impaired at learning each of the discriminations, when initially introduced, but discriminations were all acquired to an extent over training. Training on each of the discriminations continued until it appeared that an asymptotic level of performance had been reached.

In the first stage of training, which consisted of training on the first discrimination (BW+ WB-), there was a significant effect of block, F(3,42)=24.56, $p<0.05$, reflecting the increase in the level of performance for both groups over the course of training. There was also a significant effect of group, F(1,14)=11.5, $p<0.05$ and a group by block, F(2,28)=0.51. There was a significant effect of block for the HB+ BH- discrimination, F(2,28)=47.9, p<0.05, and for the BW+ WB- discrimination, F(2,28)=4.75, p<0.05, but not for the WH+ HW- discrimination, F(2,28)=0.32.

Results of the last eight sessions, blocked by two sessions, are shown in Figure 3.7. In the first four sessions, when both groups were tested, the Sham group performed at a high level on the structural discrimination. The Hippocampal group performed at a level that was close to chance. Analysis of variance revealed that there was a significant effect of group, F(1,14)=82.2, p<0.001, a significant effect of block, F(1,14)=6.83, p<0.05, but these factors did not significantly interact, F(1,14)=4.24. One-sample t-tests performed on the mean of the first four sessions of the final stage showed that the Hippocampal group were not performing significantly above chance, t(4)=1.31, but the Sham group were performing significantly above chance, t(10)=28.89, p<0.001.

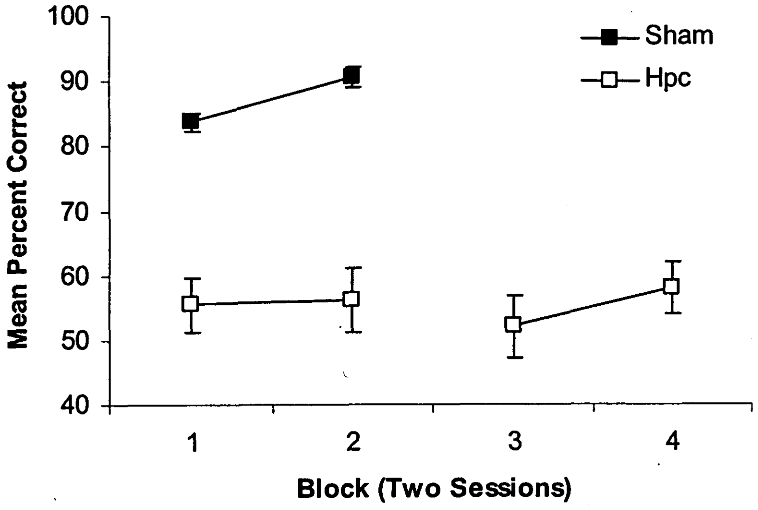

Figure 3.7. The mean overall performance on the structural discriminations in the final stage of testing for the Sham and Hippocampal (Hpc) groups. Error bars indicate ±standard error of the mean.

For the last four sessions, in which only the Hippocampal group were tested, performance was close to chance level. The mean level of performance over the four sessions was 55% correct. Hippocampal lesioned rats were still not performing significantly above chance, t(4)=1.15. The last four blocks (of two sessions) of testing (including the last two blocks in which the Sham group were no longer tested) for the Hpc group was subjected to analysis of variance to test whether performance on the structural discrimination increased over the course of training. The Hippocampal group did not significantly improve over the course of training, F(3,12)=2.54.

Discussion

The hippocampal lesioned rats were initially impaired on the simple discrimination (X+ Y-) compared to controls, but the task was quickly relearned and they did not differ from controls on the simple discrimination throughout the duration of testing of the structural discrimination. Even though, eventually, both groups were performing at a similar level, performance was at ceiling level. This may have masked any possible differences between the two groups. However, the fact that the Hippocampal group were able to solve the discrimination demonstrates that the rats were able to respond appropriately towards the visual stimuli, and performed within the constraints of the procedural demands of the task to the same extent as the control group. The initial deficit, due to its transience, may reflect recovery from surgical procedures. It could also reflect retrograde amnesia for the simple discrimination, and due to the time limit between acquisition and surgery, consolidation of the task, contingent on the hippocampus, may not have occurred (Clark, Broadbent, Zola and Squire, 2002).

discrimination interaction revealed that the Hippocampal group performed at a significantly lower level than the Sham group on the BW+ WB- discrimination, F(1,24)=7.69, p<0.05, and on the WH+ HW- discrimination, F(1,24)=48.04, p<0.05. There was a significant effect of discrimination for the Hippocampal group, F(1,14)=5.25, p<0.05, but not for the Sham group, F(1,14)=0.37. There was also a significant interaction between the effects of discrimination and block, F(5,70)=20.86, p<0.05. Simple main effects analysis of the discrimination by block interaction showed that performance significantly differed between the two discriminations for the first five blocks, F(1,14)=91.58, p<.05, F(1,14)=19.66, p<.05, F(1,14)=16.04, F(1,14)=11.41, F(1,14)=21.15, respectively. Performance did not differ on the sixth block of training, F(1,14)= 2.89. There was also no effect of block for the BW+ WB- discrimination, F(5,70)=2.03, but there was an effect of block for the WH+ HW- discrimination, F(1,14)=28.76, p<0.05.

In the third stage of training, in which the third discrimination (HB+ BH-) was introduced, performance increased for both groups (see Figure 3.6). Whilst the Sham group maintained performance on the previously learnt discriminations, improvement on the third discrimination was accompanied by a decrease in performance on the previously learnt discriminations for the Hippocampal group. Analysis of variance revealed that there was a significant effect of group, F(1,14)=54.64, p<0.05, a significant effect of block, F(2,28)=5.65, p<0.05, but there was no significant interaction between these factors, F(2,28)=8.67. There was a significant effect of discrimination, F(2,28)=38.76, p<0.05, and this significantly interacted with the effect of block, F(4,56)=28.99, p<0.05. Simple main effects analysis revealed that there was only a significant effect of discrimination for the first and second block, F(2,28)=85.35, p<0.05 and F(2,28)=3.84, p<0.05, respectively, but not for the final hippocampal damage is sufficient to impair performance on a structural discrimination this factor of extra damage to needs to be controlled. There is, for example, evidence that the parietal cortex is involved in learning of some spatial memory tasks that also depend on the hippocampus (Thinus-Blanc, Save, Poucet, and Foreman,1996; Save, 2000), although the effects of these two lesions are not the same (Chiba, Hackson and Kesner, 2002). Also rearranging visual cues presented around a radial-arm maze causes an increase of c-*fos* activation in the parietal cortex, mirroring the effects seen on activation in the hippocampus (Jenkins et al., 2004). It is unclear whether the two effects are causally related as the cortical areas that indirectly connect the parietal cortex to the hippocampus did not show any increase in activation (Jenkins et al., 2004). Nevertheless, these results point to the possible contribution of the parietal cortex.

Experiment 7b

In Experiment 7a it was found that lesions of the hippocampus impaired performance on a structural discrimination, compared to the performance of un-operated controls that had received anaesthesia. It is possible that damage to the cortex overlying the hippocampus may have confounded the results of the lesion group by either contributing to the size of the effect in an additive manner, or may have masked the effect of hippocampal damage. In this experiment, the remaining control animals from Experiment 7a were divided into two groups that were matched for their performance on the structural discrimination. One group received bilateral excitotoxic lesions of the hippocampus (Hippocampal), the other group received excitotoxic lesions of the cortex overlying the hippocampus (Cortical control). Procedures for testing the ability to solve the structural discrimination were the same as for Experiment 7a. It is

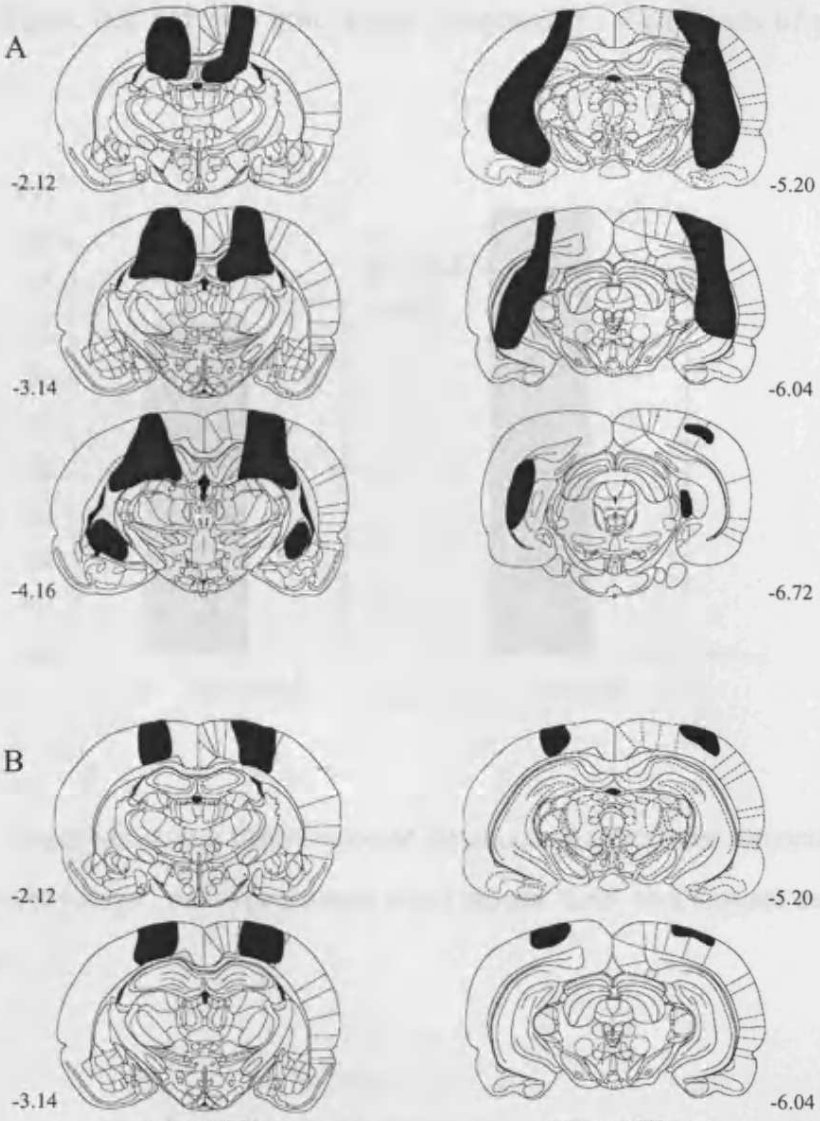

Figure 3.8 Coronal sections illustrating the extent of the lesion for rats with an intermediate amount of damage for the Hpc group (A) and for the Cortical control group (B). Distances are posterior to bregma (Paxinos and Watson, 1997).

Behavioural Testing. *Simple Discrimination.* The pre-operative performance of the two groups for the simple discrimination and also the structural discrimination is

A much more striking lesion effect was found for the structural discrimination. The Hippocampal lesion group were impaired on all stages of testing, but showed a clear ability to acquire the first two discriminations. In the first three stages in which discriminations were presented in blocks of trials, the Sham group showed quick acquisition of each discrimination. However, the Hippocampal group showed a manner of acquisition of the discriminations which was similar to the acquisition of the task of naïve rats (see Experiment 3, Chapter Two). When the second discrimination (WH+ HW-) was introduced, the Hippocampal lesion group initially performed at a level that was close to chance, and at a level that was considerably lower than their performance of the BW+ WB- discrimination. The Sham group, did not show this difference in performance of the two discriminations to the same extent. This is reflected by the significant group by discrimination interaction. It is possible that the Hippocampal group reacquired the discriminations in an elemental manner, and thus after learning one of the discriminations, there was negative transfer to subsequently learned discrimination. When the third discrimination (HB+ BH-) was introduced, both groups showed performance of the discrimination that was lower than the performance of BW+ WB- and WH+ HW- discriminations. However, performance of the third discrimination by the Sham group during the first block of testing was not below chance, whereas the Hippocampal group performed at a level considerably lower than chance. Once again, this pattern of performance is similar to that of naïve animals, and the negative transfer of learning to the third discrimination, may reflect elemental learning.

The performance by the Hippocampal group declined when all three discriminations were presented in a pseudo-random order. Thus, once rats were given the full structural discrimination, the Hippocampal group did not perform above chance. This

Behavioural procedure. Behavioural testing commenced once all animals had at least 10 days of recovery after surgery. Both groups were tested on the discriminations using a similar procedure of progressively introducing each discrimination in the same manner as in Experiment 7a.

In stage one of testing rats received four sessions of 30 trials on the simple discrimination (X+ Y-). Stage two consisted of two sessions consisting of twenty trials of the first structural discrimination (BW+ WB-). Every third trial the simple discrimination (X+ Y-) was presented, making a total of 10 trials per session. Stage three consisted of six sessions. Each session consisted of 10 trials of the first structural discrimination (BW+ WB-) followed by 15 trials of the second discrimination (WH+ HW-). The amount of times that WH and the HW pattern appeared in either the left or right goal location was counterbalanced over blocks of two sessions. On every sixth trial the simple discrimination (X+ Y-) was presented, making a total of five trials per session. Stage four consisted of four sessions. Each session consisted of five trials of the first structural discrimination (BW+ WB-), followed by five trials of the second discrimination (WH+ HW-), and finally followed by 15 trials of the third discrimination (HB+ BH-). The amount of times each stimulus pattern was presented in either the left or right goal location was counterbalanced over blocks of two sessions. The simple discrimination was presented in the same manner as in stage three, so that a session consisted of 30 trials in total. Stage five consisted of eight sessions. Each session consisted of eight trials of each of the structural discriminations presented in a random order with the constraint that the same discrimination could not be presented on two consecutive trials. On every fifth trial the simple discrimination (X+ Y-) was presented, making a total of six trials per session.

shown in Figure 3.9 The two groups were matched for their levels of performance, F<1.

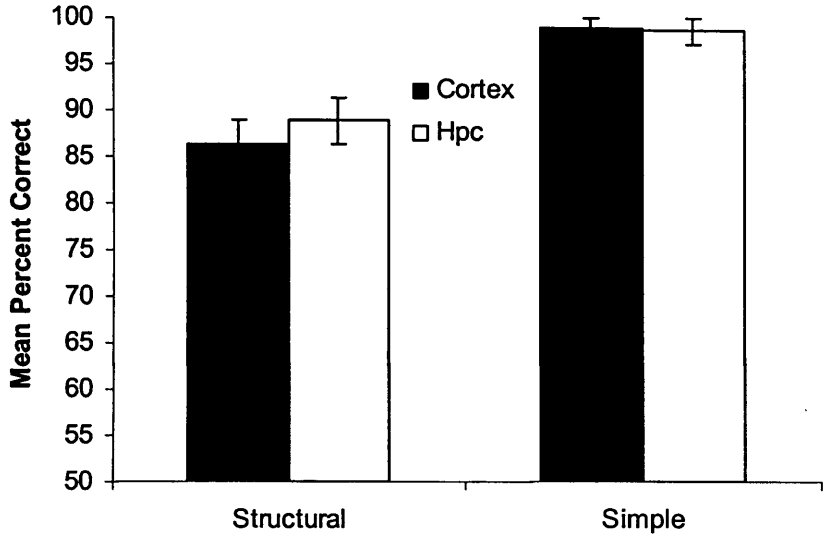

Figure 3.9. The pre-operative performance of the structural and simple discrimination for the Cortical control (Cortex) and Hippocampal (Hpc) groups. Error bars indicate ±standard error of the mean.

The post-operative performance of the simple discrimination is shown in Figure 3.10. The Hippocampal group initially performed poorly on the simple discrimination, but quickly reacquired the task and maintained performance at a level that was similar to that of the Cortical control group. The Cortical control group showed a level of performance that was similar to their pre-operative level, and initially performed at a higher level than the Hippocampal group. Analysis of variance revealed that there was no significant effect of group, F(1,5)=0.04, but, there was a significant effect of block, F(11,55)=10.24, $p<0.05$ and these two factors significantly interacted, F(11,55)=4.15, $p<0.05$. Simple main effects analysis revealed that there was a significant effect of predicted that damage to the hippocampus will impair performance on a structural discrimination compared to the performance of the rats that received cortical control lesions.

Method

Subjects. Eight rats were used from the remaining control group from Experiment 7a. Subjects were divided into two groups that were matched for their performance of the structural discrimination. One group received excitotoxic lesions of the hippocampus, whilst the other group received cortical control lesions. One animal died during surgery, thus leaving group sizes of Hippocampal lesion, n=3, and Cortical control lesion, n=4. Animals were housed and fed in the same manner as for Experiment 7a.

Surgery. The procedures for the hippocampal surgery were the same as those used for Experiment 7a. The surgical procedures for the cortical control lesions were the same as for the hippocampal surgery except that the syringe was only lowered to a depth of 1mm, and only 0.04µl of NMDA was injected at each site. The NMDA was injected over a period of two minutes and the needle was left *in situ* for 1min after injection. All other procedures were the same as for the hippocampal lesions.

Histology. The histological methods were the same as for Experiment 7a.

Apparatus. The apparatus for was the same as used for Experiment 7a.

Stimuli. The stimuli for the structural discrimination and for the simple discrimination were the same as for Experiment 7a.

Results

Histology. The extent of the lesions for the animals with the intermediate amount of damage is illustrated for both the Hippocampal and Cortical control group in Figure 3.8. The damage caused to the hippocampus was similar to the amount of damage found for the hippocampal lesions in Experiment 7a. All hippocampal lesioned rats had large lesions of the dorsal hippocampus, damaging the vast majority of cells from CA1, CA2 and CA3. The lesions extended to the ventral hippocampus, including large parts of the subiculum, but two rats showed slight caudal sparing of the ventral hippocampus. Also, in two cases there was unilateral sparing of the rostral dentate gyrus. There was slight damage to the anterior cingulate cortex in two cases. All rats had some damage to the cortex overlying the hippocampus. In all cases there was damage to the parietal cortex, but also there was damage to the retrosplenial cortex in two cases. Two rats also had slight damage to parts of the visual cortex.

Rats in the cortical control group all had cell loss in the cortex, but this damage was limited to the parietal cortex. The damage was bilateral, but two animals had larger damage to the parietal cortex in one hemisphere than in another. One rat had marginal cell loss in the CA1 region, but in all other cases there was complete sparing of the hippocampus.

group for the first block, F(1,21)=23.81, p<0.05, but the two groups did not differ for the rest of training, F<1.

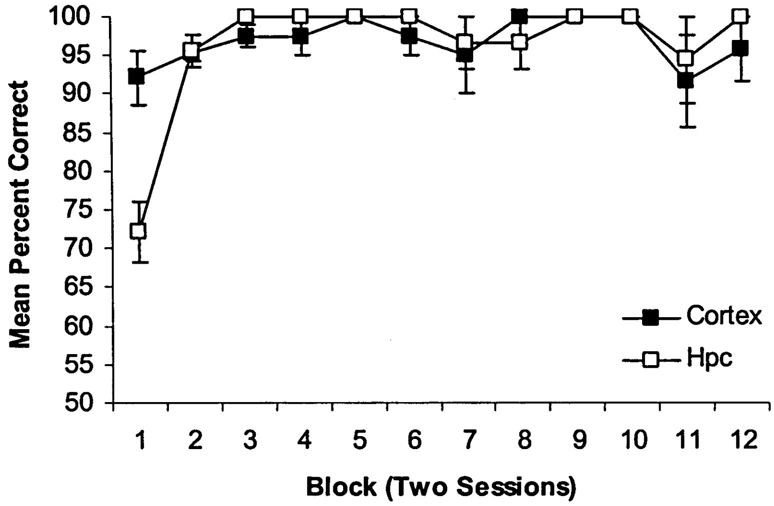

Figure 3.10. Performance on the simple discrimination for the Cortical control (Cortex) and Hippocampal (Hpc) groups. Error bars indicate ±standard error of the mean.

Structural Discrimination. The performance of both groups on the first 12 sessions of testing is shown in Figure 3.11. Both groups reacquired each of discriminations as they were introduced. Both groups showed an initial performance that was considerably below chance on the third discrimination (HB+ BH-), in a similar manner to the original acquisition of the task by naïve animals (see Experiments 3 and 4, Chapter Two). Throughout all stages the Cortical control group performed at a higher level than the Hippocampal lesion group. Individual analyses of the three stages revealed that there was a significant effect of group for the first stage of training of the first discrimination (BW), F(1,5)=7.71, p<0.05, and also a significant group by block interaction, F(1,5)=24.7, p<0.5. In the second and third stages of result strongly implies that the hippocampal lesioned rats were solving the task prior to receiving training on the full structural discrimination, by using a strategy that did not require processing of structural information. For the first two discriminations elemental learning was possible. When the third discrimination was initially introduced it is possible that hippocampal lesioned rats were showing a within-trial block acquisition of each separate discrimination, made possible by the use of blocked trials. A win-stay strategy of approach towards a stimulus, until it no longer predicts reward may have been used by the Hippocampal group. Once the discrimination trial types were pseudo-randomised the Hippocampal group did not show re-acquisition of this task. Therefore, hippocampal lesions impaired performance of the structural discrimination, which had previously been acquired prior to surgery. The fact that the Hippocampal group were initially impaired on the simple discrimination must be taken into account, but they were able to reacquire the task, whereas they did not appear to reacquire the structural discrimination. This may reflect the different levels of complexity between the two tasks. The results of this experiment support the hypothesis that the hippocampus is involved in the learning and memory of a structural discrimination, but whether this effect can be attributed to a selective deficit in processing structural information remains to be answered. This issued is addressed in Chapter Four by examining the performance of hippocampal lesioned rats on non-linear discriminations of a similar level of difficulty as a structural discrimination.

One factor that confounds the data is that, as a consequence of surgery, the hippocampal lesioned rats received extra damage to the cortical areas overlying the hippocampus. These areas include a varying amount of parietal cortex. It is possible that damage to the parietal cortex contributes, or even may be responsible, for the impairment shown by the Hippocampal group. For it to be established that above chance, whereas the Hippocampal lesion group's performance dropped to a level that was not significantly above chance. Therefore, lesions of the hippocampus, in Experiment 7a and 7b, impaired performance to the extent that their levels of performance implied an inability to solve the discrimination. Although, the performance by the two groups, in Experiment 7b, was not significantly different, the Cortical control group were still able to solve the discrimination, whereas Hippocampal lesions resulted in an inability to solve the task once the discriminations were presented in a pseudo-random order.

The Hippocampal group showed an initial performance of the third discrimination (HB+ BH-) that was below chance. This result was also found in Experiment 7a, and the pattern of results resembles the pattern of acquisition seen in naïve rats (see Experiment 3, Chapter Two). A possible account for the low performance of the discrimination is that there is negative transfer of learning from the previously acquired discriminations, which would be predicted if prior to presentation of the third discrimination, the task had been acquired by the formation of elemental associations.

In Experiment 7a the control group did not show the same pattern of performance, on third discrimination, as the Hippocampal group. Performance of the third discrimination in the first block of testing was not below chance. In the present experiment, the Cortical control showed a pattern of performance on the third discrimination that was similar to the Hippocampal group. Therefore, rats with cortical control lesions did not behave the same as the un-operated rats in Experiment 7a. However, it can be argued that the cortical control lesions did not have the same effect as hippocampal lesions, which is reflected in the significant group difference of training there were no significant effects of group and no significant interaction of this factor with block or discrimination type, F<1.

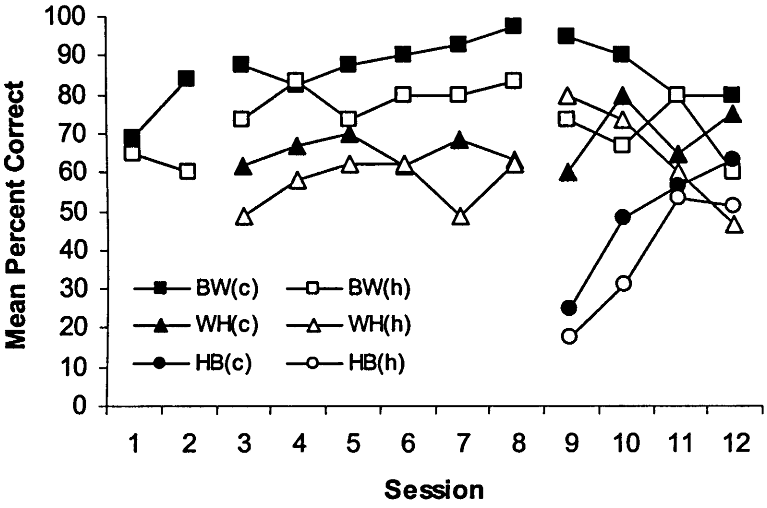

Figure 3.11. Performance on the first 12 sessions of the structural discrimination by the Cortical control (c) and the Hippocampal (h) groups.

In the final stage, in which performance of the task requires structural processing of all three discrimination, the Cortical control group performed at a higher level than the Hippocampal group, although at a level that was lower than that achieved prior to surgery. The overall performance by both groups, blocked by two sessions, is shown in Figure 3.12. An analysis of variance performed on the data from both groups, revealed that there was no significant difference between the levels of performance by both groups, F(1,5)=1.75, no significant effect of block, F(3,15)=0.57, and no significant interaction of these factors, F(3,15)=0.27. One sample t-tests on the performance on the last block of training revealed that the Cortical control group were performing above chance level, t(3)=3.77, $p<0.05$, but the Hippocampal group were not, t(2)=1.59.

this experiment, in an attempt to rule out the confounding effects of cortical damage on the performance of a structural discrimination, rats that had previously acquired a structural discrimination (see Experiment 4, Chapter Two) received bilateral radio-frequency lesions of the hippocampus (Hippocampal). Even though radio-frequency lesions will cause damage to fibres of passage that are spared when using excitotoxic lesions, it is possible to control better the extent of the cortical damage. To control for any effects of cortical damage that may be caused by the passage of a radio-frequency electrode, another group that was matched for their performance on the discrimination received sham lesions (Sham). These lesions were made using the same surgical procedures that were used for the experimental group, except the electrode, having passed through the cortex, did not enter the hippocampus, and no current was passed. The goal was to test whether damage to the hippocampus is sufficient to impair performance on a structural discrimination.

Rats initially received testing with each component discrimination being presented in blocks of eight trials. Then rats received training on two blocks of four trials of each component discrimination presented in a pseudo-random order. Finally, all three discriminations were presented in a pseudo random order, similar to the final stage of Experiment 7a and 7b. In Experiment 7a hippocampal lesioned rats were able to perform each discrimination before the trials were intermixed, therefore, blocked presentation appeared to support learning. When the trials were intermixed levels of performance fell to chance. Therefore, a blocked trial presentation of the discrimination may initially result in performance of the structural discrimination, but will be impaired when intermixed. It is has been claimed that gradually interleaving presentation of ambiguously reinforced stimuli facilitates learning of configural associations (Dusek and Eichenbaum, 1998; Mclelland, et al., 1995). Using this

Comparisons of both groups' average performance from the last stage of testing of Experiment 7a prior to surgery and the performance during the final stage of testing in the present experiment revealed that both groups performed at significantly lower levels after surgery on the full structural discrimination, F(1,5)=51, p<0.005. The group by pre/post surgery interaction failed to reach significance, F(1,5)=3.4.

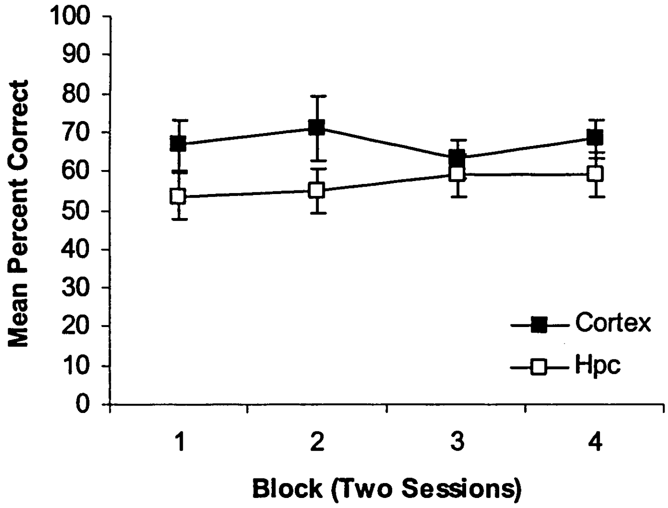

Figure 3.12. Performance on the last stage of testing of the structural discrimination by the Cortical control (Cortex) and Hippocampal (Hpc) groups. Error bars indicate ±standard error of the mean.

Discussion

It was found that rats with hippocampal lesions performed at a lower level on the structural discrimination compared to animals that had cortical control lesions, although this difference was not statistically different. The inability to find a significant difference may be due to low statistical power, as there were only a small number of animals in each group (Hippocampal, n=3; Cortical control, n=4). The Cortical control lesion group were still able to perform the structural discrimination the initial acquisition of the first structural discrimination (BW+ WB-), and also in the rate of acquisition of the simple discrimination.

Both groups showed significantly lower levels of performance after surgery. Consequently, it appears likely that cortical function (namely the parietal cortex) is contributing to performance of the structural discrimination. However, in the present experiment to ensure that lower performance after surgery is due to cortical damage a control group would have need to be provided that receives craniotomy but no further surgical interventions. This would control for possible factors such as the strain of surgery, aging of animals and extensive overtraining in the water tank which may influence performance of a structural discrimination.

It remains a possibility that there may be an additive effect of cortical damage that could contribute to the impairment shown by the hippocampal lesioned rats. Consequently, the effect of cortical damage on a structural discrimination needs to be minimised as far as possible and to be controlled, to be able to determine the role of the hippocampus on a structural discrimination. The possible role of the parietal cortex in learning and memory of a structural discrimination will be further discussed in Chapter Five.

Experiment 8

The results of Experiment 7a show that damage to the hippocampus caused impaired performance on a structural discrimination. It was found in Experiment 7b that rats with damage to the cortex overlying the hippocampus were still able to solve a structural discrimination, whilst hippocampal lesioned rats were not able to solve the task. However, the performance of these two groups did not significantly differ. In electrode (0.3 mm tip length, 0.25mm diameter) was lowered vertically and at each lesion site the tip was raised to a temperature of 70°C and left *in situ* for 40s. The co-ordinates for the lesion sites are shown in Table 3.2.

Table 3.2. Co-ordinates for hippocampal lesion. All co-ordinates were taken from bregma.

AP	ML	DV
-2.4	±1.0	-3.5
-2.7	±0.7	-3.5
	±1.8	-3.7
-3.0	±1.1	-3.7
	±2.6	-3.6
-4.0	±0.8	-3.6
	±1.5	-3.5
	±2.5	-3.5
	±3.8	-.38
-4.5	±2.6	-3.6
-5.2	±4.6	-4.4
	±3.0	-3.6
-5.6	±4.9	-5.1
	±4.9	-7.5
-5.9	±3.8	-4.0
	±4.8	-5.2
	±4.8	-6.5

method should maximise the potential of hippocampal lesioned rats to acquire the structural discrimination.

As in Experiment 7a, rats were trained on a simple discrimination prior to surgery. Animals were also tested on a spatial reference memory task in a Morris water maze to test the efficacy of the lesions on a task that is believed to be hippocampally dependent (Morris et al., 1982).

Method

Subjects. The subjects were 16 male rats (DA strain: Harlan, UK). The rats had previously been trained on a structural discrimination prior to surgery (see Experiment 4, Chapter Two). Rats were matched for their pre-operative performance. Prior to and during the experimental procedures they were allowed free access to food and water. They were housed in pairs in a room that was illuminated for 14.5 hours per day. Rats were tested at the same time every day during the period of light in the holding room. Three rats died as a consequence of surgical procedures; therefore, only 13 rats received behavioural training. All procedures used were in accordance with the United Kingdom Animals (Scientific Procedures) Act, 1986.

Surgery. All rats were deeply anaesthetised with isoflurane gas and placed in a stereotaxic headholder (Kopf Instruments) with the nose bar at 0. The scalp was then cut and retracted to expose the skull. A craniotomy was performed on all rats. Eleven rats received hippocampal surgeries, but three rats died during surgery leaving the total number of hippocampal lesioned rats as eight. Radiofrequency lesions of the hippocampus were made using an RFG4-A Lesion Maker (Radionics, UK.) The with the constraint that the same discrimination could not be present on two or more consecutive trials.

Probe session. At the end of stage four a tenth session was run in a similar manner, but in this session each discrimination was presented four times and was only presented every other trial. For the remaining trials rats received probe trials in which a reinforced pattern had to be simultaneously discriminated from a non-reinforced pattern with which it had not previously been paired. The discriminations included all combinations of the reinforced and non-reinforced patterns: BW+ HW-, BW+ BH-, WH+ WB-, WH+ BH-, HB+ WB- and HB+ HW-. Each discrimination was presented twice and was counterbalanced for reinforcement in both goal locations. Discriminations were presented in a random order.

Spatial Reference Memory

Apparatus. The pool was circular, 2m in diameter and 0.6m deep. The pool was made from fibreglass and painted white. It was mounted on a platform 0.6m above the floor and positioned in the centre of a room which was 3m by 4m and 2.3m high. The pool was filled to a depth of 0.27m, with water which was made opaque with 0.5l of opacifier E 308 (Roehm and Haas: Dewsbury, UK). The water was changed daily and maintained at 25°C (±2°C). A video camera was positioned 1.8m above the centre of the pool, mounted in a 0.3m diameter hole in the ceiling. The picture from the camera was relayed to a television screen in an adjacent room, from which the experimenter could observe the rats. The image was also relayed to a PC and the behaviour of the rats was analysed using Water maze Software (Morris & Spooner, 1990). The room was illuminated by eight 45W spotlights in the ceiling that formed a circle above the centre of the pool. Also there were 4 floor mounted 500W lamps positioned in each from the start position that was furthest way from the location where the platform had been previously.

Results

Histology. The extent of the lesions is illustrated in Figure 3.13. Two rats had substantial damage in the parietal cortex and also had some damage to the motor and visual cortices. These rats were removed from the analyses since the cortical damage caused as a consequence of surgical procedures was disproportionately large compared to the incidental cortical damage in rest of the Hippocampal group and the Sham group, thus leaving six hippocampal lesioned rats.

For the majority of rats in the Hippocampal group there was a large amount of damage to the dorsal hippocampus, although three rats had unilateral sparing of some cells in the CA2 and CA3 areas. In all but one rat there was damage to fimbria, and all rats had partial damage to the fornix. There was damage to the ventral hippocampus in all but one animal. The damage was limited to the middle regions of the hippocampus, but in four cases there was severe shrinkage of the ventral hippocampus. There was sparing of the ventral subiculum and parts of the ventral dentate gyrus. Four of the rats had incidental damage to the cortex overlying the hippocampus. This included slight damage to the cortex in two cases and one rat had a substantial amount of damage in the parietal cortex. In one case there was minor damage to the cingulum bundle.

corner of the room. An escape platform in the pool was made from clear Perspex, 0.1m in diameter, and mounted on a stick 1cm below the surface of the water. Circular indentations were drilled in the surface of the platform to a depth of 0.5cm. On the walls of the room were posters which served as room cues.

Procedure. Animals received ten sessions of training to locate a hidden platform in the pool. For half of the animals the platform was located in a constant position in the northwest quadrant of the maze, and for the other half, the platform was in a constant position in the southeast quadrant. Rats were given one session of training per day. Each session consisted of four trials. At the start of a trial animals were released into the pool facing the pool wall. They were released from a possible eight different start points around the wall of the pool. The order of release points used for the trials was random with the constraint that the same release point could not be used more than once per session. Once the rat had located the platform it was allowed to sit on the platform for 30s before being removed. A ten second period elapsed before the start of the next trial. If animals failed to locate the platform within 120s they were guided to the platform and allowed to sit there for 30s. Animals were carried to the test room, in a holding box in groups of four or less. Once an animal had finished the four trials of the session, it was placed back in the holding box, and when all animals in the group had finished they were carried back to the holding room. Rats were dried thoroughly after each trial.

On the 11th session rats received an extra session of training that consisted of three trials followed by a probe trial. For the probe trial, the platform was removed from the pool and animals were required to search in the pool for 120s. Animals were released

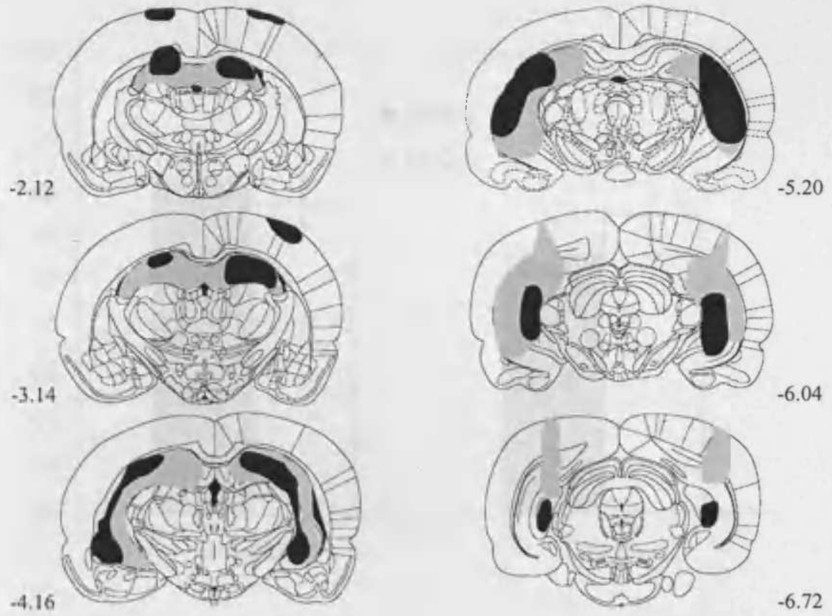

Figure 3.13 Coronal sections illustrating the extent of the largest (grey) and the smallest (black) lesions of the hippocampus. Distances are posterior to bregma (Paxinos and Watson, 1997).

The extent of damage to the neocortex was similar to that in the control group that received sham surgeries. All control rats had slight damage to the cortex, but this was more widespread in one rat that had damage to motor and parietal cortex. One control rat had slight damage to the CA1 region of the hippocampus. Performance of this rat during behavioural testing did not differ appreciably from the performance of the other control rats.

***Behavioural Testing**. Simple Discrimination.* The mean pre-operative performance for both groups on the structural and simple discrimination is shown in Figure 3.14 The two groups did not statistically differ in their performance of the tasks, F<1.

Five animals received sham lesions. Sham lesioned rats received the same surgical procedures as the Hippocampal group, but for each lesion site the electrode was only lowered to a depth of -1.7 from the top of cortex, and the temperature of the electrode tip was not raised. At the completion of all surgeries the skin was sutured and antibiotic powder was applied (Acramide; Dales Pharmaceuticals, UK). Animals were then given a 5ml injection of glucose saline, subcutaneously.

Histology. The histological methods were the same as for Experiment 7a and 7b.

Apparatus. The apparatus was the same as for Experiments 3, 4, 5, 7a and 7b.

Structural discrimination stimuli. The stimuli used were the same as for Experiments 3, 4, 7a and 7b.

Simple discrimination stimuli. The two stimuli were a black plus sign on a white background (P) and a black circle on a white background (C). Both stimuli were 28cm high and 28cm wide. The plus sign was made of a vertical rectangle and a horizontal rectangle that crossed each other at their centre at an angle of 90°. The vertical rectangle was 28cm high and 4.5cm wide. The plus sign was centred in the middle of the white rectangle. The horizontal rectangle was 7cm high and 28cm wide. The circle had a radius of 22cm and was located in the centre of the white background.

Behavioural procedure. *Pre-operative training of the simple discrimination.* Rats received three sessions of training on the simple (P+ C-) discrimination. Each session consisted of 18 trials. Stimuli were presented simultaneously, an equal amount of times in either the left or right goal areas. For half the rats the platform was always

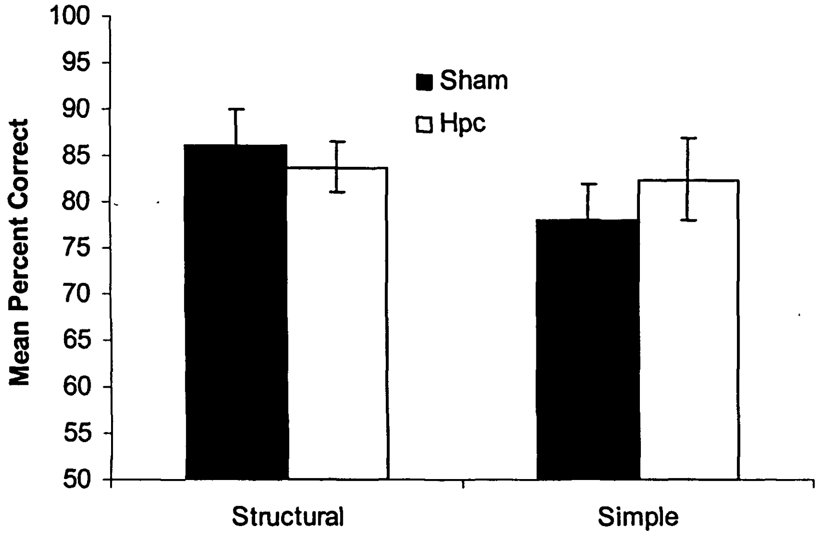

Figure 3.14. The mean pre-operative performance on the structural and simple discrimination for the Sham and the Hippocampal (Hpc) groups. Error bars indicate ±standard error of the mean.

The mean percent correct for the 15 blocks (of two sessions) of post-operative testing on the P+ C- discrimination for both groups is shown in Figure 3.15. Performance by both groups started at a level that was lower than their pre-operative performance, but was quickly regained over the initial sessions. The Sham group initially performed at a higher level than the Hippocampal group, but by the third block performance in both groups was at a similar level. An analysis of variance of the 15 blocks showed that there were significant effects of block, F(14,126)=23.55, $p<0.001$, and group, F(1,9)=18.4, $p<0.05$, and a significant interaction of these factors, F(14,126)=3.31, $p<0.01$. Simple main effects analysis of the interaction revealed that the Sham group were performing significantly better than the Hippocampal group for the first two blocks, F(1,135)=39.34, $p<0.001$, and F(1,135)=15.63, $p<0.001$, respectively, but for the subsequent 13 blocks of training there were no significant differences between the groups.

present underneath the P stimulus, and never underneath the C stimulus. For the remaining rats the platform was always underneath the C stimulus. Sessions of training on the simple discrimination were run on the same days as the last three sessions of training of the structural discrimination. A session commenced immediately after a session of training on the structural discrimination.

Post-operative testing. Post-operative testing started once all animals had at least ten days of recovery after surgery.

Stage one consisted of six sessions of 30 trials on the simple discrimination (P+ C-). All procedures were the same as for pre-operative training.

In stage two rats received six sessions of testing on the structural discrimination and the simple discrimination (P+ C-). Each session consisted of blocks of eight trials on each of the three structural discriminations. These blocks of trials were presented in a random order. Every fifth trial the simple discrimination (P+ C-) was presented, so in total it was presented six times per session. The procedure for the presentation of the simple discrimination was maintained for all stages of subsequent testing.

In stage three rats received eight sessions in which all three structural discriminations were presented in two blocks of four trials. These blocks of trials were presented in a random order with the constraint that two blocks of the same discrimination could not be presented consecutively.

In stage four rats received nine sessions in which all three structural discriminations were each presented eight times. Discriminations were presented in a random order

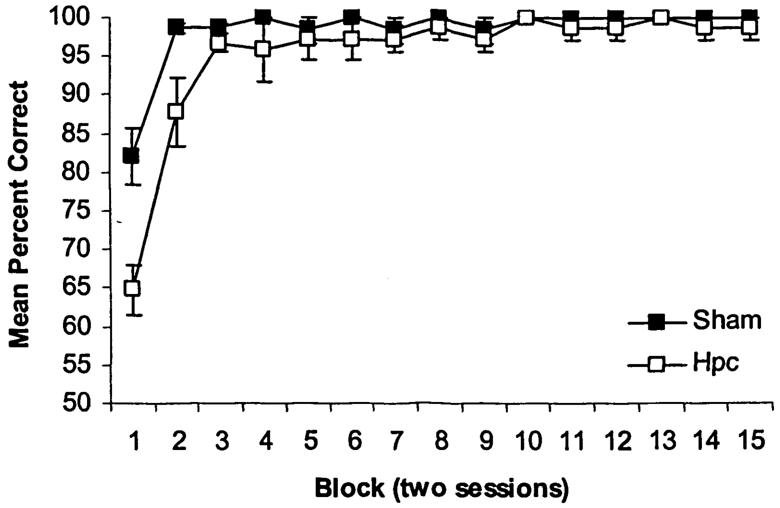

Figure 3.15. Performance of the simple discrimination by the Sham and the Hippocampal (Hpc) groups. Error bars indicate ±standard error of the mean.

Structural Discrimination. The mean percent correct for the performance of the structural discrimination, collapsed over the three discriminations, in blocks of two sessions, for both groups is shown in Figure 3.16.

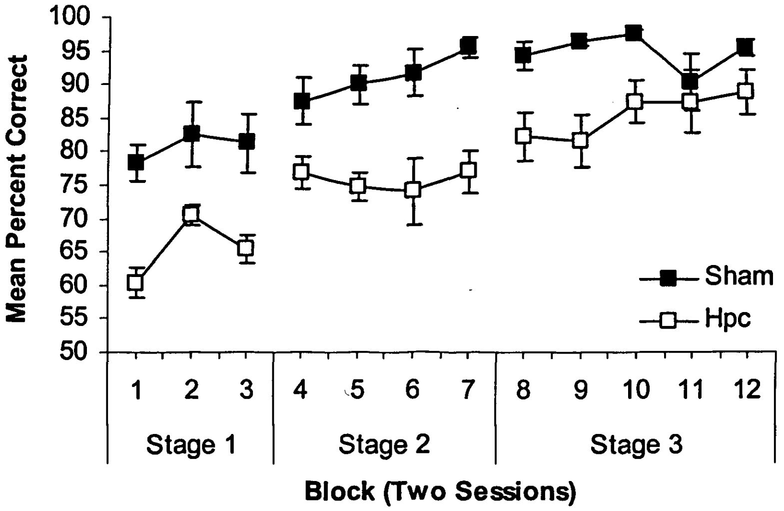

Figure 3.16. Performance of the structural discrimination over the three stages of training for the Sham and the Hippocampal (Hpc) groups. Error bars indicate ±standard error of the mean.

The Sham group consistently performed the structural discrimination at a higher level than the Hippocampal group. Over the three stages of training, performance in both groups improved, but with the Hippocampal group performing at a level lower than the Sham group. In the final stage, performance by the Hippocampal group continued to improve and by the end of training, the performance by both groups began to converge. Performance by the Sham group during the final stage remained at a level close to ceiling. In stage three of training, performance by both groups did not drop to a level lower than that in stage two. From this result it is possible to claim that animals were not using a win-stay strategy to solve the task, i.e. it is possible within a block of trials of a discrimination to relearn which features of the stimuli are relevant for solving the task. If animals had used such a strategy it would be predicted that in stage three when discriminations are presented in a pseudo-random order, thus removing the opportunity to relearn within a block of trials, their performance would be lower than in stage two. It appears that the data from the first two stages of training reflects performance of the task that is qualitatively similar to the performance in stage three.

In the three stages of testing, different procedures for the presentation of discriminations were used. For the first stage discriminations were presented in blocks of eight trials per session. In the second stage, discriminations were presented in two blocks of four trials per session. Finally, in the third stage, trials of each discrimination were presented in a pseudo-random order. Due to each stage of testing employing different procedures, each stage is analysed separately. In the first stage, in which discriminations were presented in blocks of eight trials, it was found that there was a significant difference between groups, $F(1,9)=14.77$, $p<0.01$, and a significant effect of block, F(2,18)=12.09, p<0.05 and no significant interaction of these factors, F(2,18)=2.17. In the second stage, in which discriminations were presented in two blocks of four trials, there was a significant effect of group, F(1,9)=26.38, p<0.01, but no significant effect of block, F(3,27)=0.98 nor a block by group interaction, F(3,27)=0.77. In the final stage of testing in which discriminations were presented a pseudo-random order, it was found that there was a significant effect of group, F(1,9)=5.64, p<0.05, but no effect of block, F(4,36)=2.01. The interaction between the block and group in the final stage of testing was approaching significance F(4,36)=2.62, p=0.051. It is possible that the group by block interaction was close to reaching significance due to a ceiling effect. The failure of the interaction to reach significance may be due to low statistical power from having relatively small group sizes (Sham=5; Hippocampal=6) and consequently, accepting the null hypothesis may be subject to Type II error. Therefore, the simple main effects of the interaction were explored, however, caution must be taken as significant effects may simply reflect Type I error due to an inflated alpha level of probability. Simple main effects analysis revealed that there was no significant effect of block for the Sham group, F(4,36)=1.67, but there was a significant effect for the Hippocampal group, F(4,36)=3.08, p<.05. There was a significant effect of group on blocks one, two and three: F(1,18)=6.58, F(1,18)=10.17 and F(1,18)=4.67, but no significant differences between the two groups on the last two blocks of training.

Performance in both groups increased over the stages of training. Even though the Hippocampal group were significantly impaired until the last two blocks of training, both groups were able to perform the structural discrimination. It is possible that the Hippocampal group were able to perform the task in a non-structural manner by solving a sub-set of the discriminations. Therefore, the Hippocampal group could have learned to solve two of the discriminations in an elemental fashion and consequently perform poorly on the remaining discrimination. To assess this possibility, the data were analysed across blocks of sessions by ranking the scores for each discrimination, for each subject, by order of level of performance, (i.e. First, Second and Third, in declining ability). If animals were using this strategy it would be predicted that there would be an effect of block for only the First or First and Second discriminations, demonstrating acquisition of these discriminations as training progressed, and not for the Third discrimination (i.e. the worst discrimination), which would fail to be acquired as a consequence of training.

The performance of the First, Second and Third discrimination over blocks of training is shown in Figure 3.17. It was found that there was a significant effect of block, $F(11,99)=17.83$, $p<0.001$, and a significant effect of discrimination, $F(2,18)=79.63$, $p<0.001$, and these factors significantly interacted, $F(22,198)=2.67$, $p<0.001$. There was no significant group by discrimination interaction, $F(2,18)=2.7$, and contrary to the predictions there was no significant group by discrimination by block interaction, $F(22,242)=0.89$. As, in the previous analyses of the data, the group by session interaction was approaching significance, $F(11,99)= 1.86$, $p=0.054$. It appears, that even though significantly impaired compared to controls, the Hippocampal group did perform, to some extent, the structural discrimination in a qualitatively similar manner as controls.

Performance improved on the Third discrimination for both groups, revealing that animals were not showing performance above chance by systematically making correct response for one or two of the discriminations correct, and consistently making incorrect choices on a third discrimination. The fact that there was a significant discrimination by block interaction may be because the Sham group had already reached a ceiling level for two of the discriminations. In addition the group by discrimination interaction approached significance ($p<0.06$). Simple main effect analysis of this interaction revealed that there was an effect of discrimination for the Hippocampal group, $F(2,22)=7.149$, $p<0.01$, but not for the Sham group, $F(2,22)=2.3$. From this, it appears that because there might have been a ceiling effect for the Sham group (i.e. there was not a significant difference between their ability on their best and worst discriminations), and this may explain the discrimination by block interaction.

The mean percent correct for both groups for the probe trials compared to performance of the normal structural discrimination trials is shown in Figure 3.18. In the probe trials, reinforced compounds were simultaneously tested against non-reinforced compounds, with which had not been previously paired together. Performance of the probe trials did not appear to differ from that of normal structural discrimination trials for either group. An analysis of variance confirmed that performance did not differ for the trial types, $F(1,9)=0.21$, and this did not significantly interact with the effect of group, $F(1,9)=3.27$. The two groups did not significantly differ in their overall performance, $F(1,9)=2.05$.

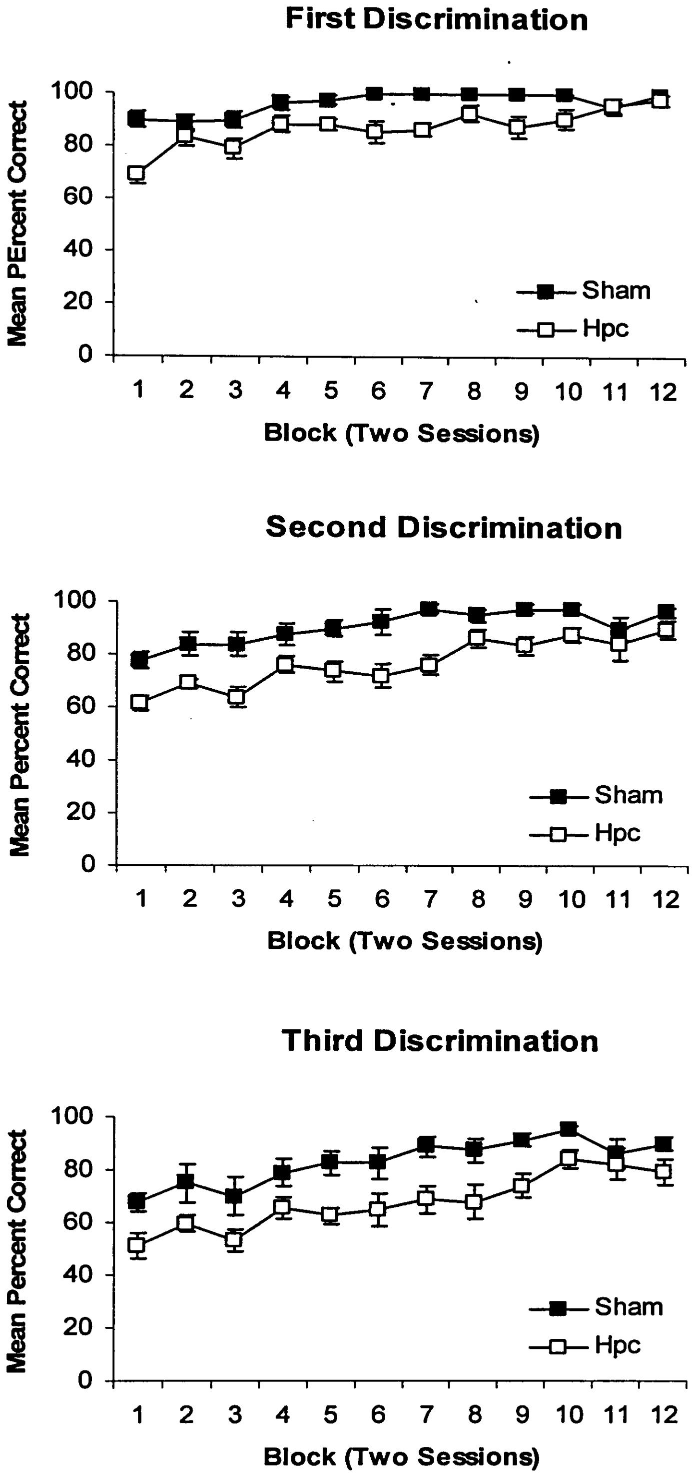

Figure 3.17. The mean performance on the discriminations of the structural discrimination ranked in the order of ability for each subject for the Sham and the Hippocampal (Hpc) groups. Error bars indicate ±standard error of the mean.

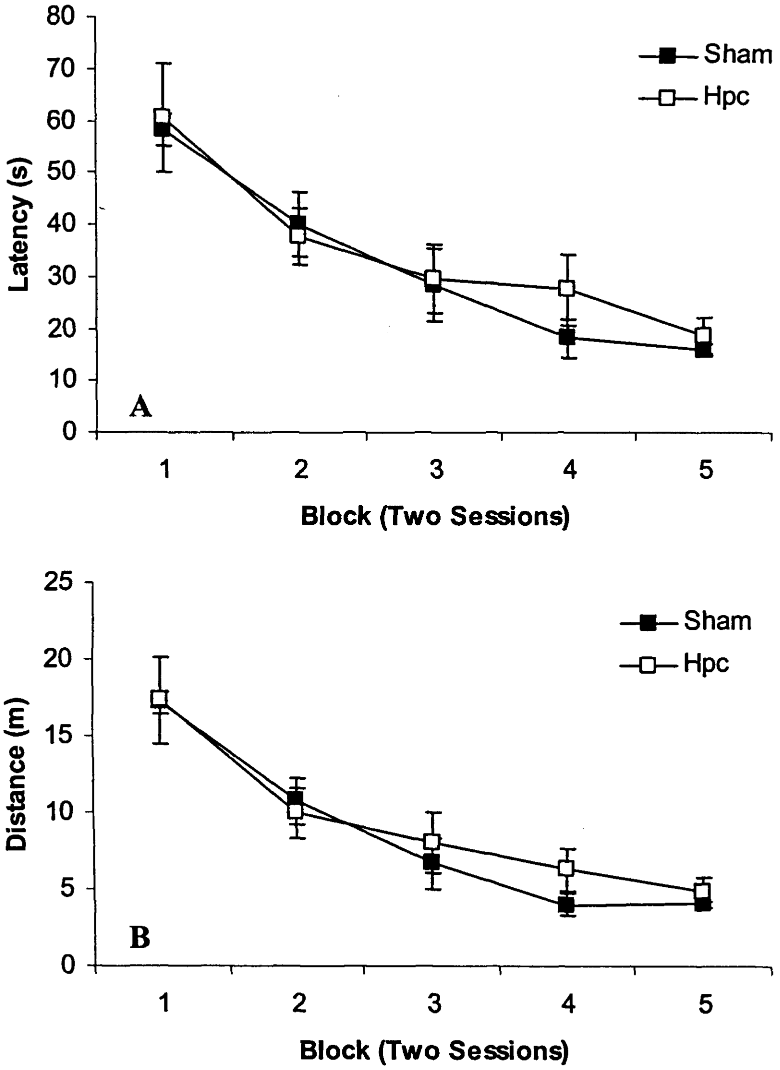

Figure 3.19. The performance of the spatial reference memory task by the Sham and Hippocampal (Hpc) groups. The mean latencies to locate the hidden platform is shown in section A, and the mean distance travelled is shown in section B. Error bars indicate ±standard error of the mean.

Probe. The mean percentage of time spent in the correct quadrant for both groups is shown in Figure 3.20. There was no apparent difference in the proportion of time spent in the correct quadrant by the two groups. Both groups appeared to show a preference for the quadrant where the platform had previously been located. An

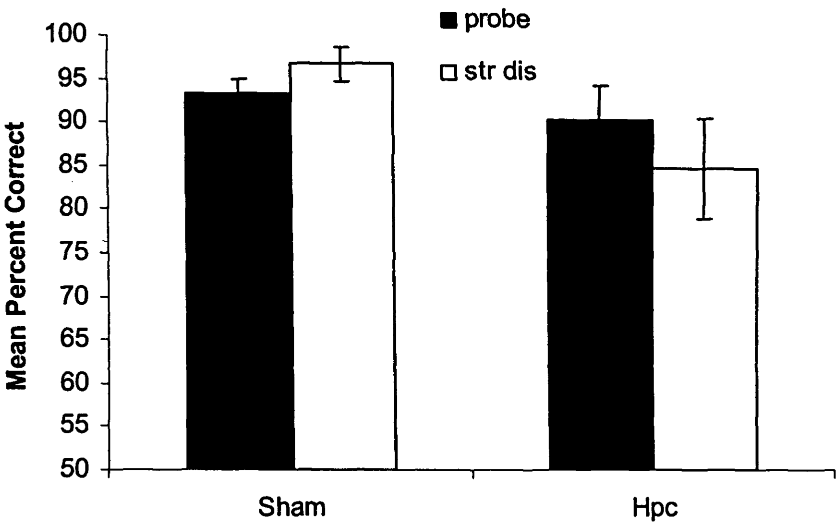

Figure 3.18. The performance on the probe trials and the structural discrimination for the Sham and the Hippocampal (Hpc) groups. Error bars indicate ±standard error of the mean.

Spatial Reference Memory. The mean latency and distance travelled to locate the platform for both groups is shown in blocks of two sessions in Figure 3.19. At first both groups were slow to locate the platform, but over the course of training the latencies decreased. Both groups showed a similar level of performance throughout training. An analysis of variance of the latency to locate the hidden platform revealed that there was no significant group difference, $F(1,9)=0.21$. There was a significant effect of block, $F(4,36)=19.37$, $p<0.001$, but there was no significant group by block interaction, $F(4,36)=0.32$. Analysis of variance of the distance travelled to locate the hidden platform similarly showed that there was no significant effect of group, $F(1,9)=0.05$, nor a group by block interaction, $F(4,36)=1.16$. There was a significant effect of block, $F(4,36)=5.92$, $p<0.05$.

independent sample t-test did not reveal a significant difference between the two groups, t(9)=1.69. One-sample t-tests demonstrated that both groups spent a significantly greater proportion of their time searching in the correct quadrant of the maze than a chance level of 25%: Sham, t(4)=9.18, $p<0.05$; Hippocampal, t(5)=3.93, $p<0.05$

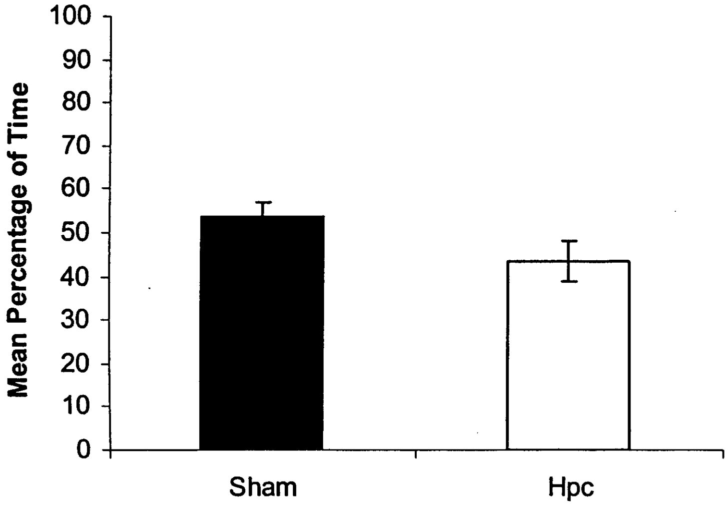

Figure 3.20. The mean percentage of time spent in the correct quadrant during the probe trial for the Sham and the Hippocampal (Hpc) groups. Error bars indicate ±standard error of the mean.

Discussion

It was found that rats with hippocampal lesions were impaired on a structural discrimination. There was an indication (from the block by group interaction approaching significance) that by the end of training performance of the structural discrimination did not significantly differ from control rats. However, the control rats were performing at a ceiling level which may have masked an effect of lesion in the final blocks of training. Even though they were impaired on the task they were able been found to reverse neo-cortical lesion deficits in a water maze task (Hoh, Kolb, Eppel, Vanderwolf and Cain, 2003). Therefore, training of the procedural demands of a water maze task is capable in some situations of eradicating impairments. The possibility that training in the water tank may have resulted in a lack of deficit on a spatial reference memory task will be discussed further in Chapter Five.

The results of Experiment 8 support the hypothesis that the hippocampus is involved in the learning and memory of a structural discrimination. Whilst it is possible that other areas may also play a role in structural learning, this experiment demonstrated that hippocampal damage is sufficient to produce a deficit on a structural discrimination.

General Discussion

In two experiments it was shown the lesions of the hippocampus impair the ability to perform a structural discrimination. In both experiments the ability to perform a structural discrimination, that had been acquired prior to receiving lesions of the hippocampus, was tested. It was found in Experiment 7a and 7b that excitotoxic lesions of the hippocampus impair performance, causing a total inability to solve the task. In Experiment 8, in which smaller radio-frequency lesions of the hippocampus were made, it was also found that damage to the hippocampus impaired the performance of a structural discrimination, but now lesioned rats were able to still solve the task to an extent. The difference in the two experiments could be attributed to two possible factors; the amount of cortical damage and the amount of damage to the hippocampus itself. In Experiment 8 the amount of cortical damage was far smaller than that in the hippocampal lesioned rats in Experiment 7a and 7b. Also, the to solve the task. An analysis of the data, to examine whether groups were using different strategies for solving the task, found that both groups solved the task in a similar manner. Both groups showed an increase in performance for all three discriminations over blocks of training. Therefore, hippocampal lesions impaired an animal's ability to perform the structural discrimination task that it had acquired prior to surgery, but lesioned animals were still able to show evidence of being able to solve the discrimination. Hippocampal lesion did not prevent relearning of the task, but whether naïve hippocampal lesioned rats would be able to show acquisition of a structural discrimination still remains to be directly tested.

The Hippocampal lesion group were initially impaired on the simple discrimination, but quickly relearned the task. Although initially impaired, the fact that hippocampally lesioned rats were able to solve the simple discrimination task demonstrated that rats were able to attend to visual stimuli and to behave appropriately within the demands of the task. The deficit on the structural discrimination does not appear to be due to an inability to learn about visual stimuli *per se*, and also to make approach and avoidance responses towards the stimuli.

It was found that the hippocampal lesioned rats were not impaired on a spatial reference memory task in the Morris water maze. The lack of a deficit is in contradiction with the standard finding that hippocampal lesioned rats are impaired on this task (Morris et al. 1982). The fact that an impairment was not found could be due to the extensive training that rats have received in the water tank apparatus before and after surgery. It has been found that training in one water maze prevents a spatial deficit in another water maze that would normally be caused by NMDA receptor blockade (Bannerman, Good, Butcher, Ramsay and Morris, 1995). Pre-training has cortical damage was controlled for by subjecting the control animals to sham surgical procedures so that cortical damage could be matched for both groups. This resolves the issue that was addressed in Experiment 7b, confirming that hippocampal damage is sufficient to produce a deficit on a structural discrimination. The extent of the deficit shown by lesioned animals in the first experiment may be due to additional damage to the parietal cortex. The issue of a contribution of the parietal cortex to structural learning will be discussed further in Chapter Five. Experiment 8 demonstrates that when the amount of cortical damage is controlled, hippocampal damage is sufficient to produce a deficit on a structural discrimination. Both Experiment 7 and 8 provide behavioural evidence for the role of the hippocampus in memory of the spatial arrangement of visual cues, implicated in c-*fos* activation studies (Wan et al., 1999; Jenkins et al. 2004). The present findings also support the hypothesis that structural encoding is crucial in creating a mental 'snapshot' of visual cues, which is claimed to a be an ability that is reliant on episodic memory, a hippocampal dependent function in humans (Aggleton and Pearce, 2001).

In Experiment 8 a different post-operative testing procedure was used to that of Experiment 7. In Experiment 7 after surgery rats were initially trained on the BW+ WB- discrimination. Subsequently the WH+ HW- discrimination was introduced and finally followed by the HB+ BH- discrimination. Once all three discriminations were being solved concurrently, the discriminations were presented in a pseudo-random order so that animals were unable to predict the order of the discriminations. The procedure was similar to the original training of the structural discrimination (Experiment 3). In contrast in Experiment 8 all three discriminations were presented in blocks of trials in a pseudo-random order from the beginning of training.

Eventually rats were tested on the three discriminations in a pseudo-random order so as to remove the possibility of within-block learning.

The method of testing in Experiment 7 is beneficial in showing that the component discriminations that form the structural discrimination can be solved by hippocampal lesioned animals, but once all three discriminations are required to be solved concurrently in a pseudo-random order performance by hippocampal lesioned animals falls to a level that is close to chance. This demonstrates that hippocampal lesioned animals are able to some extent to learn about the stimuli but are unable to discriminate the structural features of the configurations.

The testing procedure used in Experiment 7 also provides the opportunity to examine the transfer of learning from each stage to the next. For example, when the third discrimination (HB+ BH-) was introduced the Sham group performed above chance ($t(10)=4.5$, $p<0.005$), whereas the Hippocampal group performed significantly below chance ($t(4)=-4.4$, $p<0.05$). This demonstrates that the control group had remembered the HB+ BH- discrimination, whereas the Hippocampal group were showing performance that was similar to that of their pre-operative performance when rats were naïve to the task (Experiment 3).

In Experiment 8 the procedures were changed so that all discriminations were presented from the start of testing. This was done for the following reason. Testing on all three component structural discriminations demands a structural solution to the task, whereas testing one component discrimination could lead to performance above chance that need not reflect the ability to discriminate structure. It is also possible that by testing on one discrimination this may encourage new learning of an elemental solution which leads to poor performance on subsequently introduced discriminations.

would impair the ability to process structural features, therefore, not resulting in a novelty preference for the test object. This interpretation assumes that the two objects are encoded separately within the environment and not with regards to each other. If the objects were encoded as one configuration then the movement of one object would have resulted in the structural features of both stimuli being altered. If this was the case then it would be predicted that for the control rats there would be increased spontaneous exploration but not with a specific preference for one of the objects.

In contrast to the evidence for the involvement of the hippocampus in object-in-place learning, it has been found that fornix lesions do not impair a spontaneous exploration preference for an object that has had its component features reconfigured (Ennaceur and Aggleton, 1994). In this task, rats were allowed to explore in an arena that contained a familiar object and an object that consisted of the same elements as the familiar object, but the elements were placed in a novel spatial arrangement. Both control and fornix lesioned rats showed an exploratory preference for the reconfigured object. Therefore, changes in the structural features of the stimulus caused proportionately higher exploratory behaviour in fornix lesioned rats that, according to the hypothesis proposed here, should be less sensitive to structural changes. One possibility is that the reconfiguring of the stimulus resulted in qualitative changes in the appearance of the object that can not be described in terms of the sum of its features. This raises issues of how compound stimuli are learnt about; whether compound stimuli are treated as the sum of their parts or whether the combination of two or more features create new elements that are unique to their combination.

Whilst the results presented here may be attributed to an impairment in spatial processing, evidence has not been provided that the deficit is exclusively spatial. It is

Therefore, it could be argued that testing rats on all three discriminations concurrently maximises the chances of both groups showing reacquisition of the task by eliminating possible conflicting solutions. This may account for the finding that hippocampal lesioned rats showed performance that was close to chance on the full structural discrimination in Experiment 7, whereas in Experiment 8 even though hippocampal lesioned rats were impaired they were able to perform the structural discrimination to some extent. However, this may be simply due to the size of lesion, because as mentioned previously the radio-frequency lesions in Experiment 8 were somewhat smaller that the excitotoxic lesions in Experiment 7.

The finding that hippocampal lesions impair performance on a structural discrimination may reflect the same mnemonic processes that are involved in tasks that require encoding of object-in-place associations that also depend on the hippocampus (Mumby et al., 2002). It is possible that the encoding of an object in a given location may be achieved by learning the structural features of the stimuli (i.e. the stimulus in a particular spatial context). In the task used by Mumby et al. (2002) rats were exposed to a familiarization stage in which they were allowed to explore two identical objects in an open arena. In a test stage they were placed back into the arena, but one of the identical stimuli was now moved to a new location. Control rats showed a preference for exploring the object that was in the new location, whilst hippocampal lesioned rats did not show a preference in their exploration. These results can be explained in terms of a structural encoding deficit. If the test object had been encoded with regards to its structural features created by its position in the arena during the familiarization stage, then in the test phase the novel structural features created by the object in new location should cause increased exploration of that object compared to an object with preserved structural features. Damage to the hippocampus possible that hippocampal lesion deficits may be seen on a structural discrimination that does not contain spatial features, such as a temporal structural discrimination. It is not clear whether the deficit is due to learning the spatial relationships between stimuli that are presented in compound or due to a feature-binding problem. It is possible that the hippocampal lesion deficit on a structural discrimination is due to impaired learning of configurations of stimuli, and therefore, it would not be possible to dissociate structural and configural learning by the use of hippocampal lesions.

Even though there is evidence to suggest that the hippocampus is not responsible for configural learning (Whishaw and Tomie, 1991; Gallagher and Holland, 1992; Davidson et al., 1993; Mcdonald et al., 1997; Bussey et al., 1998; Bussey, Dias et al., 2000), it needs to be demonstrated that hippocampal lesioned animals are not impaired on performance of a configural discrimination that does not require the processing of structural features. Ideally such a task should use the same stimuli that were used in the structural discrimination for Experiments 7 and 8. If the deficit on a structural discrimination is explicitly due to impaired processing of the structural features, the hippocampal lesioned rats should not be impaired on a configural discrimination, in which only the featural information of the configurations are crucial for the solution of the task.

Chapter Four

The Effect of Hippocampal Lesions on the Performance of Configural Discriminations, and the Influence of Structural Information Encoding on the Transfer of Learning

Introduction

It has been claimed that the hippocampus is essential for the learning and storage of configural associations (Rudy and Sutherland, 1989). Evidence has been found to show that hippocampal lesioned animals are impaired on discrimination tasks that require configural solutions such as negative patterning (Sutherland and Rudy, 1989; Alvarado and Rudy, 1995a), and transverse patterning (Alvarado and Rudy, 1995a; Dusek and Eichenbaum, 1998). However, in contrast, it has also been shown that animals with hippocampal lesions can sometimes learn configural tasks at normal rates. For example, hippocampal lesioned rats were able to learn a feature-neutral task (A+ C-, AB-, CB+), but the same animals were impaired at learning to find a hidden platform in a Morris water maze (Gallagher and Holland, 1992). The inconsistencies in the data do not appear to be due to the extent of the lesion of the hippocampus, because ibotenic lesions, similar to the lesions made by Gallagher and Holland (1992) spare performance of a feature-neutral discrimination, but still result in a deficit on a negative patterning task (Alvarado and Rudy, 1995a). Therefore, there is still controversy as to when the hippocampus is required for configural learning.

In chapter three it was found that hippocampal lesions impaired performance of a structural discrimination. It is possible that hippocampal lesioned rats were impaired on a structural discrimination due to the task requiring a non-linear solution, and thus task is claimed to require the formation of configural associations (Alvarado and Rudy, 1992; 1995a; 1995b). Each stimulus is equally reinforced and non-reinforced. Therefore, the solution of the task requires learning of the unique configurations formed by the compound stimuli.

The transverse patterning discrimination is comparable in its level of difficulty to that of the structural discrimination, due to the size of the stimulus set and the number of reinforcement outcomes with which each stimulus is associated. The designs of the structural and the transverse patterning discriminations are shown in Figure 4.1.

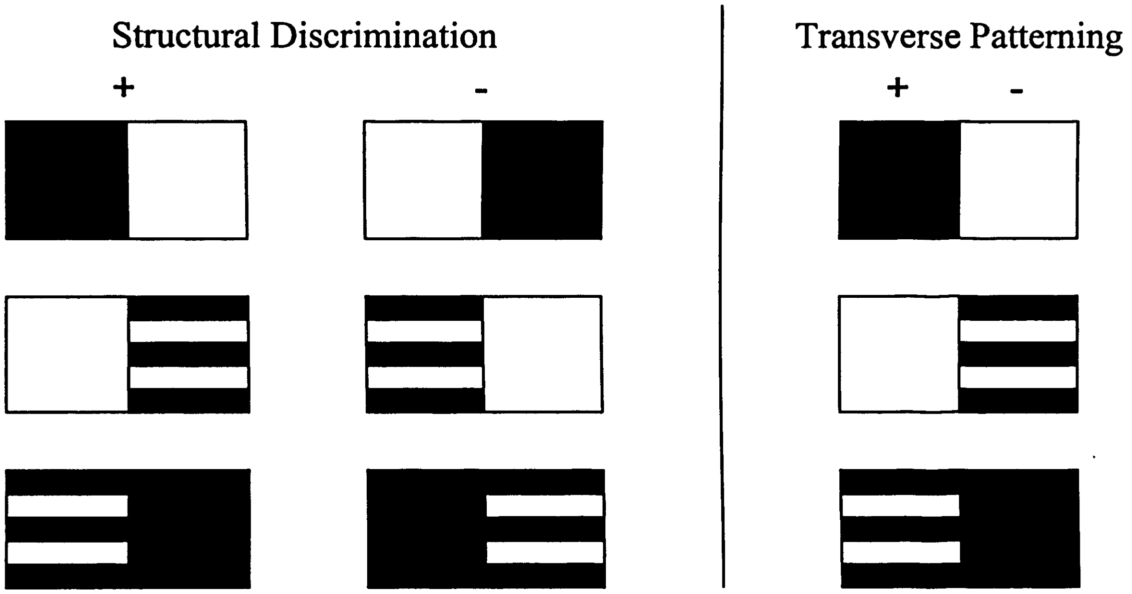

Figure 4.1. The design of a structural and a transverse patterning discriminations. Each task uses three stimuli that when paired in compounds must be discriminated from other combinations of the stimuli in three concurrent discriminations.

In both tasks there are three stimuli that are incorporated into compounds of pairs of stimuli, and each stimulus is differentially reinforced when it is presented in compound with other stimuli. Due to the design of the transverse patterning the impairment may simply reflect the necessity of the hippocampus for learning of configural associations. This interpretation of the results would fit well with the predictions of the original 'configural association' theory of the hippocampus (Sutherland and Rudy, 1989). However, if hippocampal lesioned rats are impaired on a structural discrimination due to a deficit in discriminating the spatial arrangements of pairs of stimuli, then it should be possible for hippocampal lesioned rats to demonstrate performance that is similar to controls of a configural discrimination that is comparable in its level of complexity to that of the structural discrimination.

In this chapter the effects of hippocampal lesions on the performance of two configural discrimination are investigated. The aim of these experiments is to test whether the hippocampus is required for performance on configural tasks that are of a similar difficulty level as that of the structural discrimination. In the second of these experiments, the generalisation of learning structural information is tested to investigate whether learning structural information can be dissociated from the learning of the featural information in the processing of compound visual stimuli. This will be tested by comparing the amount of generalisation of learning from a previously acquired biconditional discrimination to a novel biconditional discrimination in which the same configurations are presented but the structural information is reversed. It is predicted that rats with hippocampal lesions will show greater generalisation due to impaired learning of the structural features of the originally learnt biconditional discrimination. As a consequence, rats with hippocampal lesions will show superior performance to the control rats.

In the first experiment of this chapter the effect of post-acquisition hippocampal lesions on a transverse patterning discrimination was tested. The transverse patterning discrimination it is possible to present the subjects with the same stimuli in the same compounds that were used for the structural discrimination so that it is only the demands of the task that differ.

One difference between the transverse patterning task and the structural discrimination, other than whether learning structural information is required for the solution of the discrimination, is that in the transverse patterning discrimination subjects are required to choose between two differentially reinforced stimuli that are presented in compound. In the structural discrimination subjects are required to make a choice between differentially reinforced compounds that are presented simultaneously. In the transverse patterning task, subjects can only learn that a stimulus has multiple associations across trials, whereas in the structural discrimination a subject is presented with the same element in two different compounds, and learning can occur within a trial. It is possible that this difference in the procedures for training may influence learning, and so differences in the behaviour of hippocampal lesioned animals may not solely reflect the influence of structural learning. To rule out this possibility in the second experiment subjects were trained on a biconditional discrimination.

In a biconditional discrimination subjects are required to learn configural associations that stimuli come to acquire whilst presented in compounds. A stimulus presented in compound with another stimulus may be reinforced, but when presented in compound with another stimulus will be non-reinforced. Therefore, whole compounds are reinforced or non-reinforced rather than elements within a compound having different associations. This procedure for the training of a configural discrimination is more similar to the task demands of the structural discrimination.

In these two experiments effort has been made to use configural tasks that are comparable on two levels to the demands of the structural discrimination, so that a lack of effect of lesion would reflect the qualitative differences between structural and configural learning, rather than reflecting a quantitative difference of task difficulty due to size of stimulus set and demands of task.

Experiment 9

In this experiment it is predicted that hippocampal lesions will not affect the performance of the transverse patterning discrimination because learning of this non-linear discrimination does not require the structural features of the compound stimuli to be learnt.

Normal rats were trained on a transverse patterning discrimination in a progressive manner, until all three component discriminations were solved concurrently (see Experiment 5, Chapter Two). After acquisition of the task, the rats were divided into two groups that were matched for their performance of the transverse patterning discrimination. One group received radio-frequency lesions of the hippocampus (Hippocampal) and the other group received the same initial surgical procedures, but no damage to the hippocampus was caused (Sham). The two groups were then tested on their ability to solve the transverse patterning task. After testing on the performance of the transverse patterning task, to test the efficacy of the lesions, groups were then trained on both a spatial reference memory task and a spatial working memory task in a Morris water maze.

Stage two consisted of 24 sessions. Each session contained eight trials of each of the B+ W-, W+ H- and H+ B- discriminations. Discriminations were presented in a random order with the constraint that two trials of the same discrimination could not be presented consecutively. On every fifth trial the simple discrimination (P+ C-) was presented, making a total of six presentations per session.

Spatial Reference Memory

Apparatus. The apparatus was the same as used for Experiment 8 (Chapter Three).

Procedure. All procedures were the same as used for Experiment 8 (Chapter Three) with the exception that the day after receiving the probe test, rats received a session of three normal trials followed by a probe trial, in which the platform was removed and curtains were pulled around the perimeter of the pool, removing the use of the room cues. The probe trial lasted for 120s and the percentage of time searching in the quadrant of the pool where the platform was previously located was recorded (correct quadrant). Rats were released into the pool from the quadrant of the pool opposite the correct quadrant. If rats were using strategies other than using the room cues for navigation to the platform, then performance on the probe trial should remain above chance.

Spatial working memory

Procedure. Animals received five sessions of training to locate a hidden platform that remained in a constant location within a session, but changed location for each session. Each session consisted of four trials. For the first two trials the start location was the same, but for the last two trials the start positioned changed to different damage in the visual cortex plus damage to the parietal cortex, but in all cases there was no damage to the hippocampus.

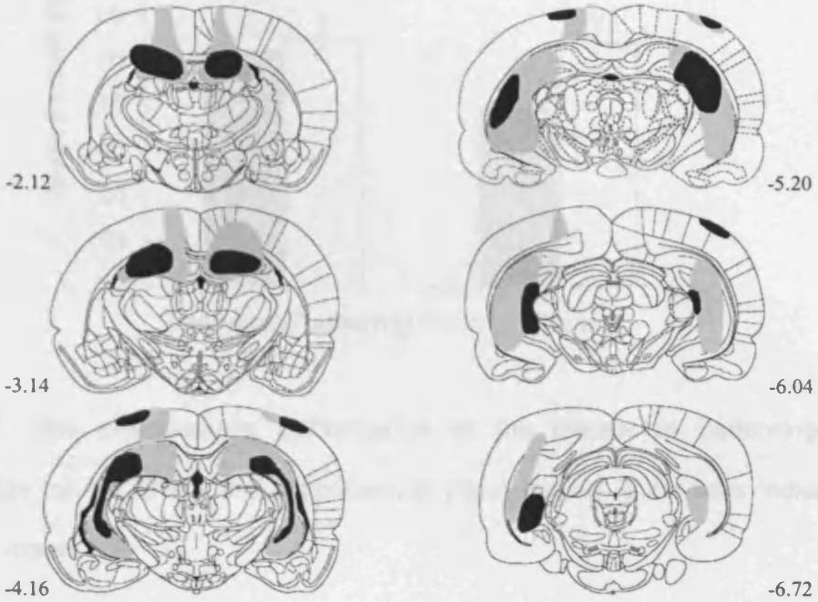

Figure 4.2. Coronal sections illustrating the extent of the largest (grey) and the smallest (black) lesions of the hippocampus. Distances are posterior to bregma (Paxinos and Watson, 1997).

Behavioural Testing. *Simple discrimination*. The pre-operative performance on the simple and the transverse patterning discrimination for the last three sessions of training is shown in Figure 4.3. The two groups were matched for their performance and did not statistically differ, F(1,9)=1.51.

locations. The start location order was random with the constraint that a start location could not be used more than once per session (with the exception of the first and second trials). Once the platform had been located rats were allowed to sit on the platform for 30s before being removed and the next trial commenced after an inter-trial interval of 10s. If a rat failed to find the platform within 120s it was guided to the platform where it was allowed to remain for 30s.

Results

Histology. One rat, from the Hippocampal group, had a large amount of cortical damage, which included parts of the visual cortex. This rat's data were removed from the final analyses. The extent of the hippocampal lesions is illustrated in Figure 4.2. All rats had large lesions of the dorsal hippocampus, except for one rat which had some unilateral sparing of CA1 and parts of the fornix. In the remaining cases the damage included large areas of CA1, CA2 and CA3, the dentate gyrus and subiculum. There was partial bilateral damage to the fornix and fimbria in these four cases. There was damage to the ventral hippocampus, but in the majority of cases there was also substantial sparing of the posterior parts of the ventral hippocampus leaving much of the ventral subiculum intact. One rat also had caudal sparing of the hippocampus. Two rats had slight damage to the dorsal thalamus, unilaterally in one case and bilaterally in another. In four cases there was cellular loss in the neocortex overlying the hippocampus. In two of these cases the damage only occurred unilaterally. The extent of damage to the cortex was similar in the control group that received sham surgeries. Thus, for the Sham group, there was very little cortical damage in one rat and in two others there was thinning of the parietal cortex. Two Sham rats had

Method

Subjects. The subjects were 14 male Dark Agouti rats (Harlan, UK). Rats were previously trained on a transverse patterning task prior to surgery (see Experiment 5, Chapter Two for details). Prior to and during the experimental procedures animals were allowed free access to food and water. They were housed in pairs in a room that was illuminated for 14.5 hours per day. All testing was carried out during the period of light at the same time each day. All procedures were in accordance with the United Kingdom Animals (Scientific Procedures) Act, 1986.

Surgery. Rats received either radio-frequency lesions of the hippocampus or sham operations using the same procedures as previously described for Experiment 8 (Chapter Three). The only difference in procedures was that the radio-frequency probe was raised to a temperature of 70°C for a period of 60s rather than 40s as in the previous experiment. The duration of exposure to the raised temperature was increased for the purpose of extending the amount of damage to the hippocampus, and also to increase the consistency of the amount of damage across animals. Nine rats received hippocampal lesions, but two rats died during surgery leaving the total number of hippocampal lesioned rats to seven. Five rats received Sham surgeries that followed the same procedures as the hippocampal lesions with the exceptions that the probe was only lowered to a depth of -1.7 from the top of cortex, and the temperature of the tip of the electrode was not raised.

Histology. All methods were the same as for Experiments 7 and 8 (Chapter Three).

Apparatus. The apparatus was the same as used in Experiment 5 (Chapter Two).

Transverse patterning stimuli. The stimuli were the same as used Experiment 5 (Chapter Two). These stimuli were also the same as used for training of a structural discrimination in Experiments 3 and 4 (Chapter Two).

Simple discrimination stimuli. The stimuli were the same as for Experiment 8 (Chapter Three), in which rats were tested for retention of a structural and a simple discrimination.

Behavioural procedure. *Pre-operative training of the simple discrimination.* Rats received three sessions of training on the simple discrimination (P+ C-). Each session consisted of 18 trials. Stimuli were presented simultaneously, an equal amount of times in either the left or right goal areas. For half the rats the platform was always present underneath the P stimulus. For the remaining rats the reinforcement contingency was the opposite (i.e. P- C+). Training on the simple discrimination commenced during the last three days of pre-operative training of the transverse patterning discrimination. A session of simple discrimination training commenced immediately after a session of training on the transverse patterning discrimination (see Experiment 5, Chapter Two).

Post-operative testing. Post-operative behavioural procedures started once all animals had at least 10 days recovery after receiving the surgery.

Stage one consisted of six sessions of 30 trials of the simple discrimination (P+ C-). All procedures were the same as for the pre-operative training of the simple discrimination.

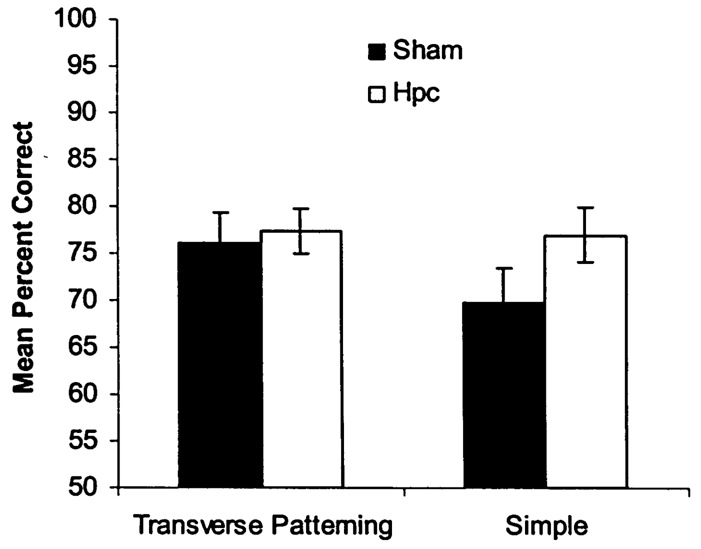

Figure 4.3. The pre-operative performance of the transverse patterning and simple discrimination for the Sham and Hippocampal (Hpc) groups. Error bars indicate ±standard error of the mean.

The post-operative performance of the simple discrimination, in blocks of two sessions, for each group, is shown in Figure 4.4. Both groups showed a drop in performance compared to that of their pre-operative level, but their performance quickly increased over days. Both groups relearned the task and maintained a high level of performance over blocks of training. An analysis of variance revealed that there was no significant effect of group, $F(1,9)=0.79$. There was a significant effect of block, $F(14,126)=15.34$, $p<0.05$, but no significant group by block interaction, $F(14,126)=0.93$.

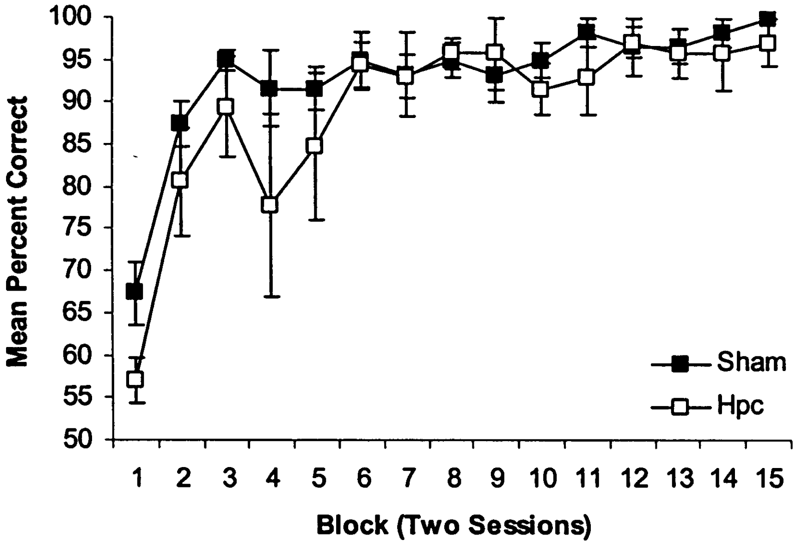

Figure 4.4. Performance of the simple discrimination by the Sham and Hippocampal (Hpc) groups. Error bars indicate ±standard error of the mean.

Transverse Patterning. The mean percent correct for each group for the transverse patterning discrimination is shown in Figure 4.5. Both groups' post-operative performance started around chance (50%), but gradually increased over sessions, reaching a level that was similar to that of their pre-operative performance. There were no apparent differences between the different groups' ability to solve the task over the course of testing. An analysis of variance of the scores, blocked by two sessions, showed that there was a significant effect of block, $F(11,99)=9.75$, $p<0.001$, but no effect of group, $F(1,9)=0.59$, and no significant interaction of these factors, $F(11,99)=1.02$. Analysis of the data from the last block training confirms that both groups were performing the task above chance by the end of training: Sham, $t(4)=5.07$, $p<0.01$; Hippocampal, $t(5)=3.88$, $p<0.05$.

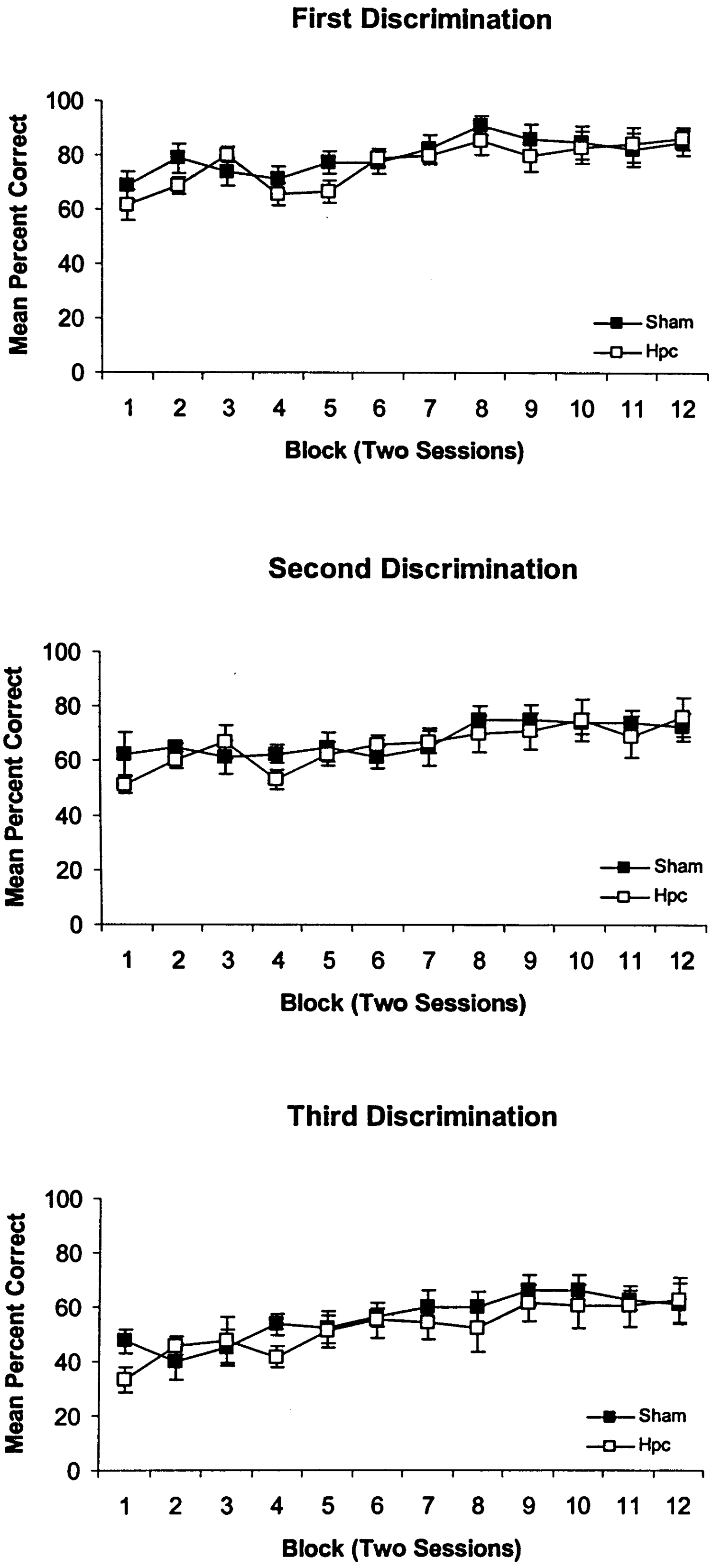

Figure 4.6. The performance on each discrimination of the transverse patterning task ranked in the order of ability for the Sham and Hippocampal (Hpc) groups. Error bars indicate ±standard error of the mean.

It is predicted that if animals are using the strategy of solving two discriminations and consequently being poor on the third discrimination, there will be an interaction between the rank of discrimination (i.e. First, Second and Third) and block, reflecting that the worst discriminations, does not improve at the same rate as the other discriminations over blocks of testing.

The results for the performance of both groups on the First, Second and Third discriminations, ranked for ability, are shown in Figure 4.6. An analysis of variance revealed that there was a significant effect of discrimination, $F(2,18)=188.1$, $p<0.0001$, a significant effect of block, $F(11,99)=9.26$, $p<0.0001$, but no significant interaction between these factors and with the effect of group, $F<1$.

Spatial Reference Memory. The mean latency and distance travelled to locate the platform, over blocks of two sessions, is shown in Figure 4.7 for both groups. At the start of training both groups were slow to locate the platform, but over the course of training the latencies decreased. Both groups' latencies decreased at a similar rate, but initially it appeared that the rate of decrease was greater for the Sham group than for the Hippocampal group. An analysis of variance of the latency to locate the hidden platform revealed that there was a significant effect of block, $F(4,36)=9.19$, $p<0.001$, but there was no significant effect of group, $F(1,9)=1.39$, and the block by group interaction did not reflect a significant difference in the rate of acquisition of the task, $F(4,36)=1.42$. Analysis of the distance travelled to locate the platform is similar to the findings of the latency data. There was a significant effect of block, $F(4,36)=12.01$, $p<0.05$, but no significant effect of group, $F(1,9)=2.05$ nor a significant group by block interaction, $F(4,36)=1.35$.

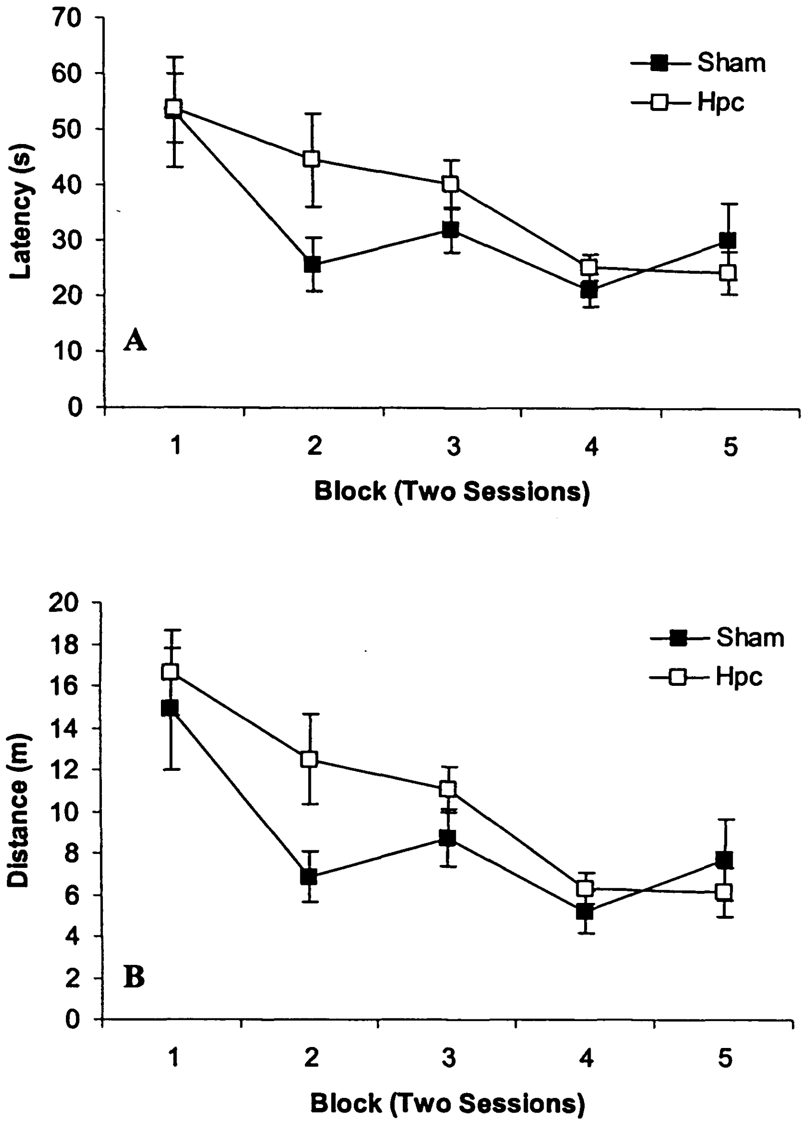

Figure 4.7. Performance on a spatial reference memory task in the Morris water maze. The mean latency to escape from the pool for the Sham and Hippocampal (Hpc) groups is shown in section A, and the mean distance travelled is shown in section B. Error bars indicate ±standard error of the mean.

Probe (i): The mean percentage of time spent in the correct quadrant for both groups is shown in Figure 4.8. Both groups showed a similar level of preference for the correct quadrant. An unpaired samples t-test revealed that there was no significant difference between the Sham and Hippocampal groups, t(1,9)=0.6. Both groups spent

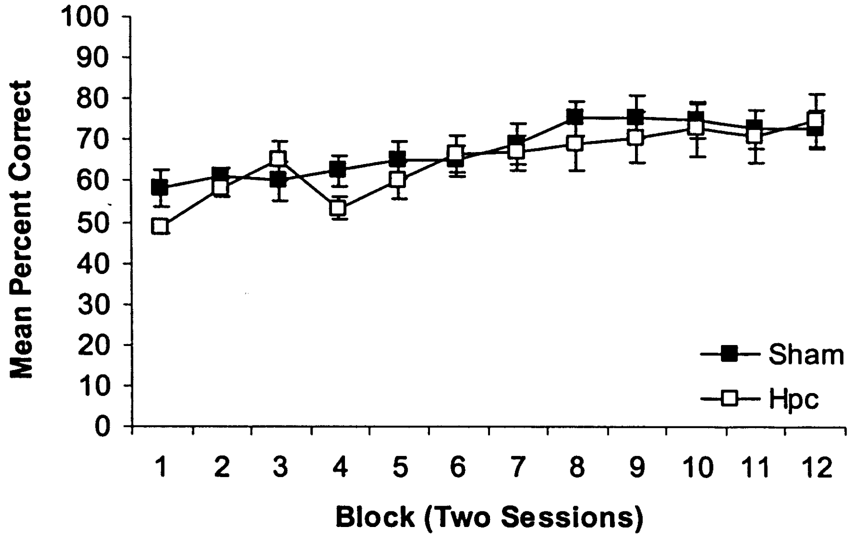

Figure 4.5. Performance on the transverse patterning discrimination by the Sham and Hippocampal (Hpc) groups. Error bars indicate ±standard error of the mean.

It is possible that even though there was no difference between the groups' ability to solve the transverse patterning task, the groups could be solving the task in qualitatively different manners. One possibility is that the Hippocampal lesion group may have used a non-configural strategy of learning about two of the discriminations and consequentially making incorrect choices on the third discrimination. This could result in performance of the task that is above chance, without reflecting configural learning. To examine whether this was the case, the scores for each discrimination for each rat were ranked as being First, Second, Third. This was done over blocks (of two sessions) of testing to allow for the possibility that rats may always be poor on one discrimination compared to the other two, but which particular discrimination on which they are poor may change over blocks of training.

trial, $F(1,9)=11.45$, $p<.05$, and a significant trial by group interaction, $F(1,9)=6.615$, $p<0.05$. However, there was a significant effect of group, $F(1,9)=6.24$, $p<0.05$, suggesting that the lack of an overall group difference for latency may have been due to the two groups differing in their swim speeds.

Discussion

The results of the experiment failed to show that hippocampal lesions impair performance of a transverse patterning discrimination, whilst being impaired on a spatial working memory task. This result supports the prediction that the hippocampus is not required for configural learning. Also, the result is in line with other research that has also failed to find impaired learning of a transverse patterning discrimination with fornix lesions in rats (Bussey et al., 1998) and hippocampal lesions in monkeys (Saksida et al., 2003; Brasted et al., 2004). Even though the hippocampal lesioned rats' performance level after surgery started near to chance, the Sham group also showed an initial drop in performance, and both groups reacquired the task at a similar rate. Analysis of the performance of the different discriminations did not reveal that the groups were learning the transverse patterning in a qualitatively different manner. The results contradict the predictions of the 'configural association' theory of the hippocampus (Sutherland and Rudy, 1989; Rudy and Sutherland, 1995).

In contrast to the present experiment, impairments on a transverse patterning task due to hippocampal lesions have previously been found (Alvarado and Rudy, 1995a, 1995b; Dusek and Eichenbaum, 1998). One of the differences between these experiments and the present experiment is that in the studies by Alvarado and Rudy (1995) and by Dusek and Eichenbaum (1998), rats were trained on the task only after significantly more time in the correct quadrant that would be expected by chance: Sham, t(4)=3.9, p<0.05; Hippocampal, t(5)=2.9, p<0.05.

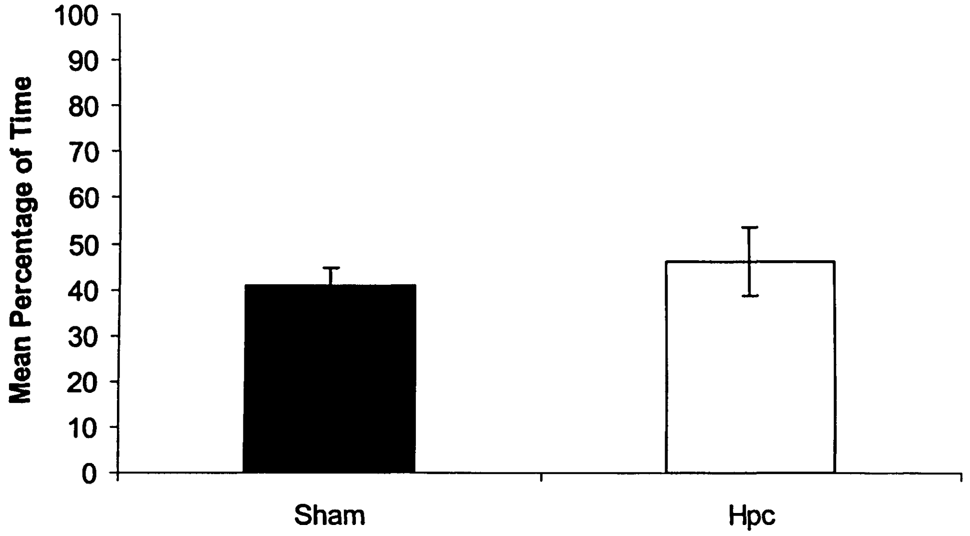

Figure 4.8. Probe (i). The mean percentage of time spent in the correct quadrant by both the Sham and Hippocampal (Hpc) groups. Error bars indicate ±standard error of the mean.

Probe (ii): The mean percentage of time spent in the correct quadrant for both groups when the room cues were removed, by concealing the pool with a curtain, is shown in Figure 4.9.

Both groups showed a level of preference for the correct quadrant that did not significantly differ from chance (Sham: t(4)=0.9; Hpc: t(5)=-0.3). An unpaired t-test showed that there was no significant difference between the groups, t(1,9)=0.67.

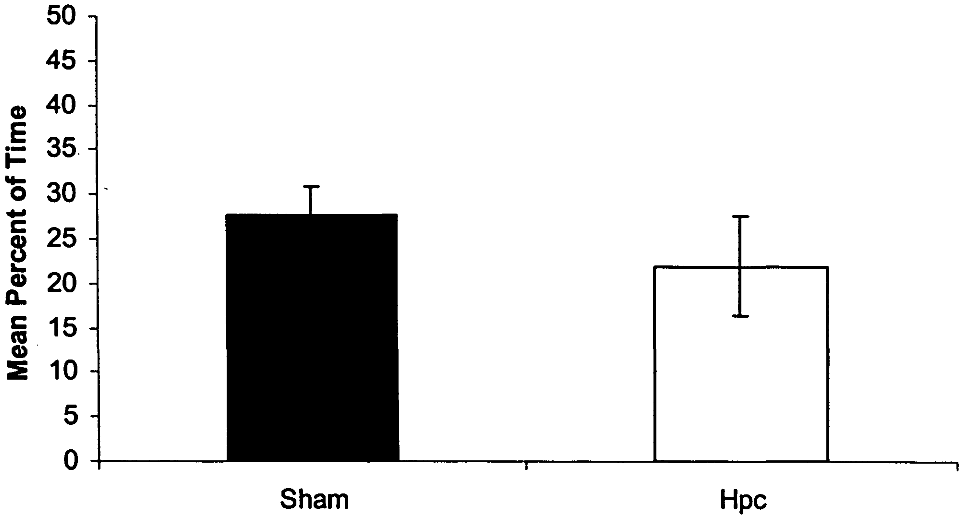

Figure 4.9. Probe (ii). The mean percentage of time spent in the correct quadrant by both the Sham and Hippocampal (Hpc) groups. Error bars indicate ±standard error of the mean.

Spatial Working memory. The performance by the Sham and Hippocampal groups, over the four trials of a session, collapsed over the five sessions of training is shown in Figure 4.10. Both groups spent a similar amount of time searching for the platform on trial one, but then showed a decrease in latency over the other three trials of training. The Sham group showed a more rapid decrease in latency than did the Hippocampal group, and this difference was most prominent for trial two. An analysis of variance of the first two trials reflected this difference between the rate of acquisition for both groups with a trial by group interaction, $F(1,9)=7.19$, $p<0.05$. There was a significant effect of trial, $F(1,9)=15.66$, $p<0.01$, but no significant effect of group, $F(1,9)=3.47$. Simple main effects analysis of the trial by group interaction revealed that there was a significant effect of trial for the Sham group, $F(1,9)=20.2$, $p<0.01$, but not for the Hippocampal group, $F(1,9)=0.89$. Also the Sham group were significantly faster to locate the platform than the Hippocampal group on trial two, receiving lesions of the hippocampus. In the present experiment rats were trained on the task before receiving lesions to the hippocampus. It could be argued from the revised 'configural association' theory of Rudy and Sutherland (1995) that the lack of a deficit could be due to the configural associations necessary for learning of the transverse patterning discrimination being stored in the neocortex. Also, once acquired, the hippocampus' modulatory effect on the similarity of configural units may not being necessary for continued performance of the task. This explanation may explain to some extent why there was no effect of lesion on the transverse pattering task. However, it must also be noted that performance by both groups dropped to a level that was close to chance after surgery, therefore, it appears the task was reacquired by groups. According to the revised 'configural association' theory of Rudy and Sutherland (1995) acquisition of the transverse patterning task should require the integrity of the hippocampus.

Another factor that may account for the differences between the experiment reported here and the data reported by Alvarado and Rudy (1995b) is that the pattern of acquisition of the three discriminations in the transverse patterning task by the control rats of Alvarado and Rudy (1995b) and by the rats of the present experiment, prior to surgery (see Experiment 5, Chapter Two) is markedly different. Both the experiment by Alvarado and Rudy (1995b) and Experiment 5 (Chapter Two) used a progressive method of training of the three discriminations. In the experiment by Alvarado and Rudy (1995b) performance on the third discrimination started at a level that is not below chance, whereas in Experiment 5 (Chapter Two) performance starts at a level that is considerably below chance. This difference may be due to the tasks being learned in qualitatively different manners. It appears in Experiment 5 (Chapter Two) that until the third discrimination is acquired, rats acquire the discriminations by

F(1,16)=9.29, p<0.01, but there was no significant difference between the groups on trial one, F(1,16)=0.001.

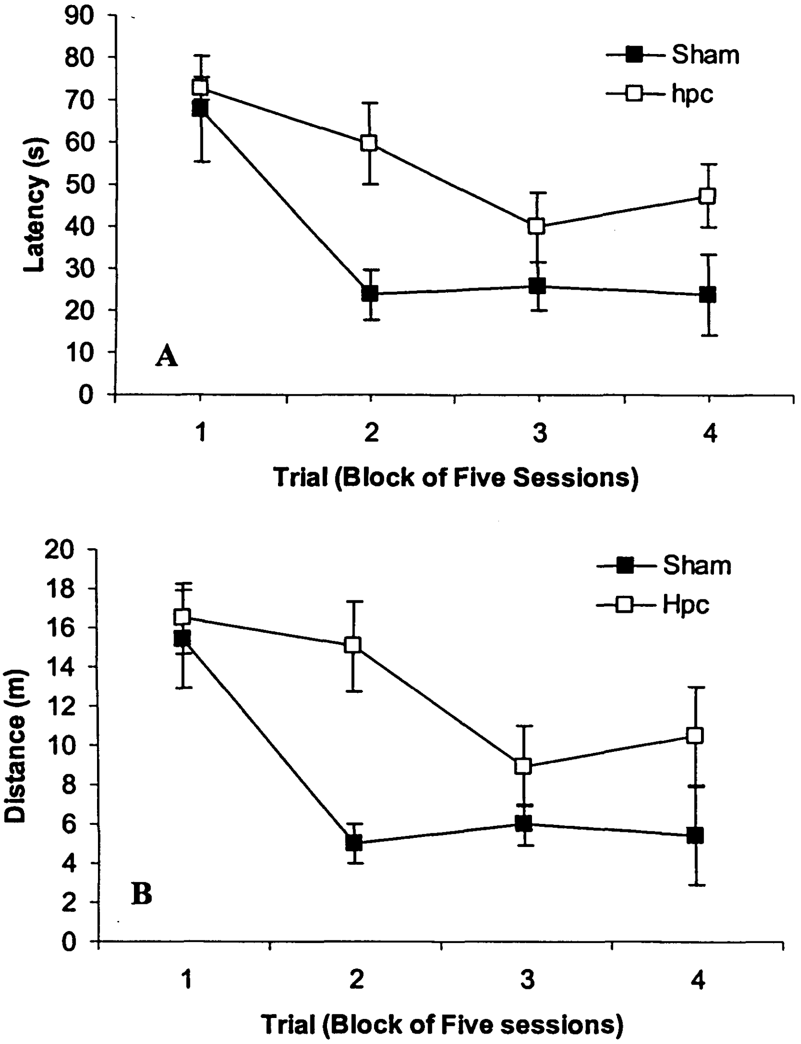

Figure 4.10. Performance of a spatial working memory task in the Morris water maze by the Sham and Hippocampal groups. The mean latency to locate the hidden platform is shown in section A, and the mean distance travelled is shown in section B. Error bars indicate ±standard error of the mean.

Analysis of variance of the distance travelled to locate the hidden platform reflected the findings from the latency to locate the platform. There was a significant effect of elemental learning. This is evident by the negative transfer of learning to the third discrimination, implying a reversal of learning of elemental associations. The control rats in the experiment by Alvarado and Rudy (1995b) do not show negative transfer of learning to the third discrimination. Alvarado and Rudy (1992) claim that learning of the second discrimination, in the transverse patterning task, encourages a configural solution to the third discrimination. This is due to the ambiguity of the stimulus that has been negatively rewarded in the first discrimination, and positively rewarded in the second discrimination (ie. Stimulus B is non-rewarded when present with A, but subsequently is rewarded when presented with C), and thus, rats adopt a configural strategy, because an elemental strategy cannot learn that a stimulus has two different associations when placed in compound with other stimuli.

The assumption that training on the second discrimination in a transverse patterning task encourages a configural solution of subsequent discriminations is supported by the findings of Alvarado and Rudy (1992). The results of this experiment are shown in Figure 4.11. In this experiment, a group of rats were trained on a A+ B- discrimination, and then received concurrent training of A+ B- and B+ C-. Another group of rats were trained on the A+ B-discrimination, but then received concurrent training of A+ B- and D+ C-. In the third stage of training both groups were required to learn a C+ A- discrimination whilst still receiving training of the previous discriminations. It was found that the group that had received training of B+ C- discrimination showed a higher level of performance on the C+ A- discrimination than the group that had been trained on the D+ C- discrimination. The group that had been trained on the D+ C- discrimination failed to acquire the C+ A- discrimination and performance of the other discriminations also declined. Alvarado and Rudy (1992) interpret this result as reflecting elemental learning. The group that was trained on the B+ C- discrimination acquired all three discriminations, thus demonstrating acquisition of the configural task, and also performance of the third discrimination (C+ A-) was facilitated, implying that a configural strategy had already been adopted prior to the presentation of the third discrimination.

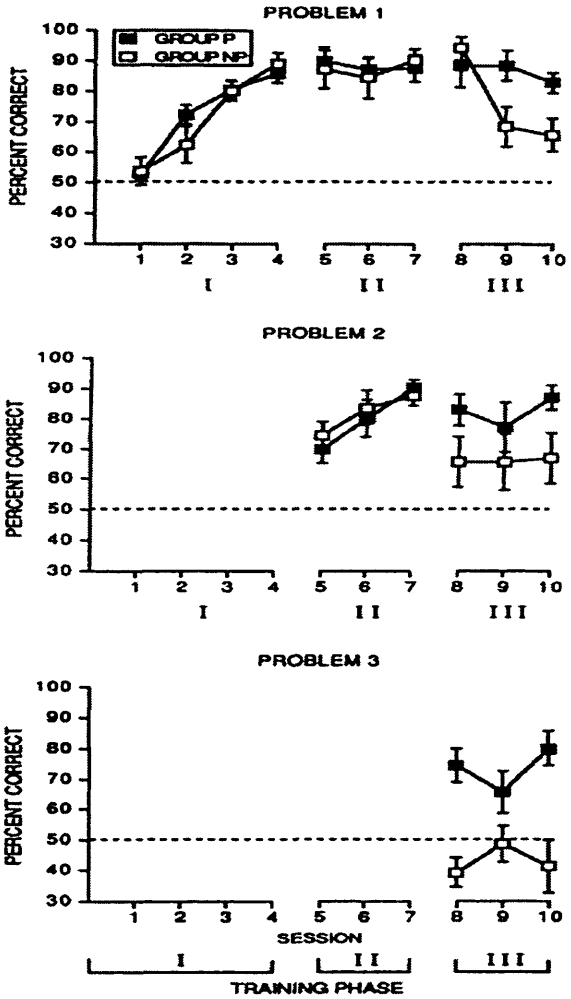

Figure 4.11. The acquisition of a transverse patterning discrimination (taken from Alvarado and Rudy, 1992). Group P were trained on a transverse patterning task (Phase 1: A+ B-, Phase 2: A+ B- and B+ C-, Phase 3: A+ B-, B+ C- and C+ A-). Group NP were trained on two elemental discriminations in the first two phases of training, and were trained on a reversal discrimination in the final phase (Phase 1: A+ B-, Phase 2: A+ B- and D+ C-, Phase 3: A+ B-, D+ C- and C+ A-).

turns the transverse patterning task into a structural discrimination in which rather than AB having to be discrimination from BA, AB-go left has to be discriminated from AB-go right, and BA-go right has to be discriminated from BA-go left. If learning of the transverse patterning task takes this form then it would be predicted that lesions of the hippocampus would impair performance of this task.

It is possible that in the experiments of Alvarado and Rudy (1995a; 1995b) impairments were found on a transverse patterning task, following hippocampal lesions, due to the task being treated as a structural discrimination. However, it is not possible to make the distinction between the use of approach/avoidance responses and conditional responses in the solution of a transverse patterning task in the experiments of Alvarado and Rudy (1992; 1995a; 1995b) and in the experiment reported here (Experiment 5, Chapter Two). Analysis of the strategies that animals use to solve transverse patterning tasks under different conditions may help to reveal when the hippocampus is required for learning of such a task.

Similar to the findings of Experiment 7 (Chapter Three), hippocampal lesions did not result in an impairment on a spatial reference memory task in the Morris water maze. However, when the rats were transferred to a working memory version of the task, in which the location of the hidden platform changes location session by session, it was found that hippocampal lesioned rats were impaired. An effect of lesion may have been found on the working memory task rather than on the reference memory task due to the greater demands of the task. Rats are required to learn a new spatial location every session, and previously learnt locations undergo extinction of learning. Even though lesioned rats were not impaired on the reference memory task their performance on average was worse than the Sham group. If the hippocampal lesioned feature of the compound stimulus whilst withholding a response to the other component feature of the compound, (i.e. approach versus avoidance). In the structural discrimination, reinforcement was dependent on animals making a response to a compound whilst withholding a response to another compound, rather than responding to an individual feature of a particular compound. It is possible that the learning required by these tasks is qualitatively different, and this raises the possibility that the hippocampus is simply required for responding to compound stimuli in a configural discrimination. To examine this possibility rats were trained on a biconditional discrimination (AB+, CD+, AD-, CB-).

Normal rats were trained on a biconditional discrimination (see Experiment 6, Chapter Two). After acquisition of the task the rats were divided into two groups. One group received hippocampal lesions (Hippocampal) and the other group received the same surgical procedures, but no damage was caused to the hippocampus (Sham). The two groups were then tested on their ability to perform the biconditional discrimination.

Method

Subjects. The subjects were 14 male Dark Agouti rats (Harlan, UK). Rats had previously been trained on a biconditional discrimination prior to training (see Experiment 6, Chapter Two for details). Prior to and during the experimental procedures animals were allowed free access to food and water. They were housed in pairs in a room that was illuminated for 14.5 hours per day. All testing was carried out during the period of light at the same time each day. All procedures were in accordance with the United Kingdom Animals (Scientific Procedures) Act, 1986.

rats were impaired due to an initial retardation in learning, it is possible that the reference memory task may have masked the difference between the groups, and the working memory task may have been a more sensitive test.

It must also be noted that whilst the hippocampal lesioned rats were not impaired on the reference memory spatial task, the control group performed poorly on the task compared to other reported results on the same task. Morris et al. (1982) found that after ten sessions of training, control rats were taking approximately 15s to locate the platform. Also, Bussey et al., (1998) reported similar levels of performance after ten sessions of training in sham lesioned Dark Agouti rats. In the current experiment, after ten sessions of training control rats were taking approximately 30s to locate the platform. Therefore, the lack of impairment may be due to the unusually poor performance of the Sham group.

Experiment 10a

In Experiment 9 it was found that hippocampal lesions did not impair performance of a transverse patterning discrimination. When rats were presented with the same stimuli that were used for the transverse patterning task arranged in a manner so that the task required the structural features of the compounds to be discriminated, it was found that hippocampal lesions impaired performance (Experiment 8, Chapter Three). Although, a lack of impairment on the transverse patterning could be due to the structural features of the compound stimuli not being necessary for solution of the task, there were other demands in the two tasks that could have influenced whether an effect of hippocampal lesion was seen. One factor is that in the transverse patterning task, reinforcement was dependent on animals making a response to a component

In contrast, performance on the third discrimination, in Experiment 5 (Chapter Two), started below chance, but increased until all three discriminations were solved. It is possible that in this experiment rats were using an elemental solution to solve the task until faced with the third discrimination in which the elemental solution was no longer appropriate. This may have a consequence in reflecting qualitative differences in the acquisition of the transverse patterning task, between the present experiment and that reported by Alvarado and Rudy (1995b). The control rats in the experiment of Alvarado and Rudy (1992) may have adopted a configural strategy earlier in the acquisition of the task that facilitated performance. In contrast in the present experiment, the perseveration of an elemental strategy until the third discrimination was introduced may have retarded the acquisition of configural associations, consequently masking differences between the hippocampal lesioned rats and the control group.

Another possibility is that the difference between task acquisition in the experiment of Alvarado and Rudy (1992) and the present experiment may be due to qualitative differences in the encoding of the configural task. In the experiment by Alvarado and Rudy (1995b) performance may have not been below chance because the compound stimuli may have been associated with a unique cue. This would result in less generalisation from the previously learnt discriminations, when the stimuli are presented in new compounds, as the configurations would fail to activate the unique cue. In the present experiment, because generalisation of learning occurs when previously learnt stimuli were presented in new compounds, it is possible that the compounds were not associated with unique cues and the task was solved by forming representations of unique configurations of the stimuli themselves. Even so, learning of unique configurations formed by stimuli is more similar to the account of learning compound stimuli's associations that Sutherland and Rudy (1989) describe than the learning of unique cues. This is because a unique cue account of configural learning allows for the unique cue to form linear associations with a US (Rescorla, 1973), and therefore, learning of this manner according to Sutherland and Rudy (1989) should not require the integrity of the hippocampus.

Although there may be factors that could account for different effects of hippocampal lesions on a transverse patterning task, the present experiment supports the hypothesis that the hippocampus plays a selective role in the processing of structural information, rather than the featural information of configural stimuli.

The conclusion that the task requires configural learning assumes that the task was solved by the approach and avoidance of cues within a configuration, rather than the initiation of conditional 'go left' and 'go right' responses to the presentation of configurations. Nissen (1953) suggested that a transverse patterning task could be solved by learning 'go left' responses to the following compounds: AB, BC and CA. For the mirror image of the compounds a 'go right' response would be required. If rats learn the structural discrimination by the use of conditional left and right responses, the task would only be soluble by encoding of the structural features of the stimuli. For example, the AB compound can be presented in two manners. Firstly, if A is presented to the left of B (AB), a conditional response strategy would be to go left (towards A). Secondly, if A is presented to the right of B (BA), the correct response is to go right (towards A). Therefore, learning of the A+ B- discrimination, may take the form of AB-go left, BA-go right, and consequently requires the structural information in the two variations of the AB compound to be learned. The conditional response strategy for learning applied to all three of the discriminations

Surgery. Surgical procedures for hippocampal lesions were identical to the methods used for Experiment 9 with the exception that for the co-ordinate sites AP: -5.6, ML: ±4.9, DV: -7.5, and AP: -5.9, ML: ±4.8, DV: -6.5 the radiofrequency probe was raised to a temperature of 70°C for 90s. The duration was increased for the purpose of causing a more consistent amount of damage to the most ventral areas of the hippocampus. The Sham lesions followed the same procedure as for the hippocampal lesions with the exceptions that the probe was only lowered to a depth of -1.7 from the top of cortex and the temperature of the tip of the electrode was not raised.

Histology. The histological methods were same as the procedures used in Experiment 8 and 9.

Apparatus. The apparatus used was the same as used for Experiment 6 (Chapter Two).

Biconditional discrimination stimuli. The stimuli were the same as used for Experiment 6 (Chapter Two).

Simple discrimination stimuli. One of the stimuli was the P stimulus that had previously been used in Experiments 8 (Chapter Three) and Experiment 9 (Chapter Four). The other stimulus was a white diablo shape (D), superimposed on a black background (28cm by 28cm). Stimulus D consisted of two white right angled triangles that both had a hypotenuse of 28cm and two shorter sides that were both 20cm in length. One of the triangles was placed with its hypotenuse at the bottom of the square. The other triangle was placed with its hypotenuse at the top of the square, so that it was pointing downwards. The right angled corners of the two triangles met in the centre of the square, thus leaving the visible black background to form two black triangles of identical proportions to the white triangles.

Behavioural Procedure. *Pre-operative training of the simple discrimination.* Rats received three sessions of training on the simple discrimination (P+ D-). Each session consisted of 18 trials. Stimuli were presented simultaneously, an equal amount of times in either the left or right goal areas. For half the rats the platform was always present underneath the P stimulus. For the remaining rats the platform was always present underneath stimulus D. Training of the simple discrimination commenced during the last three days of pre-operative training of the biconditional discrimination. A session of simple discrimination training commenced immediately after a session of training on the biconditional discrimination (see Experiment 5, Chapter Two).

Post-operative testing. Post-operative testing began once all animals had at least ten days of recovery after surgery.

Stage one of testing consisted of four sessions of thirty trials of the simple discrimination (P+ D-).

Stage two consisted of ten sessions of 24 trials of the biconditional discrimination. The 24 trials consisted of six trials of each discrimination (BW+ BH-, BW+ CW-, CH+ BH-, CH+ CW-), so that each pattern was presented a total of 12 trials per session. Discriminations were presented in a random order, with the constraint that a pattern could not be presented on more than three consecutive trials. On every fifth trial the simple discrimination (P+ D-) was presented, so that in total it was presented six times per session. Therefore, each session consisted of 30 trials in total.

Results

Histology. The extent of the lesions are depicted in Figure 4.12. One rat had damage that was confined to the dorsal hippocampus and the ventral hippocampus was completely spared. This rat's data were removed from the final analyses since the damage was not substantial. All remaining hippocampal lesioned rats had large lesions of the dorsal hippocampus, except for one rat with slight sparing of the dentate gyrus. One rat also had sparing of the dorsal subiculum. In the majority of cases the lesions did not include the fornix, but one animal had substantial damage to the fornix and two animals had unilateral fornix damage. All animals had substantial damage to the fimbria, although this was only unilateral in one case. All animals had damage to the ventral hippocampus, but in three cases there was a large amount of unilateral sparing of the posterior parts of the ventral hippocampus. In these cases there was substantial shrinkage in these areas. One rat also had minor cell loss in the most dorsal thalamus.

Three rats had incidental damage to the cortex overlying the hippocampus. The extent of cellular damage to the neocortex was similar in the control group that received sham surgeries. Damage was limited in both groups to areas of the parietal cortex, whilst one rat in the sham group had minor damage to the visual cortex.

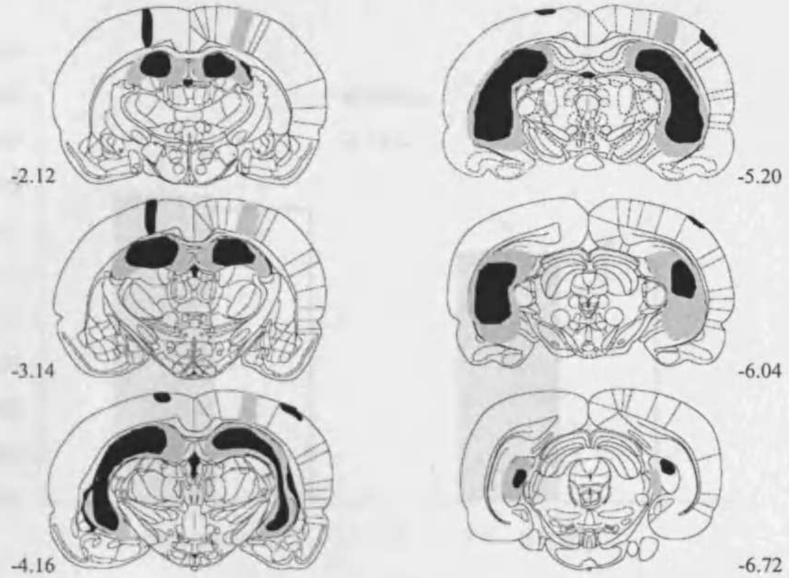

Figure 4.12. Coronal sections illustrating the extent of the largest (grey) and the smallest (black) lesions of the hippocampus. Distances are posterior to bregma (Paxinos and Watson, 1997).

***Behavioural Testing**. Simple Discrimination.* The performance of the biconditional and simple discrimination for the last three sessions of pre-operative training for the Sham and Hippocampal group is shown in Figure 4.13. The groups were matched for their pre-operative performance, and did not statistically differ, F<1.

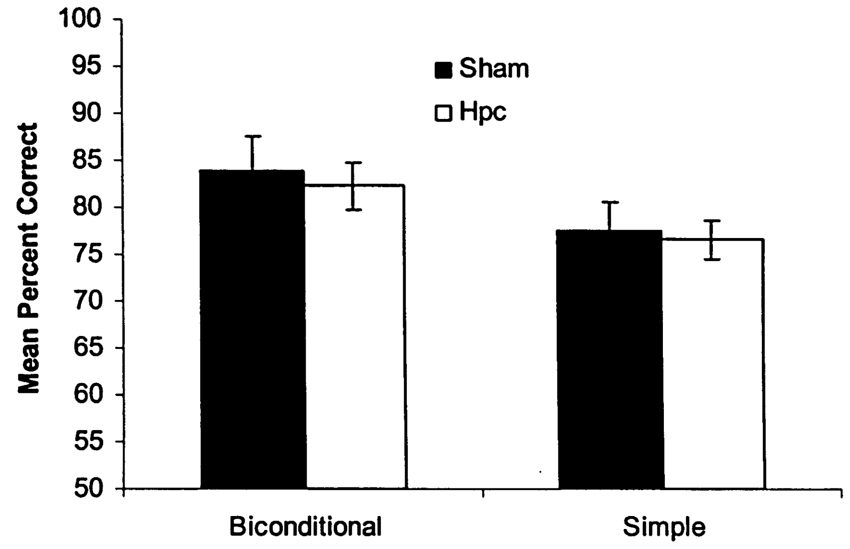

Figure 4.13 The pre-operative performance of the biconditional and the simple discrimination for the Sham and Hippocampal (Hpc) groups. Error bars indicate ±standard error of the mean.

The mean percent correct for the post-operative testing of the simple discrimination (P+ D-) for both groups are shown in Figure 4.14. While both groups started at a level of performance lower than their final pre-operative levels, this was most evident in the Hippocampal group who initially performed at a lower level than the Sham group. The Hippocampal group quickly relearned the discrimination and the two groups' performance converged. Analysis of variance revealed that there was not a significant effect of group, F(1,11)=0.7. There was, however, a significant effect of block, F(6,66)=15.92, $p<0.05$, and the interaction between block and group approached significance, F(6,66)=2.09 ($p=0.066$). Simple main effects analysis revealed that the Hippocampal group performed at a lower level than the Sham group on the first block of training, F(1,67)=8.07, $p<0.05$, but the two groups did not differ for the rest of training.

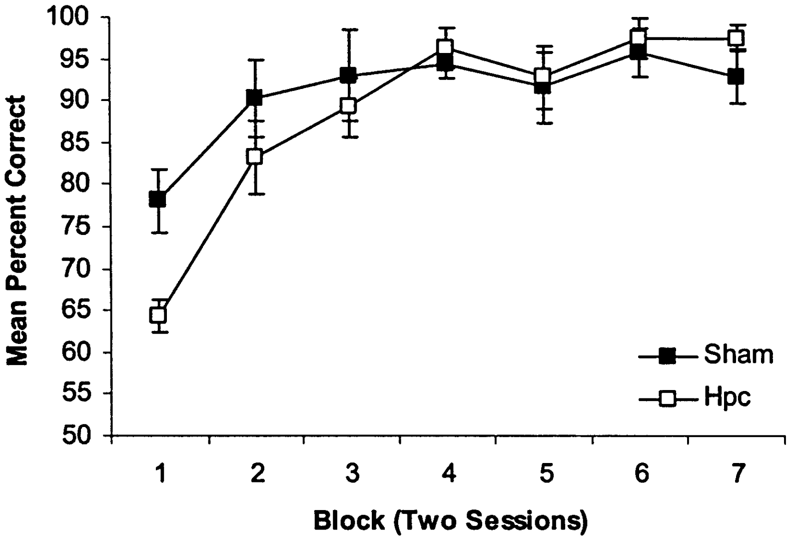

Figure 4.14. Performance on the simple discrimination by the Sham and Hippocampal (Hpc) groups. Error bars indicate ±standard error of the mean.

Biconditional Discrimination. The mean percent correct for the biconditional discrimination for both groups is shown in blocks of two sessions in Figure 4.15. Performance by both groups began above chance level, but was considerably lower than their pre-operative performance. Over the course of training, both groups' performance increased until they reached an asymptotic level that was similar to their pre-operative performance. Both groups showed a similar rate of acquisition of the task. An analysis of variance revealed that there was a significant effect of block, F(4,44)=20.67, but no significant effect of group, F(1,11)=0.63, and these factors did not significantly interact, F(4,44)=1.18. One sample t-tests performed on the data from the last block of testing confirmed that both groups were performing significantly above chance: Sham, t(5)=10.32, $p<0.001$; Hippocampal, t(6)=21.0, $p<0.001$.

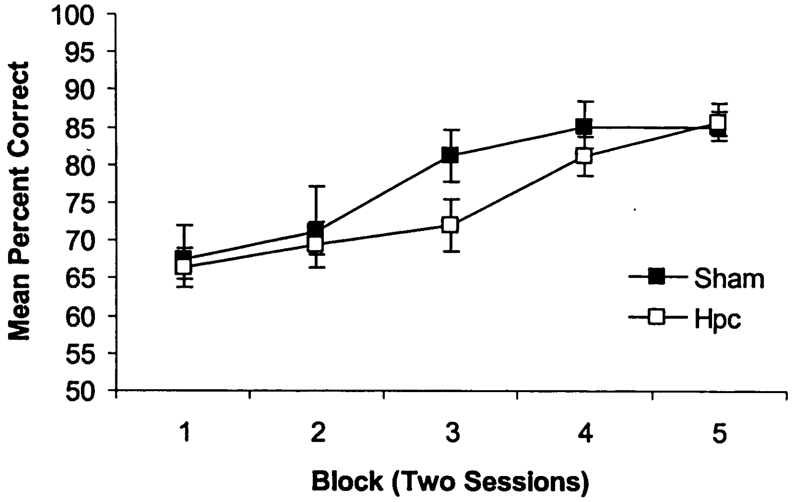

Figure 4.15. Performance by the Sham and Hippocampal (Hpc) groups on the biconditional discrimination. Error bars indicate ±standard error of the mean.

Discussion

It was found that hippocampal lesions did not impair relearning of the biconditional discrimination. Performance by both groups started at a level below their pre-operative performance, but the task was reacquired to a level similar to their pre-operative performance. The results of this experiment did not show that hippocampal lesioned rats are impaired at responding to compound stimuli in a configural discrimination. The differences in the effect of hippocampal lesions on a structural discrimination and a transverse patterning task can not be attributed to differences in demands on the tasks. In both the structural and biconditional discrimination rats were required to respond to compound stimuli in a simultaneous discrimination. Therefore, it can be concluded that the impaired performance of hippocampal lesioned rats on the structural features, correct performance on the task was contingent on their presence. It can be inferred from the findings of Wan et al. (1999) that processing of structural features may occur automatically. Wan et al. (1999) found that neurons in the hippocampus responded to changes in spatial relationships between features in a visual array. This effect was seen even though animals were behaviourally passive. Therefore, even though encoding of the structural features of the compound stimuli in the biconditional discrimination was not required, it could be assumed that normal rats will have encoded the structural features, whereas hippocampal lesioned rats will not have encoded the structural features to the same extent as control rats.

To test the prediction that structural encoding is an automatic process the two groups received continued training on the biconditional discrimination, but also received trials in which the same compounds are presented but with the spatial relationship between the component stimuli reversed. Compounds were reinforced in the same manner as they were in the biconditional discrimination. Therefore, animals now received training on the previous BW+, CH+, BH-, CW- discrimination, and also received training on the same compounds, but with novel structural features: WB+ HC+ HB- WC-. If the compound BW is encoded as BL-WR (where L refers to left and R right) then it can be predicted that when presented with WL-BR there will be a generalisation decrement between the transfer of learning of these two compounds. If BW is encoded as a configuration composing of the features B and W regardless of their structural features, then when presented with the compound WB there should be total generalisation of learning to this new compound. It is predicted that there will be greater generalisation of learning to the biconditional compounds with novel structural features for the hippocampal lesion group than for the control group.

structural discrimination is most likely due to a deficit in processing the structural features of configurations.

The lack of a deficit on the biconditional discrimination mirrors the effects seen by others on biconditional discriminations using cross-modal stimuli (Whishaw and Tomie,1991; Murphy, McDonald, Guarraci, Gotler, Baker and White, 1993). These experiments form a body of work that fails to show support for the 'configural association' theory of Sutherland and Rudy (1989). In the revised theory proposed by Rudy and Sutherland (1995) it is claimed that hippocampal lesion deficits may possibly not be seen on a biconditional discrimination due to the amount of conflict between the associative strengths of the configurations and the associative strengths that the individual stimuli possess. It is claimed that configural tasks that compose of elements that have associative strengths that are in conflict with the associative strength of the configurations will require the integrity of the hippocampus. In configural tasks in which the elements themselves do not have any associative strength, as in the biconditional discrimination, there will be less conflict between the elemental and configural associative strengths (Rudy and Sutherland, 1995). Therefore, the results of Experiment 10a can be accounted for by the revised 'configural association' theory (Rudy and Sutherland, 1995) but these results do not support the original notion of the hippocampus being necessary for learning and storage of configural associations (Sutherland and Rudy, 1989).

Experiment 10b

It was found in Experiment 10a that hippocampal lesions did not impair performance of a biconditional discrimination. Even though the compound stimuli contained

Therefore, the hippocampal lesioned rats should perform at a *higher* level that the control rats on the new biconditional discrimination that has novel structural features.

After testing the biconditional discrimination both groups were trained on two tasks that require the integrity of the hippocampus: spatial working memory (in a Morris water maze), and T-maze alternation.

Method

Behavioural procedure. Five sessions of testing were performed in which subjects received 12 trials of the biconditional discrimination and 12 probe trials in which the same biconditional discrimination was presented but the structural relationship between the component stimuli in the patterns was reversed. The design of Experiment 10b is depicted in Figure 4.16. For subjects that had been reinforced to approach BW and CH, and non-reinforced for approaching BH and CW, on probe trials they were now reinforced for approaching WB and HC and non reinforced for approaching HB and WC. To ensure counterbalancing, half of the rats were initially trained with the WB, HC, HB and WC compounds, and during probe trials they were presented with the BW, CH, BH and CW compounds. Trials of the biconditional discrimination and the probe discrimination were presented in a random order, with the constraint that two trials of the same discrimination type (i.e. biconditional or probe) could not be presented on more than two consecutive trials.

The simple discrimination (P+ D-) was presented every fifth trial of each session, in the same manner as for the testing in Experiment 10a.

T-Maze Alternation

Apparatus. The arms of the maze had wooden floors and transparent Perspex walls that were 10cm wide and 17cm high. The apparatus was a modifiable cross maze, so that one arm could be blocked to create a T-maze. The maze consisted of two arms that were 140cm long with food wells at each arm that were 2cm in diameter and 0.75cm deep. The arms of the maze intersected in the centre of each other, thus creating four arms, 70cm long. Both the South and North facing arms had guillotine doors 25cm from the end of the arms, so as to create a start area to contain an animal. The maze was supported by a stand that was 94cm high. The maze was positioned in the centre of a room 3m by 3m. There were posters on all four walls of the room, and a table was positioned along one of the walls.

Procedure. The rats were food deprived and maintained at 85% of the free-feeding weight. Rats received several days of pre-training before testing began. Pre-training ended once all animals would reliably run down a start arm to collect food reward from the food wells in the two choice arms.

A trial consisted of a forced run, in which a choice arm was blocked so that a rat would be forced either left or right. In the food well at the end of the arm was a food sucrose pellet (45mg, Sandown Instruments). Once the food had been eaten, the rat was then placed back in the start arm, where it was temporarily held by the guillotine door. The blocked choice arm was then reopened and then the rat would be allowed to make a choice between the arm it had previously visited and the arm it had not visited. The arm that had not previously been visited on the forced run was always baited on the choice run. The retention interval between the forced choice run and the choice run was 10s. Both choice arms were baited before the start of a trial so that the experimenter could provide no cues as to which arm was baited during the choice run. An animal was deemed to have made a choice if their hind feet had entered into an arm. If an animal made an incorrect choice it was retained in that arm for 10s before being removed from the maze. All trials in stage 1 were run with the start arm being the south arm.

The groups received six session of testing, one per day. A session consisted of six trials. Once a rat finished a trial it was placed back into the holding box and an interval of approximately four minutes elapsed before the next trial commenced. Animals received three trials in which they were rewarded for alternating to the right and three trials that were reinforced for alternation to the left. These types of trials were presented in random order with the constraint that reward for alternation could not appear in the same location on more than two consecutive trials.

The trial types used for Stage Two of training are depicted in Figure 4.17. In stage two there were five sessions of eight trials. Four trials were run the same as in the previous stage of testing, but for two of these four trials the North arm was used as the start arm. The other four trials were probe trials in which animals received a forced trial starting from either the North or the South arm, and then the choice trial was run starting from the opposite arm. Therefore, if an animal was forced left (East arm) from the South arm, then in the choice trial they would start from the North arm and be reinforced for turning left (West arm). For all trial types turning left was reinforced as often as turning right, and trials began from the South arm as often as they began from the North arm. Trials were run in a random order, with the constraint that there could not be more than two trials of the same type in consecutive order.

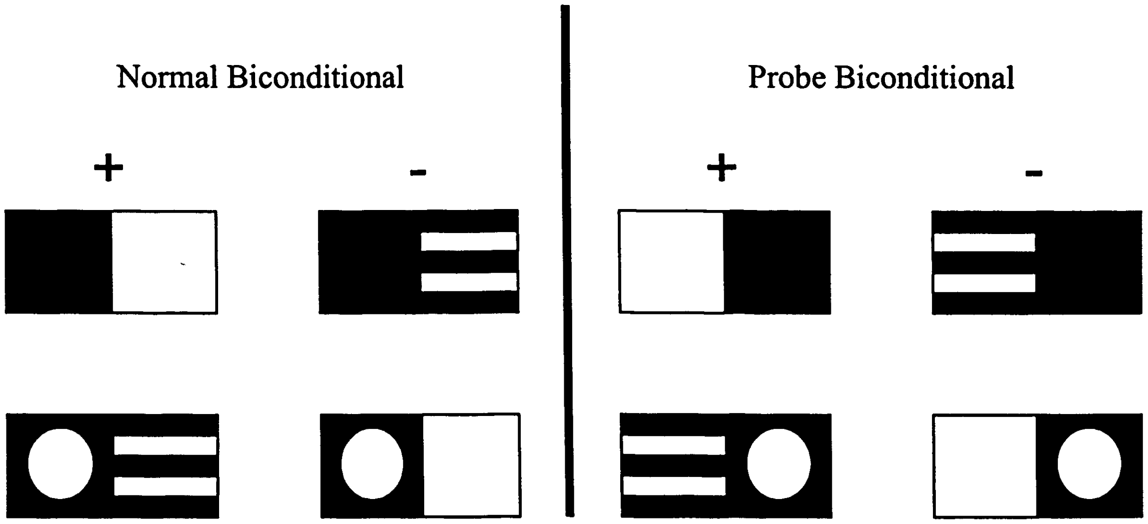

Figure 4.16. The design of Experiment 10b. Rats received continued training on a biconditional discrimination (depicted in the left-hand column) whilst receiving probe trials in which the biconditional discrimination was presented, but the structural features of the stimuli were reversed (depicted in the right-hand column).

Spatial working memory

Apparatus. The apparatus was the same as used for Experiments 8 (Chapter Three) and 9 (Chapter Four).

Procedure. Rats received eight sessions of training to locate a hidden platform that remained in a constant location within a session, but changed location for every session. An animal could be released into the pool from eight possible start locations, positioned at an equal distance from each other around the wall of the pool. Subjects received one session of training per day. Each session consisted of four trials. For the first two trials the start location was kept the same, but for the last two trials the start positioned changed to different locations. The start location order was random with the constraint that a start location could not be used more than once per session.

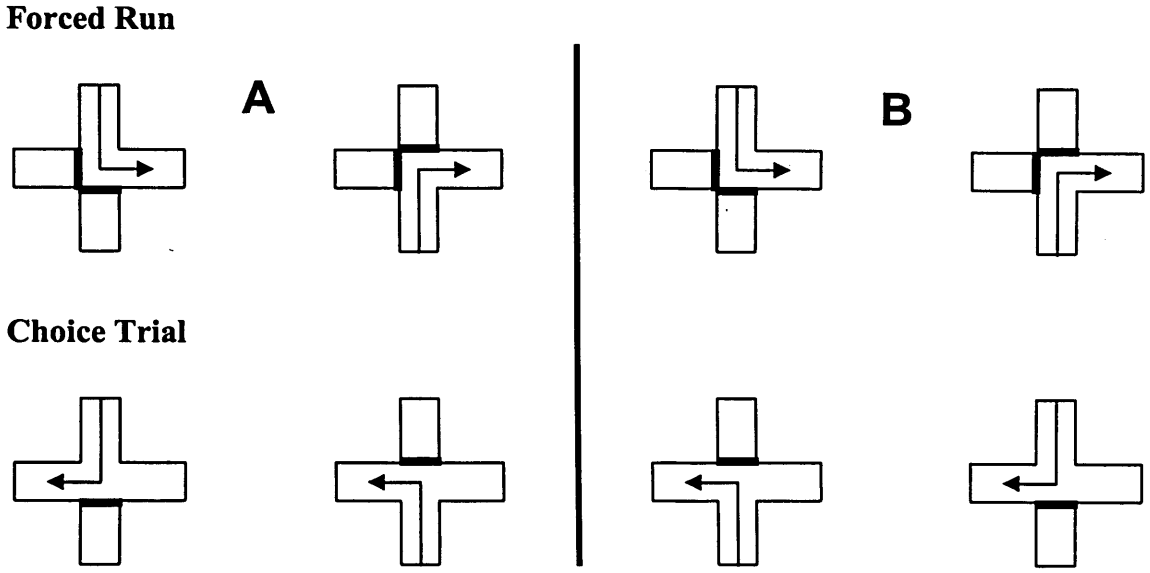

Figure 4.17. T-maze alternation trial types for Stage Two of training. Section A shows examples of the normal trials. The correct choice on a trial is depicted underneath the examples of forced runs. Animals were released from either the North or South arm for both the forced run and choice trial. Reinforcement was given for choosing the arm not previously visited. Section B shows examples of the probe trials. Animals were released from either the North or South arm on the forced run, and released from the opposite arm on the choice trial. Reinforcement was given for choosing the arm not previously visited. On all trials only the North and South arms were used as start arms, and reinforcement was never provided in these arms. The arm opposite a start arm was always blocked on a choice trial.

Results

Simple discrimination. The performance of the simple discrimination (P+ D-) was maintained at a high level during the probe test sessions. The Sham group performed at a mean level of 89% correct and the Hippocampal group performed at a mean level of 97% correct. The two groups did not statistically differ on their performance of the simple discrimination, t(11)=1.9.

Probe biconditional discrimination. The performance of the probe discrimination is shown, as a proportion of the total correct performance on the probe and biconditional discriminations, in Figure 4.18. Both groups made less correct choices when presented with the probe biconditional discrimination than the normal biconditional discrimination. However, the difference between performance on the probe biconditional discrimination and the normal biconditional discrimination was greater for the Sham group than for the Hippocampal group. Performance of the normal biconditional discrimination was maintained at a high level, by both groups, throughout testing (Sham=79.44% correct, Hippocampal=79.52% correct), and did not significantly differ, t(11)=0.2. Both groups performed significantly above chance on the normal biconditional discrimination: Sham, t(5)=7.52, p<0.001; Hippocampal, t(6)=13.22, p<0.001. Due to the groups showing a similar level of performance on the normal biconditional discrimination, performance of the probe discrimination is expressed as proportion of total correct responses on both the probe and normal discriminations. The Hippocampal group made a significantly greater proportion of correct responses on the probe biconditional discrimination than the Sham group, t(11)=2.4, p<0.05. One sample t-tests revealed that both groups made significantly less correct responses on the probe discrimination than on the normal biconditional discrimination than would be expected from chance: Sham, t(5)=8.65, p<0.001; Hippocampal, t(6)=3.61, p<0.05. However, inspection of the raw scores from the probe discrimination reveals that both groups were performing the probe discrimination above chance: Sham=60.56% correct, t(5)=3.8, p<0.05; Hippocampal=69.20% correct, t(6)=6.7, p<0.001.

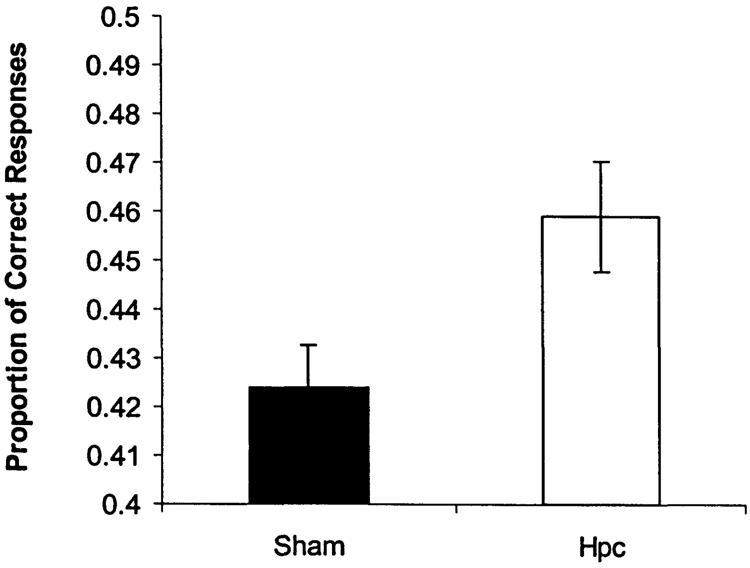

Figure 4.18. Proportion of correct responses made on the probe biconditional discrimination out of the total correct responses on the probe and normal biconditional discrimination, for both the Sham and Hippocampal (Hpc) groups. Error bars indicate ±standard error of the mean.

Spatial Working Memory. The performance on the spatial working memory task, blocked over the eight sessions, is shown in Figure 4.19. Both groups became proficient at locating the hidden platform over the four trials of training. Both groups showed a similar level of learning, and they did not appear to differ at any point of acquisition. Analysis of variance of the latency to locate the hidden platform data showed that there was no significant effect of group, F(1,11)=0.19, there was a significant effect of trial, F(3,33)=5.87, $p<0.01$, and no significant interaction of these factors, F(3,33)=0.08. Analysis of the distance travelled to locate the platform showed that similarly there was no significant effect of group, F(1,11)=0.004, and no significant group by trial interaction, F(3,33)=0.06.

***T-Maze Alternation*.** The mean percent correct for both groups for the six sessions of training is shown in Figure 4.20. Although the Hippocampal group appeared to be performing above chance, they were significantly less accurate than the Sham group, t(11)=5.55, p<0.001.

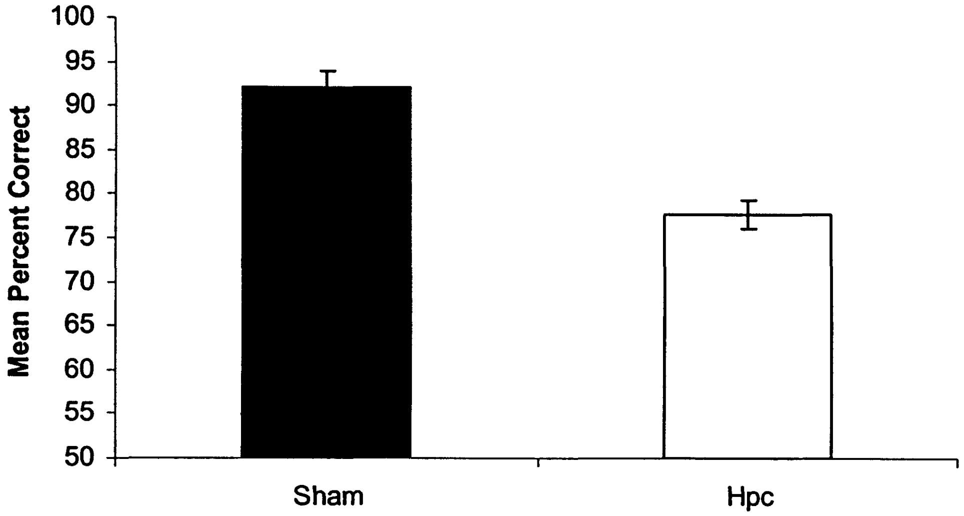

Figure 4.20. Performance on the T-maze alternation task over the six sessions of training for the Sham and Hippocampal (Hpc) groups. Error bars indicate ±standard error of the mean.

The mean percent correct for both the normal trials and the probe trials for each group are shown in Figure 4.21. Both groups performed at a lower level on the probe trials compared to the normal trials. Overall the Sham group performed at a higher level than the Hippocampal group for both tests. An analysis of variance revealed that there was a significant effect of group, F(1,11)=21.17, p<0.05, a significant effect of trial type, F(1,11)=19.85, but no significant interaction of these factors, F(1,11)=0.91. One-sample t-tests confirmed that both groups were performing above chance on both normal and probe trials: Sham (normal), t(5)=23.3, p<0.001, (probe), t(5)=10.31, p<0.001; Hippocampal (normal), t(6)=10.33, p<0.001, (probe), t(6)=4.36, p<0.01.

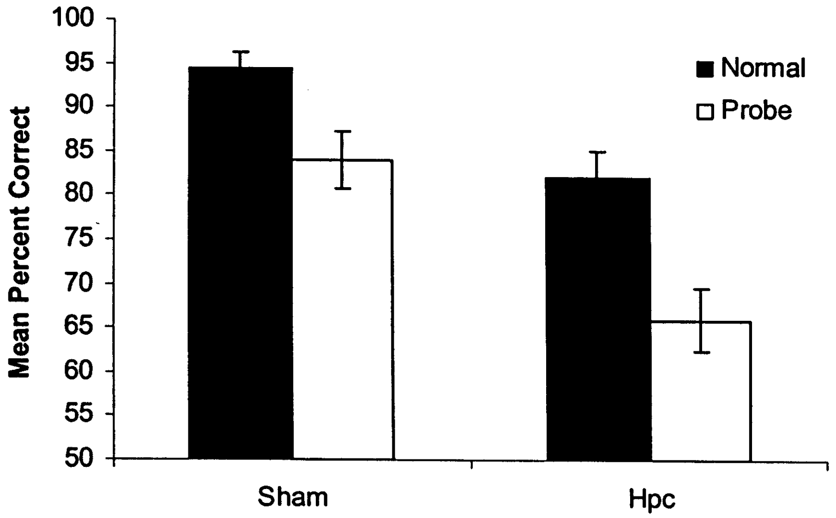

Figure 4.21. Mean percent correct for performance on the normal and probe trials of the T-Maze alternation task for the Sham and Hippocampal (Hpc) groups. Error bars indicate ±standard error of the mean.

Discussion

It was found that reversing the spatial relationship between the biconditional discrimination compounds, and thereby introducing novel structural features, caused a generalisation decrement, demonstrated by the transfer of learning, for both groups. However, the Hippocampal group showed greater generalisation to the probe discrimination than the Sham group. The greater generalisation for the hippocampal lesion rats provides support for the proposal that the hippocampus encodes spatial relationships between visual cues (Wan et al, 1999; Jenkins et al., 2004). The experiment also demonstrates through behavioural measures that the encoding of structural features appears to be automatic and does not require explicit discriminative training for the features to be learned about. There were no significant differences between the levels of performance of both groups on the biconditional discrimination

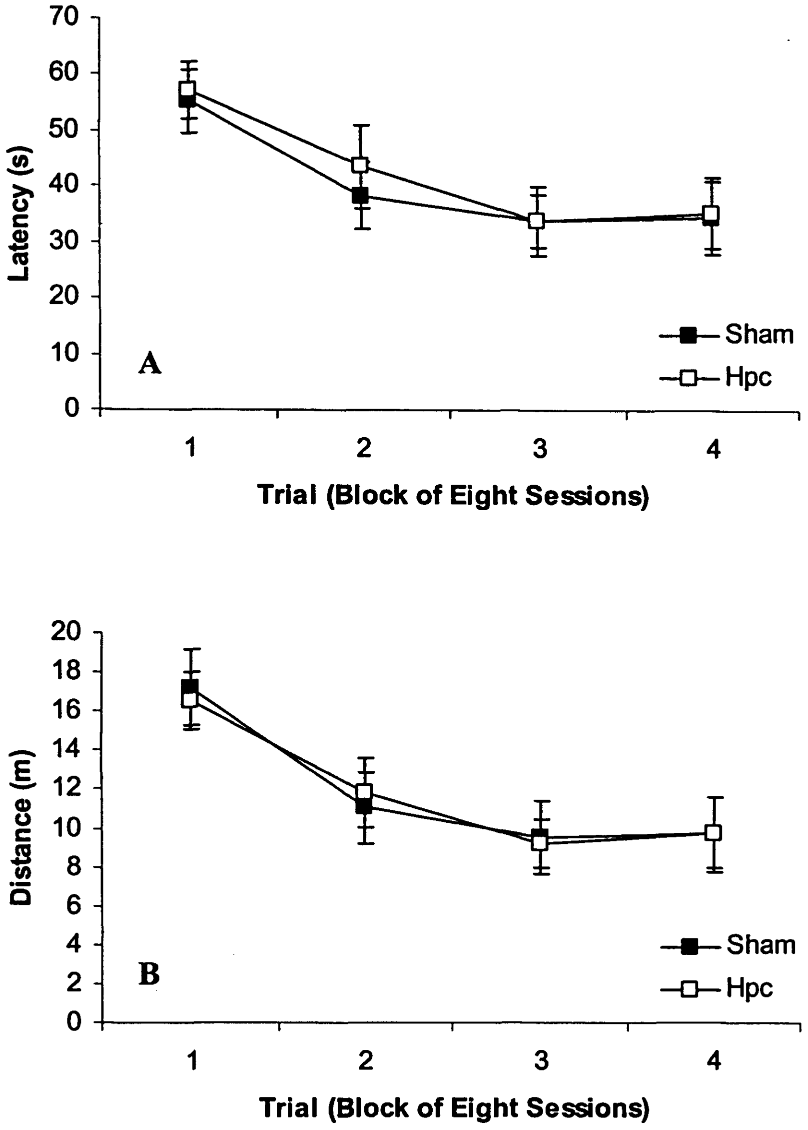

Figure 4.19. Performance by the Sham and Hippocampal (Hpc) groups on the spatial working memory task in the Morris water maze. The mean latency to escape from the pool for the four trials within a session (blocked over eight sessions) is shown in section A. The mean distance travelled to locate the hidden platform is shown in section B. Error bars indicate ±standard error of the mean.

(Exp. 10a) in which structural features were essential to the solving of the discrimination. Only when the same task was presented with novel structural features contained within the compounds, was there a significant difference between the groups' levels of performance.

Due to the novel structural features of the compounds resulting in a generalisation decrement for the Hippocampal group, it can be inferred that the hippocampus is not the only neuroanatomical region to process structural features in some manner. This may not necessarily be a surprising result, as both Wan et al (1995) and Jenkins et al. (2004) found that novel spatial arrangements of visual stimuli caused changes in the level of c-*Fos* in the parietal cortex and the postsubiculum, as well as for the subfields of the hippocampus. Although it is not clear whether lesions to these areas would have the same effect as hippocampal lesions, the additional sensitivity to novel spatial rearrangements may explain why hippocampal lesioned rats were able to perform the structural discrimination above chance (see Experiment 8), although at a lower level than of control animals.

In contrast to the findings of Experiment 9, it was found that hippocampal lesioned rats were not impaired on a spatial working memory task in a Morris water maze. In Experiment 9 it was found that hippocampal lesioned rats were not impaired on a spatial reference memory task, but when transferred to a spatial working memory, the rats were impaired. It was claimed that the working memory task may be a more sensitive test of hippocampal function in spatial learning. In the present experiment it was found that hippocampal lesioned rats were not impaired on a working memory spatial task. This is not because the hippocampal lesions were smaller in this experiment. Indeed, the changes to the surgical procedures ensured that the hippocampal lesions were more complete.

In the present experiment, hippocampal lesioned rats were found to be impaired on a T-maze alternation task. This result is consistent with other findings that demonstrate that T-maze alternation is a hippocampal dependent task, (Rawlins and Olton, 1982; Aggleton, Hunt and Rawlins, 1986). It was also found that when egocentric information was pitted against allocentric information both groups showed a reduction in performance, but still performed above chance. It is, of course, possible that hippocampal lesioned rats were still able to use odour or intra-maze cues to guide behaviour during the probe trials.

General Discussion

It was found that hippocampal lesions did not impair performance on two configural discrimination tasks. There was no effect of hippocampal lesions on a transverse patterning task, in which subjects were presented the same stimulus-compounds as for the structural discrimination, but solution of the task required discrimination of the featural information of the configurations rather than the structural features of the configurations. Also, hippocampal lesions did not affect performance on a biconditional discrimination that also required a configural solution. Whereas the transverse patterning task required responses to be made to particular components of the compound stimuli, the biconditional discrimination required responses to be made to the compounds themselves, in the same manner as the responses that had to be made to compounds in the structural discrimination. It can be concluded from these experiments that hippocampal lesioned rats were not impaired on a structural discrimination due to an inability to solve configural tasks. It appears that the deficit was due to impaired learning of the structural features.

Experiment 10b provides evidence to suggest that encoding of structural information is an automatic process, due to the generalisation decrement shown in the transfer of learning of compounds that contained the same features as in the biconditional discrimination, but with novel structural features. Hippocampal lesions lessened the effect of this generalisation decrement, as there was greater generalisation of learning to the new compounds. These results support the work of Wan et al. (1999) and Jenkins et al. (2004), by providing behavioural evidence for the sensitivity of the hippocampus to changes in spatial relationships between visual cues.

The results of these experiments have implications for the 'configural association' theory of the hippocampus, as proposed by Sutherland and Rudy (1989). They claimed that the hippocampus is responsible for the learning and storage of configural associations. In the present experiments, whilst the acquisition of these tasks was not directly tested, it can be seen that hippocampal lesions did not affect the post-operative performance of the transverse patterning task and the biconditional task. Rudy and Sutherland (1995) have postulated that configural associations may be stored in the neocortex, and the hippocampus plays a modulatory role in the acquisition of the configural associations. Therefore, the lack of impairment shown by lesioned animals on the two configural tasks may be due to the hippocampus being no longer required for the performance of the discriminations once they have been acquired. Although this is possible, in both experiments there was a clear relearning effect, as both groups reacquired the tasks. This evidence of equivalent new learning by both groups is contrary to the predictions of Rudy and Sutherland (1995). Rudy and Sutherland (1995) also claim that lesions of the hippocampus will most affect configural tasks in which the associative strengths of the individual stimuli are in conflict with associative strengths of the configurations. This account may explain why there was no effect of hippocampal lesion on the biconditional discrimination, due to the individual stimuli having an associative strength of zero. For the transverse patterning discrimination, even though individual stimuli are equally reinforced as non-reinforced, within the configurations, stimuli gain associative strength due to one stimulus being reinforced and the other being non-reinforced. The transverse patterning task should, on this basis, involve a high level of conflict between the associative strengths of the individual stimuli and the configurations Therefore, the lack of impairment on the reacquisition of the transverse patterning task after surgery does not support the predictions of the revised 'configural association' theory (Rudy and Sutherland, 1995). This result is consistent with the results of Bussey et al., (1998), Saksida et al., (2003) and Brasted et al., (2004), who also found that lesions of the hippocampal system do not impair acquisition of a transverse patterning discrimination.

It is important to note that the different effects of hippocampal lesions on configural and structural discriminations are not due to differences in the size of lesions. The size of hippocampal lesion in Experiments 9 and 10, in which there was no effect of lesion on a transverse patterning task and a biconditional discrimination, were typically more extensive than the size of lesions in Experiment 8, in which there was an effect of lesion on a structural discrimination.

To conclude, the data do not support the proposal that the hippocampus is responsible for the learning and storage of configural associations. This implies that the deficit in performance shown by hippocampal lesioned animals on a structural discrimination can not be explained in terms of an impaired ability to learn about configural associations. Also, the structural deficit is not likely to be due to the difficulty of the discrimination, as the performance of hippocampal lesioned rats did not significantly differ from the performance of control animals on two complex configural discriminations.

Chapter Five

General Discussion

5.1 Introduction

The experiments reported in this thesis have attempted to test whether a 'configural association' theory of the hippocampus (Sutherland and Rudy, 1989; Rudy and Sutherland, 1995) can account for the learning of certain non-linear discriminations. Whilst it was found that hippocampal lesions spared performance of two configural discriminations, it was found that hippocampal lesions impaired performance of a configural discrimination that required the discrimination of the structural features of the compound stimuli for the solution of the task. The 'configural association' account of hippocampal function (Sutherland and Rudy, 1989) does not account for the learning of certain discriminations by hippocampal lesioned rats, and thus the assumption that configural learning underlies allocentric spatial learning does not hold true. The novel prediction that damage to the hippocampus will impair performance of structural discriminations was supported. The results of the experiments reported in this thesis suggest that the hippocampus is not essential for learning of configural associations *per se*, but does play an important role in the learning and memory of the structural features of configurations of stimuli.

5.2 The hippocampus and learning the structure of configural stimuli

In Chapter Three two experiments were reported, demonstrating that hippocampal lesions impair performance of a previously acquired structural discrimination. The structural discrimination is a non-linear task; each element is equally reinforced and non-reinforced, but unlike most configural tasks, the unique configurations formed by the combinations of stimuli, still do not reliably predict reinforcement. Consequently,

(1996) rats were originally trained to either approach or avoid pairs of objects in a Y-maze apparatus. The pairs of objects were presented in a goal box at the end of an arm of the maze and were located in a constant position from each other in the goal box. Hippocampal lesioned rats were not impaired on this task. In a test phase the same pairs were presented, but now stimuli were rearranged so as to form their mirror image, by switching the locations of the objects. Both the hippocampal lesioned group and the sham control lesioned group showed a decrease in performance to this probe test, but the groups did not significantly differ from one another. According to the prediction that hippocampal lesioned rats will show greater generalisation of learning across spatial alterations, the probe test performed by Deacon and Rawlins (1996) should have resulted in facilitated performance by the hippocampal lesioned group. It is possible that learning of the structural features of the pair of objects did not occur due to the possible influence of elemental learning. This would appear unlikely due to the pairs of objects being learnt with regards their configuration, because each pair of objects was used previously in either a positive patterning or negative patterning task (Deacon and Rawlins, 1996). However, when the objects were moved, novel features of the objects may have been displayed which were not visible previously, therefore, the decrement in performance by both groups could be attributed to novelty of features rather than the novelty of structural features.

The results of Experiments 7, 8, 9 and 10 point towards the role of the hippocampus in the processing of structural features of configurations of stimuli. However, this analysis does not fit with other accounts of learning about configurations of stimuli. Eichenbaum, Matthews and Cohen (1989) trained fornix lesioned rats to discriminate between odour cues. Two odours were presented simultaneously, one from a location on the left and the other on the right. One of the odours was reinforced and the other odour was not reinforced. The location of presentation of the two odours was pseudo-randomised. Although impaired, fornix lesioned rats were able to acquire several pairs of odour discriminations, concurrently. In a test phase, reinforced and non-reinforced odours were presented in novel pairings. Whilst control rats maintained performance of the discriminations during the test phase, fornix lesioned rats' performance initially fell to chance level. Eichenbaum et al. (1989) concluded that control rats are able to learn about reward contingencies of a stimulus within a simultaneous discrimination trial, and also across trials. This assumes that novel pairings of rewarded and non-rewarded stimuli should have no effect on performance of the control rats. However, Eichenbaum et al. (1989) suggested that fornix rats may have originally learned each pair of odours as a configuration with regards to their spatial arrangement. Therefore, an odour pair, AB, could have been encoded as 'A to the left of B' or 'B to the left of A'. These different arrangements of the compound AB can be associated with go left/go right conditional responses that can lead to the solution of task. Consequently, when fornix rats are presented with novel pairings of reinforced and non-reinforced stimuli, performance falls to chance, as the task, learnt in this manner, is now not soluble.

The interpretation of the performance of fornix lesioned rats on novel pairings of stimuli learnt in a simultaneous discrimination by Eichenbaum et al. (1989) does not match well with the analysis of the present experiments. Eichenbaum et al. (1989) assume that fornix lesioned rats learn configurations of stimuli with regards to their structure, however, as reported within this thesis, when the ability to discriminate the structure of configurations is directly tested, by training on a structural discrimination (George et al., 2001), hippocampal lesioned rats are impaired on this task. In defence of the present results, in Experiment 8 a probe test was given in which rats were the task can only be solved by encoding the unique spatial structure of the elements within a configuration (George et al., 2001). From the evidence that the hippocampus is responsible for learning of spatial relationships between cues (Morris et al., 1982; Save et al., 1992), it was possible to confirm the novel prediction that hippocampal lesions would impair the performance of a non-linear discrimination in which spatial relationships are required to be learned.

In Experiment 10b it was found that hippocampal lesioned rats show greater generalisation of learning, compared to control rats, to a novel biconditional discrimination in which the same compounds as the original discrimination were presented but the structural features were reversed. Control rats discriminated between the compounds of AB, CD, AD and CB from the same compounds but with their structure reversed (BA, DC, DA and BC). Hippocampal lesioned rats showed significantly less change in performance between these two sets of compounds, demonstrating less discrimination. It can be concluded that control rats encoded, to a greater extent than hippocampal lesioned rats the spatial relationships between the stimuli, and this led to the poorer discrimination of configurations formed from the same elements but differing in their structure. The results of Experiment of 10b together with the results of Experiments 7 and 8, in which it was found that hippocampal lesioned rats are impaired on a structural discrimination, demonstrate the role of the hippocampus in encoding the spatial relationships between cues.

The results of Experiment 10b contrast with the findings of Deacon and Rawlins (1996) who found that hippocampal lesioned rats did not differ from control rats in a concurrent discrimination of positively or negatively reinforced pairs of objects that were spatially altered in the test stage. In the experiment by Deacon and Rawlins presented with novel pairings of the reinforced and non-reinforced configurations used for the structural discrimination. The probe test did not disrupt performance of the simultaneous discriminations, implying that rats were not making conditional go left/go right response to the pairings of configurations.

In contrast to the results of Eichenbaum (1989), Driscoll, Sutherland, Prusky and Rudy (2004) found that rats with hippocampal damage showed normal transfer of learning simultaneous discriminations to novel combinations of reinforced and non-reinforced stimuli. Driscoll et al (2004) trained rats on visual simultaneous discriminations using a water tank apparatus similar to the apparatus used in the present experiments. Therefore, there may be differences in the perception of visual and odour cues, and this may influence the effect of hippocampal damage. The fact that the fornix lesioned rats used in the study by Eichenbaum et al. (1989) were impaired at learning multiple simultaneous odour discriminations may reflect the impaired perception of the individual odours from their combined configurations. However, it is evident from the results of Driscoll et al. (2004) that hippocampal lesioned rats trained on simple visual simultaneous discriminations learn in an elemental manner that is not disrupted by novel pairings of stimuli, and thus do not learn conditional responses to the structure of the configurations of reinforced and non-reinforced stimuli

Gaffan, Bannerman, Warburton and Aggleton (2001) reported that fornix lesions facilitate discrimination of an array of visual cues from spatially rearranged version of the same cues. This contradicts the conclusions drawn from the present experiments. However, Gaffan et al. (2001) claim that the facilitation is due to the effect of fornix lesions narrowing attention. The control rats performed worse on the task due to non-reinforced. For the transverse patterning discrimination, elements within a configuration are either reinforced or non-reinforced. Therefore, for the structural discrimination, rats were required to choose between a reinforced or non-reinforced configuration, whereas for the transverse patterning task, a choice was required to be made towards one of the stimuli within a configuration.

To test whether the difference in the nature of the response was sufficient to account for the differences seen between hippocampal rats on a structural discrimination and on a transverse patterning task, the effects of hippocampal lesions were tested on a biconditional discrimination (Experiment 10a). The biconditional discrimination requires responses to be made towards configurations of stimuli rather than elements within a compound. The task is similar in this respect to the structural discrimination. Hippocampal lesions did not impair performance of a biconditional discrimination, therefore, the differences in whether a response has to be made towards a configuration or an element in a configuration does not account for the impairment seen on a structural discrimination (Experiments 7 and 8).

The results of Experiments 9 support other work that has found that damage to the hippocampus itself (Saksida et al., 2003; Brasted et al., 2003) or to the hippocampal system (Bussey, et al., 1998) does not impair learning of a transverse patterning discrimination. However, impairments have been seen with hippocampal lesions on a transverse patterning task (Alvarado and Rudy, 1995a; 1995b; Dusek and Eichenbaum, 1998). The procedures that were used for Experiment 9 were very similar to those used by Alvarado and Rudy (1995a; 1995b). As previously discussed in Chapter 4, although the procedures for training of a transverse patterning task were very similar, there were marked differences in the acquisition of the task by normal treating the cues that formed the visual array as one configuration, whereas fornix lesioned rats treated the items in the visual array as unique elements (Gaffan et al., 2001). In Experiments 7 and 8, it was not possible for hippocampal lesioned rats to solve the structural discrimination by elemental encoding of the features. Therefore, from the present experiments and the results of Gaffan et al. (2001) it can be argued that damage to the hippocampal system will impair learning of a structural discrimination when the task demands processing of the structural features. When the task does not require processing of structural features, hippocampal system damage may facilitate learning due to promoting elemental learning of items in a configuration.

5.3 The hippocampus and learning of configural discriminations

In Chapter Four, the effects of hippocampal lesions on two configural tasks were tested. It was found in Experiment 9 that damage to the hippocampus did not impair performance of a transverse patterning task and also in Experiment 10 there was no effect of hippocampal lesions on a biconditional discrimination. These results contradict the predictions of Sutherland and Rudy (1989). It has been claimed previously in Chapter Two and Chapter Four that the transverse patterning task and the biconditional discrimination are appropriate control tasks for testing the importance of learning structural information in configural discriminations. The transverse patterning discrimination is similar to the structural discrimination due to the amount of stimuli used and the amount of configurations that are formed by combinations of the stimuli. However, the structural discrimination differs from the transverse patterning discrimination in the nature of the response required for learning of the task. For the structural discrimination, compounds of stimuli are reinforced or animals in Experiment 9 and the control animals as described by Alvarado and Rudy (1995a; 1995). Therefore, there may be qualitative differences in the learning profiles across the two studies.

The difference in the results of Experiment 9 and the experiments by Alvarado and Rudy (1995a; 1995b) could be accredited to the type of lesion used. In Experiment 9 rats received radio-frequency lesions of the hippocampus and control rats received sham operations that matched the incidental damage, caused by surgery, to the cortex overlying the hippocampus. Alvarado and Rudy (1995a) compared the effects of kainic plus colchicine lesions with the effects of ibotenic acid lesions. Control animals received the same surgical procedures as lesioned animals, but the needle was only lowered through the cortex and no drug was injected. Alvarado and Rudy (1995a) report that all lesioned rats had thinning of the neocortex, but it is not clear whether this damage was matched in the control group. It is possible that a deficit was found by Alvarado and Rudy (1995a) due to sparing of the cortex in the control rats, whereas no impairment was found in Experiment 9 in which cortical damage was matched.

Even though the radiofrequency lesions used in Experiment 9 are less selective than the ibotenic acid lesions used by Alvarado and Rudy (1995a) that spare fibres of passage, it was found that radiofrequency lesions of the hippocampus had no effect on the performance of a transverse patterning discrimination. It is possible that hippocampal lesions of Experiment 9 were not large enough to find a difference between groups on a transverse patterning discrimination, but it was found that the two groups did differ on their ability to learn a spatial working memory task. The groups did not, however, differ on a spatial reference memory task. The possible factors that may have contributed to the lack of deficit on a spatial reference memory task will be discussed subsequently.

The results of Experiment 10a, also support the findings of other work in which hippocampal lesions do not impair learning of a biconditional discrimination (Whishaw and Tomie, 1991; McDonald et al., 1997; Good et al., 1998, Coutereau, et al., 2002). However, it must be noted that both Whishaw and Tomie (1991) and Mcdonald et al. (1997) report that hippocampal lesions cause a slight retardation of the task. In Experiment 10a, hippocampal lesioned rats were marginally slower to learn the task, but there was no statistical difference between the rates of acquisition of the two groups.

In Experiment 10b, hippocampal lesioned rats were not impaired on a spatial working memory task in the Morris water maze. However, the same rats were impaired on a T-maze alternation task. The results of performance of hippocampal lesioned rats on spatial tasks from Experiments 8, 9 and 10 will be discussed to a greater extent, later in this chapter.

5.4 Implications for configural association theories of the hippocampus

Whilst the results of Experiments 9 and 10a do not support the predictions of Sutherland and Rudy (1989) these findings, to some extent, can be accounted for by the revised 'configuration association' theory of Sutherland and Rudy (1995). It can be claimed that because the effects of hippocampal lesions were tested after acquisition of the configural discriminations, that the hippocampus was no longer necessary for the performance of the task. This is due to the assumption that the hippocampus plays a modulatory role in amplifying the salience of configural features, which are subsequently encoded, and stored in the neocortex (Sutherland and Rudy (1995). Therefore, it can be predicted that hippocampal lesions will not have an effect on the retention of configural associations. The notion that the hippocampus is not responsible for the retention of long terms memories is also assumed by Gluck and Myers (1993). It is claimed that the hippocampus consolidates memories but memories are actually stored in the neocortex (Gluck and Myers, 1993).

In answer to the assumption that the hippocampus does not store configural associations (Rudy and Sutherland, 1995), in Experiments 9 and 10, post-operative performance of the task started at levels that were appreciably lower than the levels reached in pre-operative performance. Performance then increased over the course of training. Therefore, the tasks were reacquired, which, according to Sutherland and Rudy (1995) should require the integrity of the hippocampus.

The results of Experiment 10a can also be accounted for by the revised 'configural association' theory (Rudy and Sutherland, 1995) by assuming that the hippocampus' modulatory role in amplifying the salience configural features is not necessary for the biconditional discrimination. The hippocampus is assumed to facilitate learning of configural discriminations when there is a high level of conflict between the associative strength of individual elements and the associative strength of a configuration. In the case of a biconditional discrimination, individual stimuli do not acquire levels of associative strength that are in competition with the associative strength of the configurations. Therefore, the hippocampal role of amplifying the salience of configurations will not result in facilitated learning of the task due to all associations being of an equal salience. Therefore, the results of Experiment 10a support the predictions of Rudy and Sutherland (1995).

In contrast to Experiment 10a, the results of Experiment 9 contradict the predictions of Rudy and Sutherland (1995). It is claimed that the hippocampus facilitates learning of the transverse patterning task due to individual stimuli, within a configuration, acquiring positive or negative values of associative strength. The hippocampus amplifies the salience of configurations which facilitates dissociation of the individual elements' associative strength and the configurations associative strength that are in competition with each other (Rudy and Sutherland, 1995). However, as previously discussed in Chapter Four, it is not clear what value of associative strength configurations in the transverse patterning would come to acquire. Each configuration contains an element that is reinforced and another element that is non-reinforced; the configuration cannot acquire any associative strength.

5.5 The role of the hippocampus in structural learning and implications for the encoding of spatial relationships

Collectively, the results reported in Chapters Three and Four demonstrate that the hippocampus is necessary for the performance of a structural discrimination, but not the performance of configural discriminations. It can be concluded that the hippocampus is involved in the learning and memory of the structural features of compound stimuli. The assumptions of Sutherland and Rudy (1989), that the hippocampus is responsible for place learning due to its role in the learning and memory of configural associations, can be revised so that now it can be assumed that the hippocampus learns about the structural features of configurations of stimuli. Hippocampal dependent spatial learning of allocentric cues need not require configural learning, but it is now plausible to predict that allocentric spatial learning requires the structural features of configurations of cues to be learned. If the original assumptions of Sutherland and Rudy (1989) are modified to include learning of structural features, then this provides a plausible description of how spatial relationships are encoded. Whereas Sutherland and Rudy (1989) assumed that spatial cues are encoded with regards to the unique configurations that they form, and the disambiguation of these configurations provides adequate information for the learning of a goal location (as in the water maze task, described by Morris et al., 1982), it can now be claimed that this process requires learning of the structural features of the configuration. For example, viewing the configuration AB might be associated with swimming in one trajectory, whereas the configuration BC might be associated with swimming in a different trajectory. Sutherland and Rudy (1989) would assume that the configurations AB and BC are discriminated due to the different outcomes with which they form associations. It can now be claimed that the more plausible description of such learning is that the configurations are learned with regards to their structural features, therefore, the two configurations are encoded as A to the left of B, and B to the left of C. It can be assumed that in the case of using allocentric cues to navigate to a location, the addition of structural features provides greater detail with which to discriminate configurations of spatially disparate cues.

The prediction that allocentric spatial learning requires encoding of structural features fits well with the results of fornix lesioned monkeys' ability to learn conditional tasks (Gaffan and Harrison, 1989). Fornix lesioned monkeys were able learn that object A was associated with reward and object B was not associated with reward when the two stimuli were presented in one spatial location, and also that B was associated with reward and A was not when presented in a different spatial location. However, when fornix lesioned monkeys were required to learn the conditional task in the same spatial location, so that choosing object A when facing in one direction was reinforced and choosing object B when facing in the opposite direction was reinforced, the fornix lesioned monkeys were now impaired (Gaffan and Harrison, 1989). The first task, in which the discrimination was performed in two different spatial locations, could be learned by configural encoding, but the type of learning used for this task was insufficient to enable learning of the second task in which the conditional discrimination was performed in the same spatial environment. Fornix lesioned monkeys were only impaired when required to discriminate between different views of the same allocentric cues. These results contradict the 'configural associations' theory (Sutherland and Rudy, 1989), as it would be predicted that the hippocampal system would be necessary for both of the two conditional discriminations. However, it can now be suggested that hippocampus is only necessary when the structure of the allocentric cues is required for learning, not when unique combinations of cues is sufficient for the solution of a task.

Sutherland and Rudy (1989) also claim that 'navigation to a goal involves the conditional linkage of specific movement sequences with specific "local views" of the environment' (p133). It is plausible that if animals learn to navigate to a goal by moving in one trajectory until encountering another view of a configuration, this process will be facilitated by learning about the structural features of the configuration. The correct behaviour to be elicited to a configuration AB, may not be apparent until encountering other configurations such as either BC or XA. However, if AB is encoded as A to the left of B, this may facilitate learning that moving in one trajectory will lead to encountering the configuration B to the left of C, whereas moving in the opposite trajectory will lead to A to right of X. Therefore, the assumptions, about the nature of place learning in spatial tasks, of Sutherland and between stimuli to be discriminated, and the ability to map these representations would, according to the 'cognitive map' theory (O'Keefe and Nadel, 1978), require the hippocampus. Whilst both the configural tasks and the structural discrimination do not have a navigation component, it is plausible that difference between the tasks is simply due to the need for learning spatial relationships in the structural discrimination. In contrast to this, the 'cognitive map' theory would not necessarily predict the different levels of performance displayed by hippocampal lesion and control rats on the biconditional probe discrimination (Experiment 10b), since if the probe discrimination implies that control animals cognitively map the spatial features of the stimuli, then it would be predicted that hippocampal lesions would impair performance of the normal biconditional discrimination. In Experiment 10b hippocampal lesioned rats did not differ from control rats on the reacquisition of the biconditional discrimination, but the probe discrimination revealed that task had been learned in qualitatively different manners. The hippocampal lesioned rats showed less disruption by the novel biconditional discrimination compared to the control rats. This result implies that control rats had encoded the spatial features of the configurations to a greater extent that the hippocampal lesioned rats, thus resulting in a larger generalisation decrement to the probe discrimination. Whilst the biconditional discrimination does not explicitly require spatial learning, control rats attribute spatial features to the stimuli, but this does not result in impaired performance following hippocampal lesions. Learning of the structural features of the compounds is incidental to learning of the biconditional discrimination, but is not essential for normal performance of the task, as displayed by the results of the hippocampal group. It is possible if it is assumed that hippocampal lesioned rats acquired the biconditional discrimination by the use of a 'taxon' system and control rats used a 'locale' system, Rudy (1989) can be modified so that the encoding of structural features provides a plausible description of such processes.

Whereas a configural association theory of the hippocampus has failed to account for learning of certain non-linear discrimination, and leaves the question of how animals learn about spatial relationships unanswered, the encoding of structural features can provide an adequate account of learning of certain tasks. McGregor, Hayward, Pearce and Good (2004) have shown that hippocampal lesioned rats fail to learn the location of a hidden platform in a rectangular shaped water maze. The platform was positioned in one corner of the maze, and navigation to the platform could only be achieved by learning of the spatial features of the maze. Control rats showed a preference to swim to the correct location, but they also made the error of swimming to the diagonally opposite corner. This was claimed to be due to the two corners having the same geometric features, e.g. a long wall to the left of a short wall (McGregor et al., 2004). Control animals learned the location of the hidden platform by use of the geometric features of environment. However, hippocampal lesioned rats did not show a preference for searching in any of the corners of the maze (McGregor et al., 2004). This result can be interpreted as reflecting a failure of the hippocampal lesioned rats to learn about the structural features of the environment.

The finding that hippocampal lesions impair performance of structural discriminations can be accommodated to some extent, by the 'cognitive map' theory of the hippocampus (O'Keefe and Nadel, 1978). If it assumed that that both the transverse patterning task and the biconditional discrimination have no explicit spatial component, then it would be assumed that the hippocampus would not be required for these tasks. However, the structural discrimination requires the spatial relationships that in the biconditional discrimination there is no benefit of cognitively mapping the stimulus representations, but these two systems can be dissociated by the use of the probe discrimination. Thus, it is possible to apply a 'cognitive map' (O'Keefe and Nadel, 1978) interpretation of the data, but this is only achieved *a posteriori*.

The theory proposed by Gluck and Myers (1993) predicts that hippocampal lesions will result in increased stimulus generalisation. The proportionally higher level of performance on the probe biconditional discrimination by hippocampal lesioned rats (Experiment 10b) can be explained in terms of increased similarity between the configural stimuli used that were used for training of the original biconditional discrimination and the probe discrimination. Paradoxically, Gluck and Myers (1993) predict that simple discrimination learning is facilitated by hippocampal lesions. They claim that this is due to the intact cortical system learning associations between reward and a constant mental representation of a stimulus. Discrimination learning in normal animals is retarded due to the hippocampus modulating the representation of the stimuli as a consequence of redundancy compression of irrelevant features and predictive differentiation of the relevant features of predictive stimuli. In contrast to this prediction, enhanced discrimination by hippocampal lesioned rats was not evident on a transverse patterning task (Experiment 9) nor on a biconditional discrimination (Experiment 10a). However, in keeping with the Gluck and Myers (1993) theory, the probe discrimination demonstrates that animals with hippocampal damage can show performance on some tasks that does not differ from control animals, but the underlying associations that are formed, are distinct from each other due to the representation of stimuli.

The ‘stimulus representation’ theory (Gluck and Myers, 1993) does not make specific claims about the ability of hippocampal lesioned animals to learn configural discriminations. The advantages of predictive differentiation and redundancy compression in intact animals is offset by the facilitated learning of stable representations of stimuli in hippocampal lesioned animals (Gluck and Myers, 1993). Consequently, it is not necessarily predicted that hippocampal lesioned animals will be impaired on the acquisition of configural tasks. The finding that hippocampal lesions impair rats’ ability to perform a structural discrimination, whilst sparing performance of non-structural configural discrimination, is not readily predicted by the theory of Gluck and Myers (1993) and is more in line with a spatial interpretation of hippocampal function (O’Keefe and Nadel, 1978).

Eichenbaum (1992) claims that a feature of hippocampal dependent declarative memory is the ability to encode ‘relational representations’. This includes learning arrays of spatial cues that can be used flexibly to solve spatial tasks. It is possible that hippocampal lesioned animals can learn about cues, but the representations of the stimuli are inflexible and evidence of learning can only be demonstrated in repetition of the learning event (Eichenbaum, 1992). Thus, it could be claimed that structural discriminations require the use of relational memory whereas configural learning does not require this process to the same extent. It is possible that hippocampal lesions impair structural learning, but not configural learning, due to a high level of demand to compare and contrast reinforced and non-reinforced configurations. This, however, also follows from the assumption that structural discriminations are more complex than configural discriminations due to the reinforced and non-reinforced sharing a greater amount of common features. As discussed in Chapter Two, whether structural discriminations are harder to solve than configural discrimination is not readily evident.

Both structural and configural discriminations require learning that stimuli predict different outcomes when placed in compound with other specific stimuli. Therefore, there is not a clear distinction why configural learning should be spared but structural learning impaired if the hippocampus is required for relational processing. The probe biconditional discrimination (Experiment 10b) in terms of Eichenbaum's (1992) relational theory, can be described as hippocampal lesioned rats demonstrating 'inflexible' memory. Therefore, this demonstrates that the hippocampus may not be essential for learning of certain tasks, but is required when learning is demonstrated in novel situations (Eichenbaum, 1992).

The dissociation of structural learning from configural learning may appear at odds with the assumption that both types of learning require the formation of unique representations of the cues that individually fail to predict whether reinforcement will occur. However, configural discriminations may require learning about the simple features that are present in a compound stimulus (e.g. A, B, left, right), whereas structural learning may depend on the additional learning that specific conjunctions of simple features predict a reward contingency (e.g. A-left, B-Right). These assumptions underlie the formation of the connectionist network proposed by George et al. (2001). The hippocampus may be involved in the learning of the conjunction of simple features, but is not required for learning of the simple features. Thus, hippocampal damage can impair structural discrimination, whilst sparing non-structural configural discrimination. As is evident from the difference in the transfer of learning between sham and hippocampal lesioned rats (Experiment 10b, Chapter

Rudy, 1995a; Sutherland and Rudy, 1989). Secondly, hippocampal lesions impair tasks that have no apparent demands on spatial learning. For example hippocampal lesioned rats are impaired on operant schedules that differentially reinforce low rates of responding (DRL) (Johnson, Olton, Gage and Jenko, 1977; Rawlins, Winocur and Gray, 1983). Effects of hippocampal lesions have also been found on trace conditioning (Quinn, Oomen, Morrison and Fanselow, 2002; Weiss, Bouwmeester, Power and Disterhoft, 1999; Weisz, Solomon and Thompson, 1980 as cited in Rawlins, 1985).

It is possible that the role of the hippocampus in DRL tasks and trace conditioning could be explained in terms of temporal structural learning. The effect of hippocampal lesions on learning the relationship between temporally discontiguous events may be due to a failure to encode the structural relationship between the two events. This assumption is problematic, however, as it could be claimed that all learning of simple associations requires structural learning if the onset of a CS does not coincide with the onset of the US. But, whereas hippocampal lesioned rats were able to learn a biconditional discrimination (Experiment 10a), a probe test revealed that the effects of learning were different for lesioned rats than for control rats (Experiment 10b). Therefore, this raises the question of whether normal acquisition of some tasks by hippocampal lesioned animals is achievable even though the learning may be qualitatively different to normal animals (Eichenbaum, 1992; Gluck and Myers, 1993; O'Reilly and Rudy, 2001).

Some theories suggest that the hippocampus is necessary for learning of tasks in which there is a temporal delay between a conditioned stimulus and a reward outcome (Olton et al., 1979; Rawlins, 1985). The hippocampus is viewed as a mechanism that stores the trace of a memory until the US is presented, so that an association can be formed. Therefore, the possibility that the hippocampus is responsible for learning not only spatial, but temporal structure is not dissimilar to the claims of these theories.

5.6 The role of the parietal cortex in structural learning

In all of the experiments reported in this thesis, it was found that as a consequence of surgery, hippocampal lesioned rats also sustained damage to the cortex overlying the hippocampus. The effect of cortical damage was controlled for in Experiments 8, 9 and 10, by giving a control group sham lesions in which rats received the same surgical procedures as for hippocampal lesions, but no damage to the hippocampus was caused. All differences between the groups tested on the various visual discriminations can be attributed to the effect of hippocampal damage rather than to an effect of cortical damage. This may simply demonstrate the additive effect of hippocampal and cortical damage, compared to cortical damage alone. It is possible that the effects of hippocampal lesions, reported in this thesis, may not have occurred if damage was limited to only the hippocampus. An un-operated control group could have been used to assess the effect of cortical damage in the sham operated group, but if it had been found that there was no effect of sham surgery, it does not necessarily follow that the effect of cortical damage does not contribute to the effect of hippocampal damage: the cortex may be involved in tasks that are assumed to be hippocampal dependent, but may not be essential to the tasks.

As discussed previously, it has been suggested that the neocortex encodes and stores memories that are mediated by the function of the hippocampus (Gluck and Myers, 1993; Rudy and Sutherland, 1995; O'Reilly and Rudy, 2001). Accordingly, damage to

Four), the hippocampus may provide additional information about conjunctions of stimuli that are not necessarily essential for the discrimination.

The interpretation of the role of the hippocampus in providing additional structural information about configurations of stimuli is similar to some extent to the account of hippocampal function proposed by O'Reilly and Rudy (2001). The hippocampus automatically encodes stimulus conjunctions regardless of their necessity for the solution of a task. The cortex is able to encode conjunctions of stimuli, but only does so when a task demands the formations of these representations (O'Reilly and Rudy, 2001). This can account for the findings of Experiment 10b (Chapter Four). In contrast, the model of O'Reilly and Rudy (2001) assumes that the cortex can acquire the same conjunctive representations of stimuli as the hippocampus, and the rate of learning may not differ between the cortex and hippocampus due to the a trade off of pattern separation and pattern completion. The model does not necessarily predict that for a structural discrimination, in which discrimination of the structural features of the task is explicitly required, that there will be an effect of hippocampal damage. In contrast the findings of the present experiments suggest that the hippocampus is involved in explicit and incidental structural learning.

The role of the hippocampus in learning structural discriminations may help in understanding the possible associations underlying hippocampal allocentric spatial learning. However, an exclusively structural learning account of hippocampal function would not account for many effects of hippocampal lesions. Firstly, structural learning does not help to resolve why some non-linear discriminations are not affected by hippocampal lesions (Alvarado and Rudy, 1995a; Gallagher and Holland, 1992, McDonald et al., 1997), but sometimes impairs others (Alvarado and the neocortex may contribute to memory deficits as a result of hippocampal lesions. More specifically, a reason for predicting that damage to the cortex overlying the hippocampus may have an effect on structural discriminations is that the damage sustained by rats in both the hippocampal lesioned groups and the control groups in Experiments 8, 9 and 10, included areas of the parietal cortex. Damage to the parietal cortex has been associated with visuo-spatial deficits in rats (Davis and McDaniel, 1993). Rats with parietal cortex lesions also show deficits similar to the effects of hippocampal lesions on object-in-place discriminations (DeCoteau and Kesner, 1998), and also on spontaneous exploration behaviour of novel object-in-place combinations (Save et al., 1992). Parietal cortex lesions result in deficits on spatial navigation tasks that require processing of proximal cues, similar to the effects of hippocampal lesions, but, in contrast, do not affect learning of distal spatial cues (Save and Poucet, 2000). It has also been found that parietal cortex lesioned rats are impaired at learning to return to a location in which they had previously been fed (Thinus-Blanc et al., 1996). Although, the parietal cortex appears to be important for learning about allocentric cues, Chiba et al., (2002) have demonstrated that it is possible to dissociate the effects of parietal lesions from hippocampal lesions by using different spatial tasks. Chiba et al. (2002) found that control and parietal cortex lesioned rats showed a greater latency to traverse arms in a radial-arm maze which, within a session had previously provided food, but no longer contained reward. Hippocampal lesioned rats did not show this tendency, implying a failure to remember that a particular arm had previously been visited. In another task, in which arms of a radial-arm maze were continuously reinforced, control and hippocampal lesioned rats were faster to traverse an arm to if it had already been visited within a session compared to the latency to traverse an arm on a first visit of a session. Parietal cortex lesioned rats did not show this behaviour.

Chiba et al. (2002) claim that whilst the hippocampus is involved in memory of locations cue by the presence of allocentric cues, the parietal cortex is responsible for perceptual memory of allocentric spatial information, that is independent of the role of the hippocampus.

It is also possible that the parietal cortex and the hippocampus may be involved in mnemonic functions that are dissociable from each other, but when damage in the two areas is combined this may result in impairments on tasks that separate lesions of these areas could not produce. Lesions of the neocortex that include areas of the posterior parietal cortex also impair concurrent learning of object discriminations, but this effect is not seen in hippocampal lesioned rats (Deacon and Rawlins, 1996). Therefore, damage to the cortex and the hippocampus may be necessary to produce deficits on a structural discrimination, but not on a configural discrimination.

It must be noted that whilst hippocampal lesioned rats in Experiment 8 were impaired on the structural discrimination, the rats were able to acquire the task to an extent. In Experiment 7 it was found that excitotoxic lesions of the hippocampus, which also damaged large amounts of the overlying cortex, were unable to perform the structural discrimination to any extent. It is possible that the larger impairment seen in Experiment 7 was due to the extra damage to the cortex.

In Experiments 8, 9 and 10, post-operative performance by control groups was considerably lower than levels of performance reached prior to surgery. Damage to the parietal cortex may have caused a loss of retention of the tasks. To make this claim, however, an extra group would have been needed to control for the effects of craniotomy. It can be noted, that if a loss of retention of a task after surgery reflects the effect of parietal damage in the control groups, that this effect appeared to be most marked for performance of the transverse patterning discrimination, whereas the effect was only transient on the structural discrimination. This may reflect the difficulty of the task, due to the transverse patterning discrimination taking considerably longer to learn than the structural discrimination. However, the reduction in performance of the control group, after surgery, does not appear to relate to the effects of hippocampal lesions on the three tasks used to test hippocampal function.

To test the effects of sham surgery on the performance the structural, transverse patterning and biconditional discriminations, the post-operative performance of the control groups can be compared to their pre-operative performance. This can be done by examining how many sessions of post-operative testing were required to reach the level of performance achieved prior to surgery. The criterion set for this analysis of the data is that a rat must perform within a session at a level the same or greater than their average performance over the last three sessions of pre-operative training. Post-operative testing of the biconditional discrimination only continued for ten sessions (Experiment 10a, Chapter Four), whereas post-operative testing of the structural discrimination and the transverse patterning task continued for twenty-four sessions. As two Sham rats trained on the biconditional discrimination failed to reach criteria within ten sessions, animals on the three tasks were given a maximum score of ten if they failed to reach criteria before this limit. Figure 5.1 shows the sessions to criteria for sham lesioned and hippocampal lesioned rats on the structural, transverse patterning and biconditional discrimination. On average sham lesioned rats were quicker to reach criteria on the structural discrimination than on both the transverse patterning task and the biconditional discrimination. In contrast hippocampal lesioned rats show little difference in the number of sessions to acquire the structural discrimination compared to the transverse patterning task. Acquisition of the biconditional discrimination was more readily achieved than the other two tasks and on average the hippocampal lesioned rats take fewer sessions than the sham lesioned rats to acquire the task.

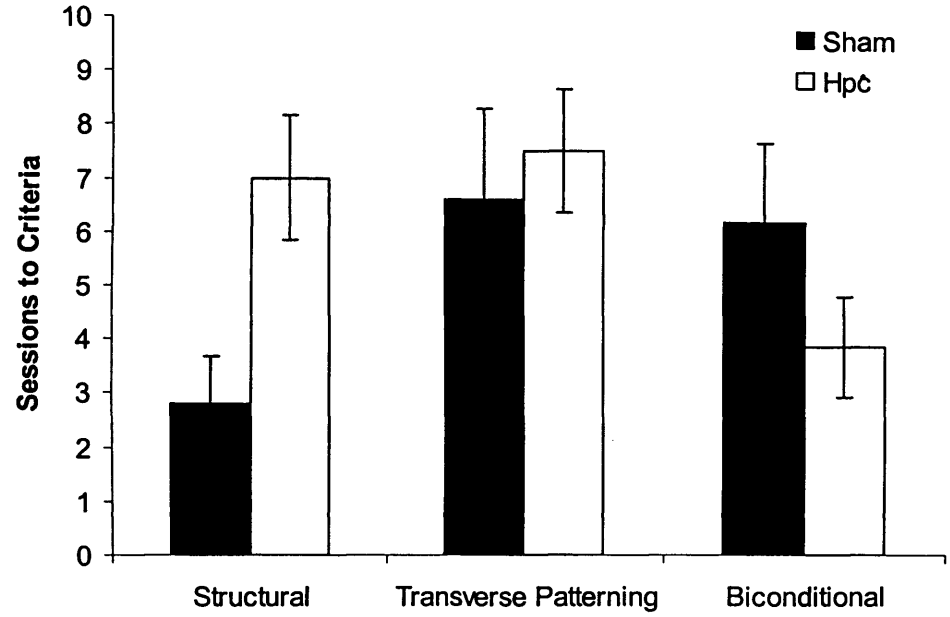

Figure 5.1. Sessions to criteria on post-operative performance of a structural, transverse patterning and biconditional discrimination for hippocampal (Hpc) and sham lesioned rats (Experiments 8, 9 and 10). Error bars indicate ±SEM.

Analysis of variance reveals that there was no significant overall effect of lesion, F(1,29)=0.9, and the no significant effect of task, F(2,29)=1.9, but there was a significant lesion by task interaction, F(2,29)=3.6, $p<0.05$. Simple main effects analysis reveals that the hippocampal lesioned rats took more sessions to acquire the structural discrimination than the sham lesioned rats, F(1,29)=5.5, $p<0.05$, but the groups did not differ on either the transverse patterning task or the biconditional discrimination. There was no effect of task for hippocampal lesioned rats nor for sham lesioned rats. It does not appear that cortical damage in the control lesioned rats resulted in selectively impairing performance of the structural discrimination. There may be differences in the effects of the tasks that are masked in this analysis due to some sham lesioned rats taking more than the maximum of ten sessions to reach criteria. However, this would only suggest that the two configural tasks were harder to acquire after surgery due to the average number of sessions to criteria being lowest for the structural discrimination. At the least it can be concluded that cortical damage did not affect performance of the structural discrimination to a greater extent than for the two configural tasks.

Even though hippocampal lesioned rats took significantly more sessions to reach criteria than the sham lesioned rats on the structural discrimination, their performance on this task was not significantly different from the performance of the two configural discriminations. With this considered and due to the fact that sham lesioned rats were on average faster to acquire the structural discrimination than for the two configural tasks, it appears that the hippocampus may facilitate learning about structural information, but does not selectively enhance learning of configural information in the same manner.

5.7 The effect of training of visual discriminations in water tank apparatus on the subsequent performance of spatial tasks in a Morris water maze

In Experiments 8, 9 and 10 after testing of complex visual discriminations in the water tank, rats were transferred to spatial tasks that tax the ability to learn about allocentric cues. In Experiment 8, it was found that hippocampal lesioned rats were not impaired on a spatial reference memory task in the Morris water maze. There was a tendency for hippocampal lesioned rats to be slower and to travel a further distance, than control rats to locate a hidden platform but this difference was not significant. Similar results were found in Experiment 9. Hippocampal lesioned rats were not impaired on a spatial reference memory task in a Morris water maze, but were impaired when transferred to a spatial working memory task. It was concluded that spatial reference memory tasks may be less sensitive to the effects of hippocampal lesioned rats after training in a water tank apparatus. Consequently, in Experiment 10 rats were again tested on a spatial working memory task in the Morris water maze after completion of testing in the water tank apparatus on a biconditional discrimination. In contrast to Experiment 9, rats were not impaired on a spatial working memory task, but were, however, impaired on a T-maze alternation task.

The results of Experiments 8, 9 and 10 are surprising due to the reported deficits following hippocampal damage, reported on spatial reference memory tasks (Morris et al., 1982) and spatial working memory (Steele and Morris, 1999). It is possible that the lesions of the hippocampus were not large enough to impair learning of allocentric spatial tasks. However, the lesions in Experiments 8, 9 and 10 included the majority of the dorsal hippocampus, and it has been shown that lesions of the dorsal hippocampus, but not ventral hippocampus, are sufficient to impair allocentric spatial learning (Moser and Moser, 1998). It is unlikely that the lesions of the hippocampus in Experiments 8, 9 and 10 were not large enough to impair learning in the Morris water maze.

In contrast to the reported deficits following damage to the hippocampus on spatial reference memory (Morris et al., 1982) and spatial working memory (Steele and Morris, 1999), in Experiments 8, 9 and 10 rats had received extensive training in the water tank apparatus before training commenced in the water maze. All rats had been trained in a water tank prior to and after surgery, and even though, in Experiment 8, hippocampal lesioned rats were impaired on a structural discrimination, they were able to perform a simple visual discrimination to high degree of accuracy. It is possible that the prior training in the water tank facilitated learning of spatial tasks in the Morris water maze. It has been found that prior training of a spatial reference memory task reverses the spatial deficit caused by NMDA blockade, which impairs hippocampal long-term potentiation, on a new spatial reference memory task (Bannerman et al., 1995). In contrast to Experiments 8, 9 and 10, Bannerman et al. (1995) did not find that there was an effect of prior spatial reference memory training for rats with hippocampal lesions, which were impaired after surgery. It is possible that the training in a water tank to search for a hidden platform for Experiments 8, 9 and 10 was sufficient to mask an effect of hippocampal lesion.

It has been found that prior training of searching strategies reverses the effects of some pharmacological interventions on learning spatial reference memory tasks in the Morris water maze. Cain (1997) found that diazepam impairs performance of spatial reference memory task in rats, but this effect was not found if rats received training to swim to a hidden platform that changed location every trial and with no room cues available. Cain (1997) claims that the pre-training procedure aids familiarization of the behavioural requirements of the task by eliminating the tendency to swim close to the walls of the maze and helping to learn to climb onto the platform. The ameliorating effect of pre-training of searching strategies in reducing spatial deficits has also been shown with the treatment of ethanol (Cain, Finlayson, Boon and Beiko, 2002), following neocortical lesions (Hoh et al., 2003), and NMDA blockade (Saucier and Cain, 1995). Similar to these findings, it has also been shown that training of rats with cerebellar dentate nucleus lesions on a T-maze alternation task eliminates deficits on a spatial reference memory task (Noblett, and Swain, 2003).

Even though training of the water maze task does not result in spared performance of a new water maze task following lesions of the hippocampus (Bannerman et al., 1995), under certain conditions rats with hippocampal damage can show a place response. Day, Schallert, Weisand and Sutherland (1999) claimed that hippocampal lesioned rats fail to show a place response on a spatial reference memory task in the Morris water maze due to an inability to switch from non-spatial strategies such as a thigmotaxic response. When trained on the Morris water maze task, using platforms that progressively decreased in size, thus deterring the use of a thigmotaxic response, it was found that hippocampal lesioned rats showed a place response that did not significantly differ from controls (Day et al., 1999). Whishaw, Cassel and Jarrard (1995) have shown that fornix lesioned rats that are trained to swim to a visible platform will search in the correct location when the platform is removed. If trained to locate a hidden platform, fornix lesioned rats fail to learn the location of the platform. Whishaw et al. (1995) claim that fornix lesioned rats are impaired at learning the sequence of movements to locate a platform, which may be underlined by impaired path integration. The impairment lies in not knowing how to get to a location rather than learning that a location is rewarded. There is also evidence that hippocampal lesioned rats will show a place response when trained to locate a visible platform which is subsequently removed on a probe trial (Whisaw and Jarrard, 1996). The findings of Whishaw et al. (1995) and Whishaw and Jarrard (1996) demonstrate that rats with either hippocampal or hippocampal system damage can learn a place response when trained under certain conditions, therefore, there are factors that learn that no one spatial location predicted the presence of the platform. In contrast, in the water maze rats could only show learning by the decrease of latency, or distanced traversed, to locate a platform in a constant location over trials of training. The effect of prior training in the water tank may result in inappropriate spatial behaviours in the water maze.

Whilst it is likely that prior training of locating a hidden platform in a water tank affects learning in a water maze, there is an alternative possibility that the lesions were insufficient to cause impairments on spatial memory tasks. This appears unlikely due to the findings of Experiments 9 that hippocampal lesions spared spatial reference memory, but impaired subsequent training of a spatial working memory task. Also in Experiment 10b, hippocampal lesions spared spatial working memory, but impaired the ability to learn a T-maze alternation task. Even though hippocampal lesioned rats in Experiment 8 were not impaired on a spatial reference memory task, they were impaired on a structural discrimination. Therefore, there is behavioural evidence to show that hippocampal lesions affected performance of certain tasks. It was typical that hippocampal surgeries in Experiments 8, 9 and 10 spared parts of the ventral hippocampus. This is unlikely to have resulted in spared performance of spatial tasks, due to the findings that dorsal hippocampal lesions, but not ventral hippocampal lesions, are sufficient to cause impaired spatial learning (Moser and Moser, 1989; Bannerman et al., 1999).

Although it is possible that prior training in the watertank influenced subsequent learning in the Morris watermaze it is worth noting that measures were taken in the surgical procedures used in Experiments 9 and 10 to increase the amount of hippocampal damage. Thus differences in the effects of hippocampal damage in the mediate whether an impairment will be seen following hippocampal damage on spatial tasks.

It is possible that in Experiments 8, 9 and 10, training in the water tank aided the ability of hippocampal lesioned rats to locate the hidden platform in a Morris water maze task by training of searching strategies. In Experiment 10 hippocampal lesioned rats were not impaired on a working memory task in the water maze, but were impaired on a T-maze alternation task. These results indicate that hippocampal lesioned rats had learnt searching strategies which aided acquisition of a place learning task in a water maze, but this did not transfer to a T-maze alternation task due to the different demands of the task.

In contrast to the assumption that prior training in a water tank may aid acquisition of spatial tasks, it was found in Experiment 9 that hippocampal lesioned rats were not impaired on a reference memory task, but were impaired on a working memory task. As stated previously, this may be due to the working memory task being more sensitive to the effects of hippocampal lesions. It is also possible that the lesioned animals perseverated by returning to the location in which the platform had previously been located for the reference memory task. Thus, the impairment could be due, not to a failure learn, but to a failure to inhibit learning that was no longer relevant for the task.

As noted in Chapter Four, control rats performed poorly on the working memory task compared to the levels of performance of normal rats reported by Steele and Morris (1999). It is possible that the control rats in Experiments 8, 9 and 10 had learnt behaviour that retarded learning in the water maze. In the water tank the platform was never consistently in one location (i.e. left or right goal location) so that rats had to

Morris watermaze in Experiments 8, 9 and 10 may be due to differences in the size of lesion. On average hippocampal lesions tended to be larger in Experiment 9 than in Experiment 8, and hippocampal lesions in Experiment 10 tended be larger than in Experiment 8 and 9. Lesion size cannot account for the effects of hippocampal lesions on the structural, transverse patterning and biconditional discriminations, as hippocampal lesions impaired performance of a structural discrimination, but lesions that tended to be larger did not impair performance of a transverse patterning task nor a biconditional discrimination. However, it is possible that the difficulty of finding effects of hippocampal lesions on Morris watermaze tasks is due to insufficient damage.

Insufficient damage to the hippocampus may explain why acquisition of a spatial reference memory task may be spared not spatial working memory in Experiment 9 if it is assumed that learning of the spatial working memory task is more demanding than the reference memory task. In contrast to Experiment 9, in Experiment 10 hippocampal lesions, which if anything tended to be larger than in Experiment 9, spared acquisition of a spatial working memory task whilst were sufficient to impair T-maze alternation. Therefore, it is possible that it is the order in which the tasks are run rather than the extent of lesions that influence performance in the Morris watermaze. Indeed, it has been shown that lesions limited to the dorsal hippocampus, occupying 50% of total hippocampal volume, result in deficits in spatial reference memory (Bannerman et al., 1999) and spatial working memory (Bannerman, Deacon, Offen, Friswell, Grubb and Rawlins, 2002) that are indistinguishable from complete hippocampal lesions.

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To resolve the issue of whether prior training in the water tank effects subsequent learning of spatial tasks in the Morris water maze, it needs to be shown that lesions of the hippocampus, that are similar to size and locus of lesions reported for Experiments 8, 9 and 10, are sufficient to impair spatial learning in the Morris water maze, without the added factor of training in the water tank. If deficits on spatial tasks in the Morris water maze are found, this would suggest that training on visual discriminations in a water tank apparatus may influence learning subsequent water maze tasks.

5.8 Conclusion

The 'cognitive map' theory of hippocampal function (O'Keefe and Nadel, 1978) claims that the hippocampus encodes and stores representations of spatial environments. Thus the hippocampus learns the spatial relationships between cues that form an environment. The 'configural association' theory of the hippocampus (Sutherland and Rudy, 1989; Rudy and Sutherland, 1995) proposes that learning of spatial cues occurs due to the formation of associations between configurations of cues and a reward outcome, and that these configural associations are dependent on the hippocampus. The predictions of Sutherland and Rudy (1989) were tested on three non-linear discriminations. It was found that hippocampal damage spared performance of two configural discriminations, but impaired learning of a task that required the spatial structure of configurations to be discriminated. These results contradict the predictions of Sutherland and Rudy (1989). It is proposed that a role of the hippocampus is to learn about the structural features that are created by two stimuli that are treated as a configuration. This idea can be used to infer that learning of spatial environments, as described by O'Keefe and Nadel (1978), requires the ability to learn the spatial relationships between allocentric cues.

5.9. Future directions

A recent theory of the perirhinal cortex (Bussey and Saksida, 2002) has proposed that the perirhinal cortex is involved in learning about objects that contain features that have ambiguous associations. The theory predicts that lesions of the perirhinal cortex will impair visual discriminations in which there is a high level of 'feature ambiguity' (Bussey and Saksida, 2002). Accordingly, it can be predicted that lesions of the perirhinal cortex will impair learning of the three non-linear discriminations that were used in the present thesis to test the function of the hippocampus. A deficit should be caused regardless of whether the structure of compound visual stimulus is required to be learned.

In this thesis, it is concluded that learning deficits of spatial allocentric cues can be accounted for by the assumption of impaired learning of structural features of compound stimuli. It has been found that lesions of the perirhinal cortex can spare performance of Morris water maze tasks (Machin, Vann, Muir and Aggleton, 2002; Burwell, Saddoris, Bucci and Wiig, 2004), although this is not always the case (Liu and Bilkey, 2001). It is possible that lesions of the perirhinal cortex will impair learning of a structural discrimination due to the high level of feature ambiguity (Bussey and Saksida, 2002) between the reinforced and non reinforced compounds. But, if lesions of the perirhinal cortex do not impair the learning and memory of allocentric spatial tasks, then the prediction that structural learning underlies allocentric spatial learning would not be supported. It is, therefore, possible to test whether the same mnemonic function underlies learning structural discriminations and allocentric spatial cues.

Even though large excitotoxic lesions of the hippocampus resulted in chance performance of a structural discrimination (Experiment 7, Chapter Three), in Experiment 8 smaller radio-frequency lesions of the hippocampus did not result in a total inability to solve the task. The use of immediate early gene activation (IEG) studies may help to further identify the neural substrates that may support structural learning. Increased levels of c-*fos* have been found as a consequence of spatial learning in the entorhinal and postrhinal cortices (Vann, Brown, Erichsen and Aggleton, 2000). Investigation of the IEG activation in these areas as a consequence of structural learning would help reveal whether the hippocampus and parahippocampal cortices are sensitive to changes in the structure of configural stimuli in a similar manner to changes of the cues present in an environment.

Testing IEG activation as a consequence of structural learning could be possible by training rats on a biconditional discrimination. Once the task had been acquired, the probe task as described for Experiment 10b (Chapter Four) could be presented. The mismatch between the structural relationships of the probe stimuli and the previously learned biconditional discrimination would result in new learning of structural features. IEG activation as a correlate of learning would indicate the neural substrates that are sensitive to changes in spatial structure.

Testing the role of the perirhinal cortex and examining IEG activation in structural learning would help to reveal whether the neural substrates that underlie allocentric spatial learning are similar for those that are responsible for structural learning. It is possible that allocentric spatial learning is disrupted by hippocampal damage due to the ability to encode the structural features of stimuli. Examination of the nature of how structural relationships are encoded may reveal the role of the hippocampus in learning and memory of tasks that have structural demands but are not explicitly spatial in their design.

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