The role of the perirhinal cortex in visual learning in the rat

Penelope Elizabeth Machin

THE ROLE OF THE PERIRHINAL CORTEX IN VISUAL LEARNING IN THE RAT

Penelope Elizabeth Machin

Thesis submitted for the degree of Doctor of Philosophy

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DEDICATION

I dedicate this thesis to my sisters, Alice and Melanie, and to the memory of my grandfather.

DECLARATION

Statement of Copyright

I confirm that no part of the material offered has previously been submitted by me for a degree in this or any other University. If material has been generated through joint work, my independent contribution has been acknowledged and quotations and paraphrases suitably indicated.

Signed: P Machin

Date: 16/5/00

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ABSTRACT: The role of the perirhinal cortex in visual discrimination learning in the rat.
Thesis submitted for degree of Doctor of Philosophy, University of Durham, 1999.
P. E. Machin
The aim of this thesis was to investigate the role of the perirhinal cortex in visual discrimination learning in the rat.
Experiment one measured postoperative reacquisition of two sets of concurrent visual discriminations acquired at different time intervals prior to surgery. Perirhinal ablation did not result in a temporally graded retention deficit, but a deficit limited to immediate postoperative performance.
Experiment two measured postoperative acquisition of a new set of concurrent visual discriminations, with a stimuli set of 15 pairs, thereby increasing demands on stimuli identification. It was found that perirhinal ablation did not affect postoperative acquisition.
Experiment 3a measured postoperative acquisition of a two choice visual discrimination and generalisations to it. Perirhinal ablation led to an impairment in performing the visual discrimination when presented in the generalisation task. Experiment 3b measured the effects of perirhinal ablation on postoperative performance in generalisation to a visual discrimination learnt prior to surgery. It was found that perirhinal ablation led to a deficit in generalising to transformations in stimuli form, but not to transformations in stimuli size.
Experiment four measured acquisition of a titrating visual generalisation task that increased demands on stimuli identification. Perirhinal ablation impaired acquisition of this task. Experiment five was designed to measure the effects of perirhinal ablation on acquisition of a generalisation task with complex visual stimuli. However, neither the sham or perirhinal animals succeeded in learning the task.
The final experiment measured postoperative acquisition of a simple visual discrimination and its partial reversal and acquisition of a biconditional visual discrimination task. Perirhinal ablation impaired acquisition of the biconditional discrimination, whereas acquisition of the simple discrimination and its reversal remained intact.
Therefore, perirhinal ablation in the rat leads to selective impairments in the acquisition and retention of visual discrimination learning. These findings suggest that the perirhinal cortex may contribute to discrimination learning tasks that require the identification of complex visual stimuli.

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Chapter 1:Introduction

1.1 Introduction and Evidence that the Medial Temporal Lobe is Involved in Memory

This review focuses on the contribution of medial temporal lobe structures to the processes of memory, with particular emphasis on the role of the perirhinal cortex in visual mnemonic processes. The main theories of memory in the medial temporal lobe are considered along with behavioural studies outlining the mnemonic contributions of the hippocampus, parahippocampal, entorhinal and perirhinal cortices.

Present research into the role of medial temporal lobe structures in mnemonic and perceptual processes originated from early documentation of the effects of temporal lobectomies in both humans and animals. Temporal lobe structures were implicated in human memory impairments as early as 1899, with documentation of a female patient with severe anterograde amnesia following pathology in the hippocampus and adjacent medial temporal cortices (Bekhterev, cited in Baxendale, 1998). Following this, early physiologists searching for the cortical areas responsible for sensory processes found large bilateral temporal lobe ablations in monkeys produced deficits in memory and general intelligence (reviewed in Gross, 1994). Since then, more thorough investigations into the behavioural outcome of bilateral temporal resection in monkeys have been conducted, leading to the categorisation of the Kluver Bucy syndrome (Kluver & Bucy, 1937). The syndrome is characterised by psychic blindness or visual agnosia, strong oral tendencies, hypermatamorphosis, lack of emotional responsiveness and loss of aggressiveness.

Findings from studies of the Kluver Bucy syndrome led to the use of temporal lobe resection as an intervention technique in psychotic or epileptic patients and attempts to reveal how different temporal lobe structures may be responsible for causing different aspects of the syndrome. These two areas of research led to the functional division of structures within the medial temporal lobe and a clearer understanding of how these structures contribute to mnemonic and visual perceptual processes.

Localisation studies in monkeys have mapped a perceptual area within the temporal lobes, namely the middle and inferior temporal gyri or inferotemporal cortex (Mishkin, 1954). Inferotemporal cortex has since been linked with the rest of the visual system, by reports of its anatomical and functional links with striate and prestriate cortex, via the ventral visual pathway (Ungerleider & Mishkin, 1982). Electrophysiological studies in primates suggest this area is crucial for object recognition processes, as cells in this area show stimulus selectivity for highly complex visual stimuli, such as hands, faces and computer generated geometric forms (Gross et al., 1972).

The consequences of using temporal lobectomies as therapeutic interventions in psychoses and epilepsy provide compelling evidence of the involvement of medial temporal lobe structures in memory processes. Scoville & Milner (1957) documented nine patients, one epileptic and eight psychotic, who had undergone bilateral temporal lobe resection. It was noted that whenever the hippocampal gyrus and hippocampus proper were included in the lesion, severe anterograde amnesia ensued. The most

striking example of this was patient HM, who underwent a radical bilateral temporal lobe resection to relieve intractable epilepsy. The surgeon's notes indicated that the damage extended posteriorly along the medial surface of the temporal lobe for a length of approximately 8 cm, thereby including the anterior two thirds of the hippocampus, the hippocampal gyrus, the amygdala and the rhinal and parahippocampal cortices. Psychological examination of HM following recovery from surgery revealed severe anterograde amnesia and partial retrograde amnesia for at least 3 years prior to surgery (Scoville & Milner, 1957). Further tests revealed that HM's motorskill acquisition and perceptual learning abilities remain intact (Corkin, 1984), suggesting that the human memory system is functionally divisible.

A recent MRI analysis of HM 's lesion indicates it may not be as extensive as originally suggested, with intact tissue in the hippocampus, and perirhinal and parahippocampal cortices (Corkin et al., 1997). Therefore, heavy cell loss within the hippocampus and surrounding cortices appears to be sufficient to produce severe anterograde amnesia in humans.

1.2 Anatomy and Connectional Characteristics of the Medial Temporal Lobe

1.2. i The Hippocampus

Situated within the medial temporal lobe, the hippocampus consists of several distinct areas, which include the dentate gyrus, CA1 - 3 of Ammons Horn and the subicular complex (Eichenbaum & Buckingham, 1992). The hippocampus assumes robust cortical connections with the rhinal cortex and parahippocampal cortex, via the perforant pathway

(Primates: Suzuki & Amaral, 1994a; Rodents: Burwell et al., 1995), and with the mamillary bodies and anterior thalamus via the fornix (Primates: Aggleton et al., 1986a). Within the primate and rodent hippocampus the flow of afferents is unidirectional, passing through the perforant pathway, the dentate gyrus, CA1 - 3 and the subiculum (Burwell & Amaral, 1998). In the rodent, septal levels of the hippocampus receive more cortically derived afferents than temporal levels, leading to the suggestion that these areas may be functionally distinct (Burwell & Amaral, 1998).

Figure 1.1. The location of the perirhinal, entorhinal and parahippocampal cortices in the primate reproduced from Burwell et al. (1995). The shaded area shows the perirhinal cortex, the striped area the parahippocampal cortex and the dotted area the entorhinal cortex. Abbreviations: amts, anterior medial temporal sulcus; ots, occipitotemporal sulcus; rs, rhinal sulcus; STG, superior temporal gyrus; STS: superior temporal sulcus; TH, TF of parahippocampal cortex: TE, temporal cortex.

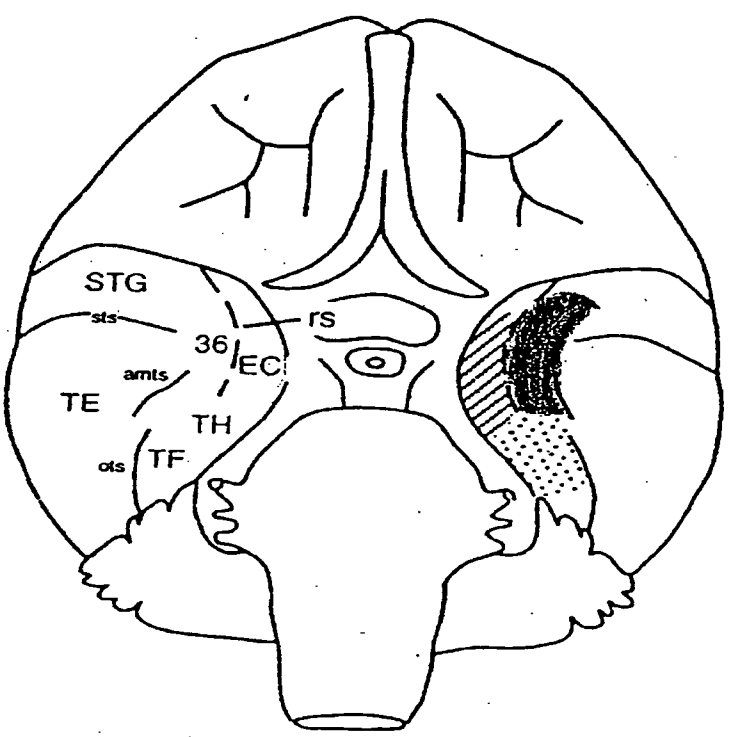
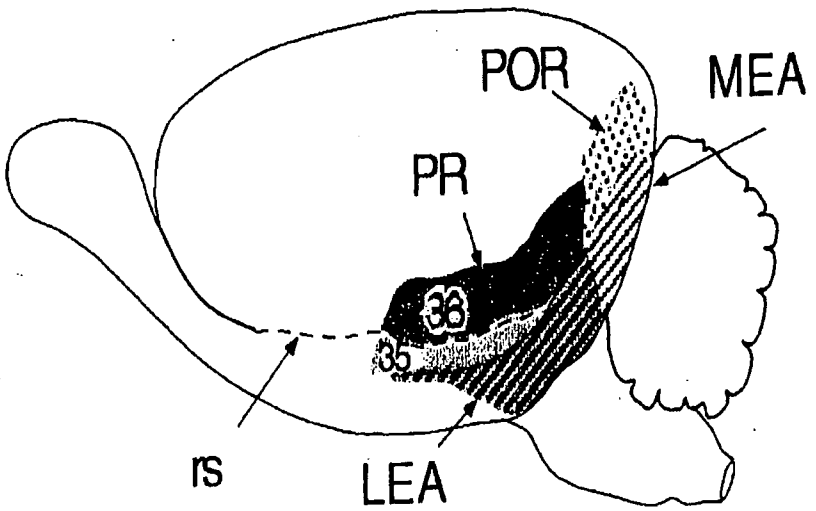


Figure 1.2. The location of the perirhinal, entorhinal and postrhinal cortices in the rodent, reproduced from Burwell and Amaral (1998). Abbreviations: MEA, medial entorhinal cortex; LEA, lateral entorhinal cortex; PR, perirhinal cortex; POR, postrhinal cortex; rs, rhinal sulcus.



1.2. ii Parahippocampal/Postrhinal Cortex

In primates the parahippocampal cortex is caudally adjacent to the perirhinal and entorhinal cortices, and is divided into areas TF and TH that differ in terms of cortical connectivity (Von Bonin & Bailey, 1947). In rodents, parahippocampal cortex is termed postrhinal cortex, occupying the caudal extent of perirhinal cortex (Burwell et al., 1995). Figures 1.1 and 1.2 show the locations of the parahippocampal cortex and the postrhinal cortex in the primate and rodent respectively. Parahippocampal cortex is deemed to form part of the dorsal or occipitoparietal pathway, coursing from the occipital lobes to the parietal cortex and deemed to be necessary for spatial vision and visuomotor control (Ungeleider & Haxby, 1994).

Area TF in the primate receives predominantly visual sensory information from the parietal and rhinal cortices and visual association

areas TE and TEO, as well as non-visual afferents from the ventrolateral, orbitofrontal, cingulate and retrosplenial cortices (Suzuki & Amaral, 1994a). In contrast, area TH in the primate receives substantial projections from auditory association areas in the superior temporal gyrus (Suzuki & Amaral, 1994a). Postrhinal cortex in the rodent also receives afferents from visual areas, including visual association areas in the occipital lobe, parietal and perirhinal cortices and area TE (Burwell & Amaral, 1998). The cortical connections of the postrhinal cortex may facilitate the integration of visuospatial and visual object recognition processes (Aggleton & Brown, 1999). The postrhinal cortex receives afferents from both parietal cortex, an area deemed to contribute to visuomotor and spatial tasks in rats (Save & Moghaddam, 1996), and from perirhinal cortex and area TE, areas deemed to contribute to object recognition in rats (Zhu, Brown & Aggleton, 1995). The postrhinal cortex in rats has subcortical connections to the striatum, claustrum and lateral nucleus of the thalamus (Burwell, Witter & Amaral, 1995). Tables 1.1 and 1.2 show the cortical and subcortical connections of the parahippocampal cortex in the primate and the postrhinal cortex in the rodent, respectively.

1.2. iii Entorhinal Cortex

In the primate and rodent, entorhinal cortex is situated medial to the caudal half of the rhinal sulcus, occupying Brodmanns area 28 and is thereby adjacent to areas 35 and 36 of the perirhinal cortex (Brodmann, 1909). Figures 1.1 and 1.2 show the location of the entorhinal cortex in the primate and the rodent, respectively. The entorhinal cortex in rodents can be subdivided into lateral and medial sections, characterised by contrasting

neuronal circuitry (Rodents: Empson et al., 1996; Primates: Witter, Van Hoesen & Amaral, 1989) that may facilitate the differential processing of incoming information before being relayed to the hippocampus. Both rodents and primates demonstrate highly similar topographies of cortical connections within entorhinal cortex (Burwell et al., 1995). The lateral entorhinal area receives afferents from piriform cortex, temporal and frontal regions, whereas the medial entorhinal area receives stronger projections from cingulate, parietal and occipital areas (Burwell & Amaral, 1998).

In rodents, the perirhinal cortices provide substantial converging efferents from both poly- and uni-modal association areas to the lateral entorhinal areas, whereas postrhinal cortex projects to both lateral and medial entorhinal areas (Burwell & Amaral, 1998). This pattern of incoming information from the postrhinal and perirhinal cortices allows for the integration of information from the ventral and dorsal visual pathways. In response, the entorhinal cortex provides return projections to the postrhinal and perirhinal cortices, although these return projections are more robust in the monkey than in the rodent (Burwell & Amaral, 1998). The entorhinal cortex also provides a substantial forward projection to the dentate gyrus of the hippocampus, via the perforant pathway (Rodents: Burwell et al., 1995; Primates: Witter & Amaral, 1991).

The entorhinal cortex in primates also projects to the medial thalamic region, including the anterior thalamic nuclei, medial dorsal thalamic nuclei and the mamillary bodies (Aggleton & Saunders, 1997). The neuronal organisation of entorhinal cortex allows the maintenance of

electrical activity over relatively long time periods which may allow the entorhinal cortex to assimilate incoming information before relaying it to the hippocampus (Iijima et al., 1996). Tables 1.1 and 1.2 show the cortical and subcortical connections of the entorhinal cortex in the primate and the rodent, respectively.

1.2. iv Perirhinal Cortex

The perirhinal cortex can be subdivided into two cortical areas, corresponding to Brodmanns areas 35 & 36 (Brodmann, 1909). In humans and other primates it is situated lateral to the full rostrocaudal extent of the rhinal sulcus, thereby occupying the anterior medial portion of the inferior temporal gyrus (Suzuki & Amaral, 1994a,b). In rodents, perirhinal cortex occupies the area lateral to the rostral levels of the rhinal sulcus only, the caudal area is termed postrhinal cortex and deemed to be functionally equivalent to primate parahippocampal cortex (Burwell et al., 1995). In both species it is bound medially by uni-modal visual area TE, together these areas occupy what is termed inferotemporal cortex. Figures 1.1 and 1.2 show the location of the perirhinal cortex in the primate and the rodent.

In primates the perirhinal cortex forms a crucial component of the occipitotemporal or ventral visual pathway, that extends from cortical area V1 in the occipital lobe to ventrolateral and orbitofrontal regions of the frontal lobe (Gross, 1992). In both primates and rodents the perirhinal cortex receives substantial cortical inputs from uni-modal and poly-modal association areas, however the relative strengths and comparable topographies of cortical inputs differ between the two species (Burwell et al., 1995). In primates the primary uni-modal perirhinal inputs originate in

somatosensory, auditory and visual association cortices (Suzuki & Amaral, 1994a). The most substantial of these uni-modal inputs arises from visual association areas TE and TEO of inferotemporal cortex (Suzuki & Amaral, 1994a). In rodents uni-modal perirhinal inputs also originate in somatosensory, auditory and visual association cortices, however the visual input in rodents is not as robust as that from olfactory areas (Burwell et al., 1995). In the rodent, perirhinal areas 35 and 36 differ in terms of their cortical connectivity (Burwell & Amaral, 1998). Area 36 receives a higher number of cortical afferents and in turn projects heavily to area 35 and the postrhinal cortex, whereas area 35 provides more substantial projections to the entorhinal cortex.

Therefore poly-modal inputs to the perirhinal cortex in both primates and rodents are widespread, subcortical connections also exist in both species with projections to the lateral, basal and accessory nuclei of the amygdala (Primates; Herzog & Van Hoesen, 1976; Rodents: Vaudano et al., 1990). The perirhinal cortex also projects to the medial dorsal thalamic nucleus of the diencephalon (Primates: Aggleton et al., 1986a; Rodents: Burwell, Witter, Amaral, 1995). The extensive cortical and subcortical connections of the perirhinal cortex suggest it could play an invaluable role in the collation of poly- and uni-modal sensory information for associative, mnemonic or perceptual purposes. The subcortical and cortical connections of the perirhinal cortex in the primate and the rodent are shown in tables 1.1 and 1.2.

Table 1.1. The cortical and subcortical connections of the rhinal and parahippocampal cortices in the primate. The relative strengths of the cortical connections are given (Suzuki, 1996).

CORTICAL CONNECTIONS IN THE PRIMATE			
ENTORHINAL CORTEX	**PERIRHINAL CORTEX**	**PARAHIPPOCAMPAL AREA TF**	**PARAHIPPOCAMPAL AREA TH**
Perirhinal cortex, 40%	Areas TE, TEO of temporal cortex, 64%	Areas TE, TEO of temporal cortex, 41%	Parahippocampal area TF, 51%
Parahippocampal cortex, 22%	Parahippocampal cortex, 25%	Cingulate cortex, 21%	Cingulate cortex, 24%
Cingulate cortex, 15%	Superior temporal sulcus, 6%	Superior temporal sulcus, 16%	Superior temporal sulcus, 8%
Frontal cortex, 9%	Frontal cortex, 3%	Posterior parietal cortex, 8%	Auditory superior temporal gyrus, 10%
Superior temporal sulcus, 8%	Auditory superior temporal gyrus, 1%	Perirhinal cortex, 4%	Visual areas V4, TE, TEO, 3%
Parainsular cortex, 3%	Cingulate cortex, 10%	Insular cortex, 1%	Frontal cortex, 1%
Olfactory bulb, 4%	Insular cortex, 2%	Frontal cortex, 3%	Insular cortex, 1%
SUBCORTICAL CONNECTIONS			
Hippocampus	Hippocampus	Hippocampus	
Striatum	Striatum	Striatum	
Amygdala	Amygdala	Amygdala	
	Thalamus		

Table 1.2. The cortical and subcortical connections of the rhinal and postrhinal cortices in the rodent. The relative strengths of the cortical connections are given (Burwell & Amaral, 1998).

CORTICAL CONNECTIONS IN THE RODENT				
LATERAL ENTORHINAL CORTEX	**MEDIAL ENTORHINAL CORTEX**	**AREA 35 OF PERIRHINAL CORTEX**	**AREA 36 OF PERIRHINAL CORTEX**	**POSTRHINAL CORTEX**
Piriform cortex, 45%	Piriform cortex, 33%	Piriform cortex, 26%	Ventral temporal cortex, 30%	Temporal cortex, 30%
Temporal cortex, 24%	Temporal cortex, 20/25%	Insular cortex, 22%	Auditory temporal cortex, 10%	Occipital cortex, 35%
Insular cortex, 21%	Frontal cortex, 10%	Entorhinal cortex, 22%	Postrhinal cortex, 10%	Cingulate cortex, 35%
Frontal cortex, 9%	Insular cortex, 6%	Temporal cortex, 13%	Entorhinal cortex, 10%	Parietal cortex, 7%
Cingulate cortex, 2%	Cingulate cortex, 10%	Frontal cortex, 8%	Insular cortex, 13%	Entorhinal cortex, 8%
Parietal cortex, 2%	Parietal cortex, 10%	Parietal cortex, 5%	Frontal cortex, 8%	Frontal cortex, 4%
	Occipital cortex, 10%		Parietal cortex, 8%	
			Piriform cortex, 5%	
			Occipital cortex, 5%	
SUBCORTICAL CONNECTIONS				
ENTORHINAL CORTEX		**PERIRHINAL AND POSTHRINAL CORTICES**		
Hippocampus		Hippocampus	Striatum	
Amygdala		Amygdala	Thalamus	

1.3 Theories of Medial Temporal Lobe Memory Systems

In humans, memory is typically divided into two systems, known as declarative and non-declarative. Declarative memory can include both episodic and semantic information and is characterised by the conscious recollection of events or facts that can be subject to verbal reflection or other means of expression (Shapiro & Eichenbaum, 1997). Non-declarative memory is characterised by non-conscious recollection of information that is only revealed by implicit measures of performance, for example, learning perceptual tasks or motor skills. In human amnesia declarative memory is usually impaired, whereas non-declarative memory remains intact (Shapiro & Eichenbaum, 1997). Human memory can also be divided into anterograde and retrograde processes. Anterograde processes refer to the acquisition of new declarative information, whereas retrograde processes refer to the recollection of declarative information acquired prior to the onset of amnesia (Shapiro & Eichenbaum, 1997). Therefore, human amnesia can be characterised by deficits in anterograde learning processes or retrograde deficits of varying severity (Parkin, 1996).

The neuropsychological data from amnesic patients prompted the development of animal models of medial temporal amnesia. Early comparative studies replicated the large bilateral temporal resection of patient HM in monkeys, resulting in severe impairments in visual recognition memory (Mishkin, 1978; Murray & Mishkin, 1984; Zola Morgan & Squire, 1985). Combined lesions to the amygdala and hippocampus were considered responsible for these severe memory impairments. However, this view was soon discredited, as equally severe impairments in recognition memory are evident following hippocampal

and rhinal lesions (Meunier et al., 1993). Furthermore, discrete stereotaxic lesions to the amygdala are shown to have no effect on primates performance in visual recognition memory tasks (Zola Morgan et al., 1989b). Consideration of the mnemonic capacities of the rhinal and parahippocampal cortices then emerged (Murray & Mishkin, 1986).

Bilateral perirhinal ablation in primates result in a deficit in recognition memory as severe as that following combined hippocampal and amygdala lesions (Meunier et al., 1993), whereas entorhinal ablation results in only a mild deficit (Leonard et al., 1995) and parahippocampal lesions produce no deficit (Ramus et al., 1994). Consequently, emphasis on the role of the rhinal cortex in recognition memory tasks has developed. Behavioural studies demonstrate distinct impairments in visual recognition memory tasks following rhinal ablation in both primates (Gaffan & Murray, 1992) and rodents (Mumby & Pinel, 1994), suggesting that the rhinal cortex is capable of sustaining recognition memory processes. Therefore, evidence from amnesic patients and intervention studies in primates and rats led to the discovery of medial temporal lobe structures involved in the processes of memory and visual perception. The exact nature of the contributions of medial temporal structures to memory remains undetermined. Present research focuses on the development of theoretical accounts of the mnemonic capacities of the hippocampus and surrounding cortices.

One theory of medial temporal memory proposed by Squire & Zola Morgan (1991) suggests declarative memory is sustained by the hippocampal memory system, composed of the hippocampus and

neighbouring parahippocampal, entorhinal and perirhinal cortices. The authors propose that temporal lobe amnesia is pathologically distinct from diencephalic amnesia, but the two systems may sustain memory by similar mechanisms (Squire & M. Zola, 1997). The hippocampus receives sensory information from association cortex passed via the entorhinal cortex from either perirhinal or parahippocampal cortex. The incoming sensory information is then bound by the hippocampus into a coherent memory trace to be stored in neocortex. This consolidation process is deemed to be time limited, resulting in temporally graded retrograde amnesia following pathology to the hippocampal memory system (Squire & Zola Morgan, 1991).

It is suggested that pathology to any area within the hippocampal memory system will result in an anterograde impairment in episodic memory, with the extent of damage determining its severity (Squire & M Zola, 1997;Zola Morgan et al., 1994). The view that structures within the hippocampal memory system are functionally uniform is supported by findings of deficits in recognition memory tasks following either hippocampal (Zola Morgan et al., 1992) or rhinal (Eacott et al., 1994) lesions in both primates and amnesic patients (Buffalo, Reber & Squire, 1998). However, reports of functional divisions within the hippocampal formation are also evident (see Aggleton & Saunders, 1997; Gaffan, 1994).

Another theory regarding the hippocampal memory system has been proposed by Eichenbaum et al. (1996), which also stresses the importance of hippocampal cortical interactions in maintaining the

existence of declarative memories. Eichenbaum outlines a memory system with three structural components; namely storage sites in neo-cortex, the hippocampus and the parahippocampal region. The rhinal and parahippocampal cortices form the parahippocampal region. Each area maintains distinct contributions to memory: the cortical areas send sensory information to the hippocampus via the parahippocampal region, the hippocampus then organises this information into a form of cortical codings to be passed back to cortical areas for storage. The authors cite supporting evidence from the study of olfactory learning in rats. Cells in piriform and orbitofrontal cortex undergo neuronal tuning and response biasing to particular odours. This process occurs independently of hippocampal activation and can facilitate odour recognition and odour-odour associations. Outputs from the hippocampus are necessary for the formation of long term memory traces in olfactory neurones that allow information regarding individual odours to be used in novel situations. This process enables the encoding of the representation of a stimulus in terms of its relationship to other stimuli and their representations in memory. Therefore the hippocampus facilitates the flexible and relational expressions of memory processes thought to be characteristic of an episodic memory system (Eichenbaum et al., 1996).

The two theories discussed so far suggest the hippocampus and surrounding cortical areas are capable of sustaining episodic memory processes (Eichenbaum et al., 1996; Squire & Zola Morgan, 1991). However, alternative theoretical approaches exist that consider the role of diencephalic structures. Delay & Brion (1969) suggest that episodic

memory is sustained by an extended hippocampal system, comprised of the hippocampus, fornix, mamillary bodies and anterior thalamus. Therefore, pathology in any component of this extended system produces comparable memory deficits. The notion of a hippocampal memory system that includes diencephalic structures, but not rhinal or parahippocampal cortices, forms the basis of a new categorisation of medial temporal memory systems (Aggleton & Saunders, 1997; Gaffan, 1998).

It has been suggested that conventional distinctions between medial temporal lobe and diencephalic amnesia are invalid as, together, structures within the medial temporal lobe and the diencephalon form one functional memory system (Aggleton & Brown, 1999; Aggleton & Saunders, 1997; Gaffan, 1998). The view that the hippocampus and diencephalon are functionally unified is supported by findings from studies of the connectional characteristics of these two regions (Aggleton & Brown, 1999; Aggleton & Saunders, 1997). The hippocampus in both primates and rodents sends efferents to the medial diencephalon, via the fornix, with the principle projection being to the anterior thalamic nuclei; in return, the anterior thalamic nuclei project back to the hippocampus (see Aggleton & Saunders, 1997). It has been suggested that these connections form a functional circuit that enables the medial diencephalon and the hippocampus to influence each other (Aggleton & Brown, 1999). This proposed circuit is thought to sustain recall memory that is necessary for the encoding and retrieval of episodic memories (Aggleton & Brown, 1999). Therefore, anterograde amnesia is thought to occur following

disruption to part of the extended hippocampal system, composed of the hippocampus, the fornix, the mamillary bodies and the medial thalamus (Aggleton & Brown, 1999; Gaffan, 1998).

The authors suggest that the extended hippocampal system is not necessary for all forms of recognition memory processes (Aggleton & Brown, 1999). Recognition memory can be divided into two distinct processes, that is, stimulus recollection and stimulus familiarity (Mandler, 1980). Stimulus recollection requires remembering the actual experiences that involved a particular stimulus; this process is thought to be hippocampal dependent (Aggleton & Brown, 1999). In contrast detecting stimulus familiarity only requires the knowledge that an item has been experienced previously, without associated details of when the stimulus was experienced. Familiarity based judgements are considered to be sustained by the perirhinal cortex and medial dorsal nucleus of the thalamus. Therefore, two functionally distinct parallel temporal – thalamic memory systems operate, both of which interact with the prefrontal cortex to enable recall strategies (Aggleton & Brown, 1999). Although the recall and recognition memory systems are deemed qualitatively distinct, information from the perirhinal recognition system is thought to be passed to the recall system, to enable the formation of item-in-place representations (Aggleton & Brown, 1999).

This distinction between recall and recognition memory is supported by the finding that lesions to the hippocampus (Rodents: Aggleton et al., 1986b; Primates: Alvarez et al., 1995), the fornix (Rodents: Aggleton et al., 1986b; Primates: Gaffan, Gaffan & Harrison,

1984) and the mamillary bodies (Rodents: Aggleton et al., 1990; Primates: Zola Morgan et al., 1989a) all produce no, or mild, deficits in recognition memory tasks. In contrast, lesions to the perirhinal cortex or the medial dorsal thalamic nuclei do result in deficits in recognition memory tasks (Rodents: Hunt & Aggleton, 1991; Mumby & Pinel, 1994; Primates: Aggleton & Mishkin, 1983; Eacott et al, 1994). Furthermore, there is evidence that lesions to the extended hippocampal system produce deficits in spatial memory tasks (Rodents: Aggleton et al., 1986b; Primates: Gaffan, 1992, 1994b). Lesions to the perirhinal cortex in rodents (Bussey et al., 1999;Ennaceur et al., 1996; Glenn & Mumby, 1998) and primates (Gaffan, 1994b) however, do not impair spatial memory tasks. These findings suggest that the hippocampus and perirhinal cortex have complementary roles in memory: the hippocampus contributing to spatial memory and the perirhinal cortex to visual object recognition.

It has been suggested that encoding and recall of episodic information by the extended hippocampal system relies upon recognising the unique spatial composition of visual scenes that share common items (Aggleton & Brown, 1999). This view is supported by reports that disconnecting the perirhinal cortex from the fornix in primates disrupts performance in an object-in-place memory task (Gaffan & Parker, 1996). These findings provide support for the suggestion that the hippocampus contributes to allocentric spatial processes and the perirhinal cortex to object recognition processes. However, both structures are implicated in processing the spatial arrangement of multiple objects within visual scenes (Aggleton & Brown, 1999; Gaffan, 1998). For example, lesions to the

rhinal cortex in primates impair performance in a spatial scene learning task that requires animals to identify individual objects within a scene to obtain reward (Murray, Baxter & Gaffan, 1998). The authors suggest that the rhinal cortex is only necessary for normal performance in spatial tasks that require the identification of visual objects (Murray, Baxter & Gaffan, 1998). In support of this view, primates with rhinal lesions were not impaired in performing a place learning task that did not require the identification of visual objects (Murray, Baxter & Gaffan, 1998).

The previous hypothesis is similar to that proposed by Gaffan (1998), he suggests that the hippocampus, fornix, mamillary bodies and anterior thalamus sustain episodic memory by combining idiothetic information into object-place configurations. There are reports that in primates lesions to the extended hippocampal system produce impairments in object-in-place memory tasks (Gaffan, 1994b; Parker & Gaffan, 1997a, b). It is suggested that when a primate forms object-place configurations, object information is received from the perirhinal cortex and configured with idiothetic information from the hippocampus regarding the spatial location of the subject in relation to the object. These object-place configurations are then stored in synaptic associations between cells representing the object and cells representing the place.

The theories proposed by Gaffan (1998) and Aggleton & Saunders (1997) both distinguish between episodic or recall memory sustained by the hippocampus and diencephalon and recognition memory sustained by the perirhinal and parahippocampal cortices. These differing theoretical accounts of memory in the medial temporal lobe highlight the need to

explore how individual structures within the medial temporal lobe form a coherent memory system and how perception and memory are integrated. Furthering our understanding of perirhinal contributions to visual memory will help elucidate whether this cortical area forms part of a distinct recognition memory system (Aggleton & Saunders, 1997; Gaffan, 1998) or part of an integral hippocampal memory system (Eichenbaum, 1996; Squire & Zola Morgan, 1991).

1.4 The Role of the Hippocampus in Memory

The hippocampus is widely considered to contribute to normal memory processes (Eichenbaum et al., 1994), with evidence of hippocampal lesions resulting in human amnesia. Patient HM experienced profound anterograde amnesia following bilateral temporal lobe resection (Corkin, 1984; Corkin et al., 1997; Scoville & Milner, 1957), as did patient PB, following bilateral hippocampal damage due to surgery and epilepsy associated hippocampal sclerosis (Corkin, 1965; Margerison & Corsellis, 1966; Penfield & Mathison, 1974). Patients RB, GD, LM and WH all experienced anterograde amnesia as a result of cell loss predominantly in field CA1 of the hippocampus (Rempel Clower et al., 1996; Zola Morgan et al., 1986,). Although these findings suggest the hippocampus contributes to anterograde memory, they do not rule out the possibility of other areas also contributing crucially to normal memory processes. It is possible that other non-hippocampal pathology, not detected at post-mortem, contributed to the amnesia experienced by these patients.

Animal models of amnesia often rely on the recognition memory tasks, delayed match or non-match to sample (DMS/DNMS) to test for

anterograde memory impairments. Studies measuring the effect of hippocampectomy on animals' performance in DMS/DNMS tasks have produced contradictory findings. There are reports of impaired performances in recognition memory tasks following ischaemic damage to hippocampal field CA1 in primates (Zola Morgan et al., 1992). However, there is also evidence of intact recognition memory following hippocampectomies in the rodent (Aggleton et al., 1986b; Mumby et al., 1992) and impairments only at long delay intervals in primates (Alvarez et al., 1995). These inconsistencies may reflect variations in the lesion techniques used (Aggleton & Brown,1999; Gaffan, 1998). For example, in the Zola Morgan et al. (1992) study ischaemic damage may have produced more diffuse cell damage throughout the medial temporal lobe that was not detected at autopsy. In comparison, the stereotaxic radiofrequency lesions produced by Alvarez et al. (1995) may have produced more discrete hippocampal damage. Particular lesion techniques, such as aspiration, increase the risk of unintended damage to neighbouring rhinal cortex (Gaffan & Lim, 1991), an area implicated in recognition memory (Rodents: Mumby & Pinel, 1994; Primates: Eacott et al., 1994). Disruption to the main source of hippocampal efferent information by transection of the fornix, a procedure that avoids inadvertent cortical damage, has no effect on recognition memory tasks in rats (Ennaceur et al., 1997) or primates (Gaffan et al., 1984).

These inconsistencies in the effects of hippocampectomies on recognition memory tasks suggest the hippocampus may not be necessary for visual recognition processes. In contrast, behavioural and

electrophysiological evidence suggest the hippocampus contributes to allocentric spatial memory processes. Hippocampal ablation or fornix transection in rats disrupts spatial working memory tasks (Aggleton et al., 1986b; Ennaceur et al. 1996; Glenn & Mumby, 1998) and spatial learning tasks (Gallagher & Holland, 1992). Similarly, in primates, fornix transection disrupts spatial discrimination and spatial reversal tasks (Gaffan, 1994a; Gaffan & Harrison, 1989a,b). Furthermore, c-fos recording studies in rats demonstrate increased neuronal activity in the hippocampus following exposure to a novel environment (Zhu et al., 1997). In this study it was found that viewing familiar visual objects in a new location increased activity in the hippocampus of the rat, suggesting the hippocampus is involved in processing contextual or spatial information regarding familiar visual objects. There are reports that the novel arrangement of familiar visual stimuli also results in increased neuronal activity, as shown by c-fos recordings, in CA1 of the hippocampus in rats (Wan, Aggleton & Brown, 1999). Together these recording studies suggest that the hippocampus encodes the spatial arrangement or context of familiar visual objects.

Single cell recordings in primates suggest hippocampal cells signal repeat presentation of an object in a particular spatial location (Rolls et al., 1989) and idiothetic information regarding the movement of a subjects' eye (Rolls et al., 1997) and hand (Miyashita et al., 1989) in relation to visual objects. These neuronal processes could contribute to object-place configurations, where the object is a visual stimulus and the place is idiothetic information regarding position of the stimulus in relation to the

viewer's spatial environment (Gaffan, 1998). There are reports that lesions to the hippocampus (Murray, Baxter & Gaffan, 1998), the fornix (Gaffan & Harrison, 1989a,b) and the mamillary bodies (Parker & Gaffan, 1997b) impair object-in-place memory tasks. Therefore, the extended hippocampal system appears to encode the spatial arrangement of visual objects within a scene. These findings suggest that the contribution of the hippocampus to spatial memory processes extends beyond allocentric spatial memory processes. It has been suggested that the spatial processing performed by the hippocampus is not strictly egocentric or allocentric, but idiothetic, for controlling locomotion (Gaffan, 1998). For example, the hippocampus may support the spatial processing of eye movements when discriminating between visual scenes; this information may then indirectly promote a suitable motor movement, such as reaching for an object within the scene (Gaffan, 1998).

The detrimental effects of hippocampal ablation on spatial memory tasks contrast with reports that perirhinal ablation in both primates (Gaffan, 1994a) and rodents (Ennaceur et al., 1996) have no effect on spatial memory tasks. These findings contradict the view that the hippocampus and perirhinal cortex sustains functionally similar contributions to memory (Squire & Zola Morgan, 1991). However, they do support the hypothesis that the hippocampus and it surrounding cortical areas maintain functionally distinct contributions to episodic memory (Aggleton & Saunders, 1997; Delay & Brion, 1969; Gaffan, 1998,).

Evidence of retrograde amnesia following hippocampal pathology has led to the suggestion that the hippocampus contributes to the

consolidation of episodic memories (Zola Morgan & Squire, 1990). New information is held in the hippocampus until a permanent memory, independent of the medial temporal lobe is developed within neocortex. There is evidence that hippocampal and rhinal lesions in primates impair retrieval of object discriminations learnt up to 8 weeks prior to surgery, whilst retrieval of discriminations learnt 16 weeks prior remain intact (Zola Morgan & Squire, 1990). Subsequent studies in rats of spatial memory (Weisand et al., 1996), object-in-place memory (Koerner et al., 1996), and object discriminations (Astur et al., 1994) fail to replicate these findings with lesions restricted to the hippocampus. Further studies with lesions restricted to the rhinal or perirhinal cortex have also proved inconclusive, with evidence of a temporally graded memory loss (Rodents: Wiig et al., 1996) and no temporal gradient (Rodents: Astur et al., 1995; Primates: Thornton, Rothblat & Murray, 1997). The variations in time intervals and tasks used in these studies may have produced the inconsistencies in these results, it remains to be seen whether the hippocampus or rhinal cortex contribute to a time limited consolidation process.

The behavioural evidence reviewed here suggests that whilst the hippocampus is crucial for some forms of memory, its exact role in episodic and visual recognition memory systems is not yet fully understood.

1.5 The Role of the Postrhinal/Parahippocampal Cortex in Memory

Parahippocampal cortex is deemed to form part of the dorsal or occipitoparietal pathway, coursing from the occipital lobes to the parietal

cortex and deemed to be necessary for spatial vision and visuomotor control (Ungeleider & Haxby, 1994). Findings from an FMRI recording study in humans suggest that parahippocampal cortex is involved in encoding complex pictures and object position configurations (Gabrielli et al., 1997). Behavioural studies suggest that the parahippocampal cortex contributes to visuospatial tasks. There is evidence of spatial view cells within parahippocampal cortex that respond to variations in visual fixation points (Rolls & O' Mara, 1995). In primates, parahippocampal lesions result in impairments in spatial orientation tasks (Habib & Sirigu, 1987), spatial reversal tasks (Teng, Squire & Zola, 1997), and object place associations (Malkora & Mishkin, 1997). In contrast, parahippocampal lesions in primates have no effect on performance in object recognition tasks (Murray & Gaffan, 1993; Ramus et al., 1994).

There is limited evidence of the effects of postrhinal ablation on spatial tasks in rodents. However, there are reports that performance in allocentric spatial memory tasks, such as the Morris water maze and radial arm maze, is normal following combined lesions to the perirhinal and postrhinal cortex (Bussey et al., 1999). The authors suggest spatial memory processes within the hippocampus are not dependent upon interaction with the postrhinal cortex. Therefore, while the behavioural evidence from primate studies suggests that the parahippocampal cortex contributes to visuospatial processing, the behavioural evidence from rodents is less conclusive.

According to the theories of medial temporal memory proposed by Squire & Zola Morgan (1991) and Eichenbaum (1996) the

parahippocampal cortex contributes to memory by collating afferents from uni- and poly-modal association areas to the hippocampus. However, behavioural (Habib & Sirigu, 1987; Malkora & Mishkin, 1997;Teng, Squire & Zola, 1997) and electrophysiological (Rolls & O' Mara, 1995) evidence from primate studies suggest that the parahippocampal cortex may also maintain an active role in processing visuospatial information for mnemonic purposes. The behavioural evidence from primates is consistent with Aggleton & Brown's (1999) view that parahippocampal cortex provides an active integration of object recognition and visuospatial processes, necessary for encoding episodic memories in the hippocampus. Further studies are needed in rats to ascertain the role of the postrhinal cortex in visuospatial processes.

1.6 The Role of the Entorhinal Cortex in Memory

Single cell recording studies in the entorhinal cortex in primates performing object recognition and place memory tasks found stimulus selective cells that respond selectively to individual objects or places (Suzuki et al., 1997). It was shown that cells within the entorhinal cortex display stimulus specific delay activity during the object recognition task and location specific delay activity during the place memory task. These findings suggest entorhinal cells may encode sensory information regarding visual objects and their spatial locations for short- term memory processes.

However, it has been shown that entorhinal lesions in rats do not impair spatial memory in a radial maze task (Galani, Coutureau, Kelche, 1998; Kesner & Giles, 1998) or in a delayed-match-to-position task

(Marighetto, Yee & Rawlins, 1998). Furthermore, entorhinal lesions have no or little effect on performance in recognition memory tasks, such as delayed-match-to-sample (Leonard et al., 1995; Meunier et al., 1993). However, transection of the angular bundle of the perforant pathway, thereby disrupting entorhinal-hippocampal circuitry, impairs retention of object discriminations acquired post surgery in the rat (Vnek et al., 1995). Similarly, rats with entorhinal lesions acquire a delayed match to position task normally, but exhibit impaired saving of the task over a 4 week period (Marighetto, Yee & Rawlins, 1998). These findings suggest that the entorhinal cortex may contribute to the consolidation or retention of mnemonic processes by virtue of its extensive cortical and subcortical connections.

1.7 The Role of the Perirhinal Cortex in Memory

It has been suggested that the perirhinal cortex provides information regarding visual objects and their meaning for the purposes of both perception and memory (Eacott & Heywood, 1995; Murray & Bussey, 1999; Nakumura & Kubota, 1996). However, the exact nature of how mechanisms within the perirhinal cortex contribute to perceptual and mnemonic processes remains unclear.

1.7. i Findings from Electrophysiological Studies: Object Recognition

Electrophysiological evidence supports the view that the perirhinal cortex contributes to object recognition processes. In primates, perirhinal cortex and area TE form part of the inferotemporal cortex, a component of the ventral visual pathway, responsible for object recognition (Gross,

1992; Macko et al., 1982). As this pathway extends from the occipital lobes to inferotemporal cortex, the size and complexity of cells receptive fields increase, so that inferotemporal neurones frequently encode pattern and form information (Desimone et al., 1984; Gross & Bender, 1969; Gross et al., 1972). Recording studies show populations of perirhinal neurones that respond selectively to highly complex visual stimuli, such as hands, faces and geometric forms (Primates: Gross et al., 1972; Rodents: Zhu, Brown & Aggleton, 1995).

Exposure to visual stimuli in primates results in a perceptual learning process, whereby individual cells finely tune their response properties to particular visual stimuli that fall within the range of their endogenous stimulus selectivity (Sakai et al., 1994). This process is thought to subserve category related recognition processes, allowing fine form discrimination amongst highly similar items within a global form category.

Neuronal mechanisms within the perirhinal cortex also contribute to the achievement of viewpoint invariant representations of visual objects (Sato et al., 1980). Electrophysiological recordings from perirhinal cells in primates performing a delayed-match-to-sample task found that stimulus preferences within cells remain constant despite changes in the relative size and location (Sary et al., 1993) or size and orientation (Miyashita & Chang, 1988) of the test stimuli. Single cell recordings in primates performing a fixation task found that response rates in shape-selective cells also remain constant despite changes in luminance, texture or the relative motion of the visual test stimuli (Sary et al., 1993). Stimulus selective

cells in the perirhinal cortex in the primate also retain their response properties to presentations of single sections of the original stimuli (Nakumura et al., 1992). The cells continue to respond to several different parts of a complex visual stimulus that share no common visual feature, this process suggests such cells may encode abstract representations of visual stimuli (Nakumura & Kubota, 1996).

These findings suggest an active role of the perirhinal cortex in sensory processes, contradicting reports that the main capacity of the perirhinal cortex is a source of sensory afferents to the hippocampus (Squire & Zola Morgan, 1991). These studies support the view that the perirhinal cortex contributes to object recognition processes, information from which may then be passed to the extended hippocampal system for mnemonic purposes (Aggleton & Brown, 1999; Gaffan, 1998). However, most of the findings reported here are from primate studies, and so further studies in rats are needed to determine whether the same impairments exist. Ablation of the perirhinal cortex in the primate may disrupt object recognition processes by virtue of its extensive cortical inputs from visual association cortices. Therefore, deficits may not occur in the rat, as the perirhinal cortex in the rat receives less substantial visual inputs (Burwell et al., 1995).

1.7. ii Findings from Electrophysiological Studies: Object Familiarity

Recording studies suggest that cells within the perirhinal cortex also encode the relative familiarity and recency of occurrence of visual stimuli (Brown, 1996). Electrophysiological studies in primates (Brown, Wilson & Riches, 1987; Fahy et al., 1993; Li et al., 1993; Miller et al.,

1991) and rodents (Zhu, Brown & Aggleton, 1995) have found stimulus selective cells in the perirhinal cortex that respond differently upon repeat presentation of a stimulus. Neurones respond maximally to novel stimuli within their stimulus selectivity (Brown et al., 1987). However, repeat presentation of the stimulus results in a reduction of response rates (Brown et al., 1987). Other stimulus selective cells are insensitive to the relative familiarity of a stimulus, but decrease response rates when the stimulus is repeatedly presented within a short time span, regardless of the familiarity of the stimulus (Riches et al., 1991). In contrast to the perceptual learning mechanism described earlier, the recency and familiarity of visual stimuli are predominantly encoded by a repetition suppression mechanism (Brown 1996). Stimulus selective cells in primates decrease their response rates upon repeat presentation of a visual stimulus, whereas presentation of novel stimuli within the global form selectivity of a cell results in an increased response (Brown et al., 1987; Riches et al., 1991). The authors argue that this is not a process of habituation, as the response decrement survives despite presentation of intervening stimuli and increasing time intervals between presentation, with no evidence of dishabituation. The number of intervening stimuli presented ranged from five stimuli for 69% of recorded cells, to 20 stimuli for 60% of cells recorded. The memory spans of cells range from under 1 minute to 24 hours and over (Fahy et al., 1993). It has been suggested that variations in time intervals may facilitate familiarity and recency judgements in different memory tasks (Brown, 1996). It is thought that cells with decremental responses operate by a system of synaptic subsets that enable the cell to increase responses to

novel stimuli within their global form selectivity and decrease responses to familiar stimuli (Brown, 1996). This process could facilitate increased attention to novel stimuli and provide a link between perceptual and mnemonic processes.

Evidence suggests that the incidence of neurones with decremental response rates is approximately 50 % of all visually responsive cells measured within primates' inferotemporal cortex (Brown, 1996). Recording studies document smaller numbers of cells that display incremental response rates upon repeat presentation of visual stimuli (Miller & Desimone, 1993). Incremental response cells are found more frequently in rats than primates and when the task used requires the subject to hold sample stimuli in memory despite presentation of other intervening stimuli (Miller & Desimone, 1993). This process of incremental responding may facilitate familiarity or recency judgements in working memory tasks.

The response rates of familiarity and recency neurones appear to be an endogenous property of these cells, as response properties remain constant in primates performing recognition memory tasks, serial recognition tasks and even when no behavioural contingency is used (Brown, 1996). Therefore, perceptual and mnemonic information may be integrated within the perirhinal cortex (Eacott & Heywood, 1995). The information encoded by cells receptive to the sensory and mnemonic aspects of visual stimuli may contribute to performance in recognition memory tasks. For example, there is evidence of shape selective perirhinal cells in primates sustaining increased electrical activity during the delay

period of a recognition memory task (Miyashita & Chang, 1988). The delay activity continued despite manipulations of the size, colour or orientation of the target stimuli. This process of sustained neuronal activity triggered by stimuli presentation may maintain the internal image of a stimulus to aid recognition judgements (Miyashita & Chang, 1988). However, presentation of intervening non-match stimuli in the delay period of a recognition task prevents the delay activity of cells from continuing in an organised or recognisable pattern (Miller & Desimone, 1993). Therefore, the mechanisms and purposes of delay activity are unclear. They may not maintain an internal image, but instead contribute to paired associate learning, whereby an association is formed between 2 visual stimuli (Desimone, 1996).

These findings suggest that information held in memory regarding the familiarity and recency of presentation of complex visual stimuli influences the response activity of cells within the perirhinal cortex (Miller et al., 1991). The finding that perirhinal neurones respond differently to novel and familiar visual stimuli has also been found in brain activation studies (Aggleton & Brown, 1999). In addition to perirhinal neurones that respond to the sensory properties of visual stimuli, cells also encode mnemonic information regarding the familiarity and recency of presentation of visual stimuli. The location of neurones receptive to changes in the familiarity of visual stimuli has been studied by monitoring the expression of the immediate early gene c-fos, an indicator of neuronal activity (Zhu et al., 1995). Presentation of novel visual stimuli results in increased c-fos expression in perirhinal cortex and area TE in the rat,

whereas presentation of familiar stimuli results in lower expression rates (Zhu et al., 1995). The authors found no significant differences in c-fos expression in the hippocampus, entorhinal cortex, septal nuclei or mamillary bodies, supporting the view that neurones signalling familiarity of visual stimuli are located predominately within perirhinal cortex and area TE.

1.7. iii Findings from Behavioural Studies: Visual Recognition Memory Tasks

Electrophysiological evidence to suggest that the perirhinal cortex contributes to both perceptual and mnemonic processes is supported by findings from behavioural studies. Primates (Gaffan & Murray, 1992) and rodents (Mumby & Pinel, 1994) demonstrate distinct impairments in visual recognition memory tasks following rhinal ablation. Lesions restricted to the perirhinal cortex also produce a deficit in primates (Meunier et al., 1993). However, the precise role of the perirhinal cortex in recognition memory remains ambiguous. There is evidence that increasing the delay period in a delayed-match-to-sample test has a detrimental effect on performance in rats (Mumby & Pinel, 1994). Further studies demonstrate that following rhinal ablation primates retain the ability to perform a delayed-match-to-sample task providing the stimuli set used is relatively small (Eacott et al., 1994). Increasing the stimuli set, thereby rendering each stimuli trial-unique, reveals a deficit. This deficit is evident when there is no delay interval between stimulus presentations, suggesting an impairment in simultaneous matching to sample (Eacott et al., 1994). Deficits in recognition memory tasks are also evident when the stimuli are

complex and difficult to distinguish, yet animals perform the task normally when the same 4 stimuli are used repeatedly (Eacott et al., 1994).

These findings are supported by reports that cooling of the inferiortemporal gyrus in monkeys impairs performance in a delayed-match-to-sample task with a large number of visual stimuli presented simultaneously without a delay interval (Horel et al., 1987). Performance in a visual discrimination task with complex stimuli (different views of monkey faces) is also impaired, yet performance remains intact when the stimuli used are simple geometric shapes (Horel et al., 1987). Furthermore, there are reports that perirhinal ablation in the monkey produces a deficit in a delayed-match-to-sample task with trial-unique stimuli (Gaffan & Murray, 1992; Meunier et al., 1993). It could be argued that impaired performances in recognition memory tasks are due to deficits in recency memory. However, if this were the case deficits might be expected to be delay-dependent and not to be evident in simultaneous matching conditions. Indeed, there are further reports that deficits in recognition memory tasks following perirhinal and parahippocampal lesions in the monkey are not always delay-dependent (Zola Morgan et al., 1989). Furthermore, there is evidence that perirhinal ablation does not impair primates performances in a test of recency memory with 4 stimuli (Eacott et al., 1994). These findings suggest that perceptual impairments in object identification may underlie the deficits reported in recognition memory tasks following perirhinal ablation. However, it is unclear to what extent deficits in recognition memory are a result of disruption to perceptual or mnemonic processes.

There are reports that perirhinal ablation in the rat impairs recognition of real objects in a spontaneous object recognition task, following a retention delay of 15 minutes (Ennaceur et al., 1996). These findings suggest that increasing mnemonic demands in recognition memory tasks has a detrimental affect on performance in the rat. However, there are also reports that suggest that increasing the demands on the perceptual processes of object identification reveals deficits in visual discrimination learning in the primate. For example, perirhinal ablation in the monkey impairs the ability to learn a 40 pair concurrent discrimination task in which the stimuli are visual objects presented in different views in each trial (Buckley & Gaffan, 1998b). Furthermore, recognition of 10 pairs of familiar visual objects presented in new orientations or embedded within visual scenes is also impaired following perirhinal ablation in the primate (Buckley & Gaffan, 1998a).

1.7. iv Findings from Behavioural Studies: Associative Learning

Whilst both electrophysiological and behavioural studies suggest that mechanisms within the rhinal cortex contribute to visual recognition memory (Gaffan & Murray, 1992; Fahy Riches & Brown, 1993; Meunier et al., 1993; Miller and Desimone, 1993) the behavioural effects of perirhinal ablation on visual associative memory tasks are less certain. There is evidence to suggest that combined lesions to the hippocampus, amygdala and rhinal cortex have dissociable effects on visual recognition and visual associative memory tasks in the primate (Malamut, Saunders & Mishkin, 1984; Overman, Ormsby & Mishkin, 1990; Phillips & Mishkin, 1984). Despite impairments in visual recognition tasks, primates may

demonstrate normal performances in two-choice visual discrimination learning (Malamut, Saunders & Mishkin, 1984) and 8 pair concurrent visual discrimination learning (Overman, Ormsby & Mishkin, 1990), following lesions to the hippocampus, amygdala and rhinal cortex. These findings are supported by reports of deficits in recognition memory tasks, yet normal acquisition of concurrent visual discriminations, with 24-hour intertrial intervals and real objects following rhinal cortex lesions in the primate (Gaffan & Murray, 1992). These findings suggest visual associative learning is not adversely affected by perirhinal ablation in the primate.

However, recent studies suggest that the perirhinal cortex maintains associative capacities, contributing to stimulus-stimulus associations both within and between sensory modalities. Rhinal lesions in primates disrupt both the acquisition and retrieval of visual associations (Murray et al., 1993, Buckley & Gaffan, 1997), cross modal auditory-visual associations (Murray & Gaffan, 1994), flavour-visual associations (Parker & Gaffan, 1998), visual–tactile associations (Goulet & Murray, 1995) and between sensory stimuli and an aversive event in fear conditioning (Romanski & Le Doux, 1992). Furthermore, perirhinal lesions disrupt the retention of fear conditioning between an aversive event and visual (Rosen et al., 1992), auditory (Romanski & LeDoux, 1992) or contextual stimuli (Corodimas & LeDoux, 1995) acquired prior to surgery in the rat.

However, the effects of perirhinal ablation on acquisition and retrieval of visual stimulus-reward associative learning have produced

contradictory findings. There are reports that perirhinal ablation in the rat (Wiig, Cooper & Bear, 1996, Eacott, 1998) and the primate (Gaffan & Murray, 1992) impairs retrieval of visual associative learning acquired prior to surgery, whilst new post-operative learning remains intact. However, similar studies in primates reveal deficits in both retention and acquisition by increasing the number of stimuli in the discrimination learning set (Buckley & Gaffan, 1997; Gaffan, 1994). Therefore, the behavioural effects of perirhinal ablation on visual associative learning are unclear. It is possible that, following perirhinal ablation, a dissociation exists between the processes of retrieval and acquisition. Alternatively, increasing demands on the processes of visual object identification may reveal deficits in both acquisition and retention of visual associative learning (Buckley & Gaffan, 1997).

It has been shown that perirhinal lesions disrupt the acquisition and retrieval of visual stimulus-stimulus associations in the primate (Murray et al., 1993). The process of visual stimuli-stimuli association appears to be dependent upon neuronal mechanisms within the perirhinal cortex and area TE. Single cell recordings in primates performing a visual paired association task found cells operated pair coding or pair recall mechanisms (Sakai & Miyashita, 1991). The pair recall neurones respond optimally to one stimulus within a learnt paired association, maintaining activation until presentation of its paired associate. The pair coding neurones respond optimally to both stimuli within a paired association. Following perirhinal ablation in primates, pair coding and pair recall neurones within area TE still respond to visual stimuli in paired association tasks, however recall of

paired associate information is severely impaired. Therefore, activation of these associative mechanisms appears to be dependent on prominent back projections to TE from the perirhinal cortex (Higushi & Miyashita, 1991).

An additional associative mechanism has been documented within perirhinal cortex and area TE, whereby shape selective cells form associations between temporally related visual stimuli. Single cell recording studies in primates found associations between highly different visual stimuli that were presented sequentially (Miyashita, 1988). This process may encode different visual elements within a scene or viewpoints of an object as we move in relation to it. A recent study suggests that associative learning between visual stimuli and food reward is dependent upon cortical connections from visual associative area TE to the lateral hypothalamus, via the perirhinal cortex and amygdala (Easton & Gaffan, 1997). Therefore, perirhinal cortex appears to contribute to associative learning in several ways and these mechanisms may be utilised in visual associative and configural memory processes.

1.7 v Findings from Behavioural Studies: Configural Associative Learning

The associative properties of the perirhinal cortex may sustain configural learning, as it relies upon associations between a number of elemental visual stimuli to form distinctive compound stimuli. Episodic memory in humans is thought to rely upon the ability to form new memory representations that are novel configurations of existing representations, by binding visual objects into unique configurations of spatial relationships

or linguistic rules (Gaffan, 1998; Rickard & Grafman, 1998; Rudy & Sutherland, 1995).

It has been suggested that the hippocampus sustains a configural associative system, as hippocampal lesions in rats impair retention and acquisition of negative patterning tasks (Rudy & Sutherland, 1989). Subsequent studies in rats found hippocampal lesions to have no effect on performance in negative patterning tasks (Davidson et al., 1993; Deacon & Rawlins, 1996; Skinner et al., 1992), feature neutral discriminations (Gallagher & Holland, 1992) or biconditional discrimination tasks (Murphy et al., 1993). Furthermore, hippocampal lesions in rats improve performance in biconditional discrimination tasks with short intertrial intervals by reducing proactive interference from the previous trial (Han, Gallagher & Holland, 1998). These findings prompted a reappraisal of the configural associative theory. It is now suggested that the hippocampus works to promote representations of configural associations in cortical areas (Rudy & Sutherland, 1995). There are reports of cortical lesions to the dorsal prestriate cortex impairing visuospatial configural learning in primates (Gaffan & Harrison, 1993) and of lesions to the posterior parietal and prestriate cortex impairing performance in negative patterning tasks in rats (Deacon & Rawlins, 1996). Furthermore, lesions to the perirhinal cortex impair visual configural learning in primates (Buckley & Gaffan, 1998). Therefore, further studies are needed to determine the nature of perirhinal contributions to configural learning. As emphasis has been placed on the possible use of configural associations in the formation of

episodic memories, exploring the configural capacities of perirhinal cortex may help elucidate its wider role in memory.

1.7. vi Conclusions

From the studies reviewed here, the perirhinal cortex appears to contribute to sensory, associative and mnemonic processes as well as providing the main sources of uni- and poly-modal cortical afferents to the hippocampus. On the basis of the electrophysiological and behavioural studies it has been suggested that the perirhinal cortex plays a general role in visual object recognition by providing complete representations of visual stimuli (Eacott & Heywood, 1995, Murray & Bussey, 1999). The perirhinal cortex may to contribute to stimulus categorisation by forming complete representations of stimuli comprised of a number of elemental stimuli (Dean,1976; Eacott & Heywood, 1995; Murray & Bussey, 1999). Further studies regarding the mnemonic and perceptual capacities of the perirhinal cortex are needed to ascertain its role in learning about different types of visual stimuli. The wider role of the perirhinal cortex in memory remains uncertain. It has been suggested that it contributes to the consolidation of sensory information by virtue of its extensive hippocampal and cortical connections (Squire & Zola Morgan, 1991). An alternative view is that the perirhinal cortex provides information regarding visual recognition to be used for mnemonic purposes by the hippocampus (Aggleton & Brown, 1999). Further studies are needed to establish the role of the perirhinal cortex in visual mnemonic processes in order to determine whether it forms part of a distinct visual recognition memory system (Aggleton & Saunders, 1997; Gaffan, 1998) or part of an

integral hippocampal memory system (Eichenbaum, 1996; Squire & Zola Morgan, 1991). Furthermore, it is of interest to determine whether the perirhinal cortex contributes to the long-term process of identifying visual stimuli.

1.8 Human Homologue of the Perirhinal Cortex

In humans, the homologue of the perirhinal cortex occupies the ventromedial aspect of the temporal cortex, extending from the temporal pole to the rostral limit of the lateral geniculate nucleus (Amaral & Insausti, 1990). The ventral surface of the perirhinal cortex lies on the banks of the collateral sulcus; it is bordered medially by entorhinal cortex and laterally by inferotemporal cortex. However, the exact boundaries of the human homologue of perirhinal cortex are yet to be defined (Simons, Graham & Hodges, 1999).

Based on findings from behavioural studies, it has been suggested that the perirhinal cortex in both humans and animals sustains knowledge about objects and their meaning (Murray & Bussey, 1999). The study of the cognitive functions of the perirhinal cortex in humans is limited, as patients with focal perirhinal pathology are rare. However, the study of amnesic and Alzheimer's patients suggests that, in humans, perirhinal pathology disrupts the cognitive processes of memory and higher order visual processes. For example, in Alzheimer's disease the first signs of pathology occur in the perirhinal and entorhinal cortices (Braak & Braak, 1994) and these areas both lose volume in Alzheimer's patients (Juottonen et al., 1998). The early cognitive deficits in Alzheimer's disease include impairments in memory and higher order visual processing, such as

complex object recognition (Levine, Lee & Fisher, 1993; Kurylo et al., 1996; Mendez et al., 1990). There are reports that perirhinal pathology also occurs in cases of semantic dementia, producing visual semantic memory losses (Hodge et al., 1992). Therefore, it has been suggested that in humans the perirhinal cortex contributes to the semantic process of endowing objects with meaning (Murray & Bussey, 1999).

However, there are limitations to the view that the perirhinal cortex contributes to semantic memory and semantic dementia in humans (Simon, Graham & Hodges, 1999). It has been suggested that anterolateral temporal cortical damage is more closely related to semantic memory loss than pathology in the ventromedial temporal regions, therefore, the caudal extent of the perirhinal cortex may be spared in cases of semantic dementia. Furthermore, patients with semantic dementia may exhibit intact episodic and recognition memory abilities (Simon, Graham & Hodges, 1999). Bussey & Murray (1999) suggest that their model of inferotemporal function can account for these findings. They suggest that the inferotemporal cortex is organised in a functional hierarchy, in which coding of a visual object is widely distributed throughout anterolateral and ventrolateral temporal cortical regions. Therefore damage to anterolateral temporal cortex in semantic dementia patients may not disrupt recognition memory, as this may be maintained by ventrolateral temporal regions. Furthermore, damage to anterolateral temporal cortex may be sufficient to cause semantic memory impairments as this would remove representations of sensory stimuli and disconnect this region from sensory inputs from the ventrolateral temporal cortex.

It has been suggested that inferotemporal cortex is organised in a functional hierarchy, in which area TE sustains recognition of relatively simple visual stimuli and the perirhinal cortex sustains recognition of complex or configured stimuli (Murray & Bussey, 1999). The notion of functional divisions within the inferotemporal cortex is supported by findings from temporal lobectomy patients. It has been shown that patients with discrete unilateral lesions in the anterior temporal lobe perform shape recognition and object naming tasks normally (Biederman et al., 1997). However, following more extensive unilateral temporal lobectomies patients are impaired in detecting distortions in the shape of visual stimuli and recognising changes in the orientation of texture elements (Huxlin & Merigan, 1998). These findings suggest that, in humans, simple object recognition may be completed posterior to the anterior temporal inferotemporal cortex.

Amnesic patients with pathology in the ventromedial aspect of the temporal lobe usually display deficits in visual recognition memory tasks (Aggleton & Shaw, 1996; Buffalo, Reber & Squire, 1998). However, not all amnesic patients experience impairments in recognition memory tasks or sustain perirhinal cortex pathology. Amnesics with damage in the hippocampus, mamillary bodies and the fornix all fail to demonstrate a clear impairment in recognition memory tasks (Aggleton & Shaw, 1996). Therefore, it has been suggested that recognition memory in humans can be divided into retrieval and familiarity based systems. Familiarity judgements are based on knowledge regarding individual stimuli, whereas

retrieval processes require recollection of contextual information associated with individual stimuli (Aggleton & Saunders, 1997).

This assumption forms the basis of a new neuropathological grouping of anterograde amnesia in which it is suggested that the perirhinal cortex and the medial dorsal nucleus of the thalamus may sustain the processes of familiarity based recognition memory. The hippocampus, mamillary bodies and anterior thalamic nucleus are deemed to sustain retrieval of episodic memories that require the recollection of contextual information. The suggestion that recognition and recall processes are reliant upon functionally distinct temporal-thalamic memory systems is supported by the known anatomical links within the medial temporal lobe and findings from animal studies (Aggleton & Saunders, 1997). For example, the perirhinal cortex in both rodents and primates sustains links to the medial dorsal nucleus of the thalamus, an area also implicated in recognition memory in primates (Aggleton & Mishkin, 1983; Aggleton et al., 1986a). This new anatomical basis of amnesia supports the view that the perirhinal cortex in both humans and animals sustains visual recognition processes. It is uncertain how mechanisms within the perirhinal cortex sustain the processes of visual object recognition, endow objects with meaning and pass this information to the hippocampal retrieval system. Therefore, in humans, the perirhinal cortex may contribute to a temporal thalamic system that sustains visual recognition processes (Aggleton & Shaw, 1997), and may maintain knowledge regarding visual objects (Murray & Bussey, 1999). Further studies in both

humans and animals are needed to elucidate the role of the perirhinal cortex in both mnemonic and perceptual processes.

1.9 Aims of Thesis

The main aims of this thesis are to investigate the role of the perirhinal cortex in visual mnemonic processes in the rat. This work contributes to the further aim of understanding how structures within the medial temporal lobe sustain different forms of learning and memory.

As there is evidence to suggest that the rhinal cortex may contribute to the consolidation of visual associative information (see section 3.1), experiment 1 (chapter 3) measured the effects of perirhinal ablation on the retention of 2 sets of concurrent visual discriminations learnt at different time intervals prior to surgery. The aim of experiment 2 (chapter 4) was to determine whether perirhinal cortex ablation impairs the acquisition of visual associative learning when increased demands are made on object identification.

The aim of experiments 3a and 3b (chapter 5) was to determine whether the perirhinal cortex contributes to the sensory processes of identifying and generalising to familiar visual objects in a visual discrimination task learnt either prior to or following surgery.

The initial generalisation experiments 3a and 3b (chapter 5) were followed up by experiments 4 (chapter 6) and 5 (chapter 7), that were designed to place further demands on the processes of visual object identification following perirhinal ablation. The aim of these experiments was to investigate the effects of increasing demands on stimuli identification in a visual discrimination learning task.

Experiment 6 (chapter 8) measured the effects of perirhinal ablation on acquisition of a nonconfigural visual discrimination and its partial reversal, along with a biconditional visual configural discrimination task to determine whether the perirhinal cortex contributes to visual configural learning.

Chapter 2: General Method

2.1 Subjects

The subjects used in the following experimental chapters were forty-one male Dark Agouti rats, supplied by Bantin & Kingman, Hull, UK. The animals used in experiments 1 and 2, described in chapters 3 and 4, were housed individually, however, following Home Office advice, the second group of animals used in experiments 3a, 3b, 4, 5 and 6, as described in chapters 5, 6, 7, & 8, were housed in pairs. All animals were housed in diurnal conditions (12h light/12h dark cycle) and were tested during the light period of the cycle, five days a week. Except when in the testing apparatus, the rats had free access to water and were food deprived prior to testing to approximately 85% of normal body weight. All animals were weighed weekly to monitor weight gains or losses and maintain weight within these limits.

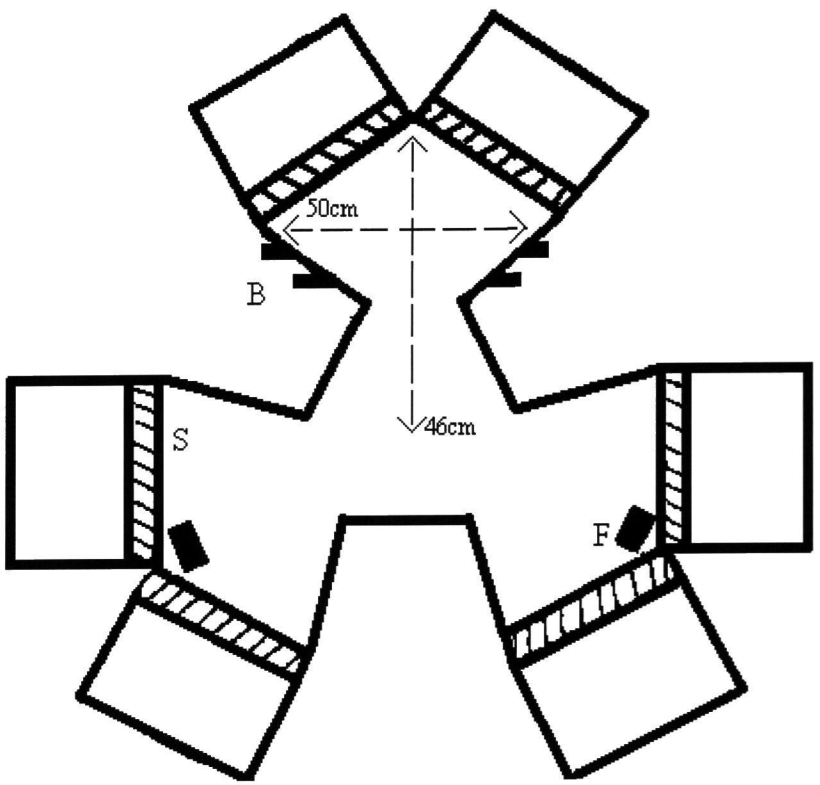
The Dark Agouti strain of rat was considered most suitable for these studies as research suggests their performance in visual discrimination tasks is superior to that of other strains (Gaffan & Eacott, 1995, Aggleton, 1996). Dark Agouti rats demonstrate better performances than pigmented Hooded Lister rats in visual discrimination tasks in the same computer operated testing apparatus used throughout this thesis (Gaffan & Eacott, 1995). Dark Agouti rats also demonstrate better performances than albino strains, Sprague Dawley and Fischer 344, and the pigmented strain, PVG hooded, in the visual discrimination task, delayed non match to sample, in a hand operated testing apparatus

(Aggleton, 1996). Tactile and olfactory stimulus cues were controlled in this study, suggesting the Dark Agouti rats were relying primarily on visual cues to perform the discrimination task (Aggleton, 1996).

2.2 Apparatus

The apparatus used throughout the following studies was a computer-operated Y-maze, which was first described in Gaffan & Eacott (1995). Figure 2.1 (adapted from Gaffan & Eacott, 1995) shows the design and dimensions of the maze.

Figure 2.1 A diagram of the automated Y-maze testing apparatus



F = Feeder, B = Photodetector Beam, S = Monitor Screen

All arms of the maze contain one feeder, two monitor screens and two photodetector Beams. Diagram reproduced from Gaffan & Eacott (1995).

The maze was fixed onto a wooden baseboard, 120 cm^2, and 49 cm above the floor. The maze consisted of three rectangular arms with two adjacent monitor screens at the end of each arm. The floor of the maze was cut from wood to fit against the monitor screens and arms of the maze. The centre of each monitor screen was situated 46.5 cm from the centre of the maze, in order that the distance of the visual stimuli displayed on the monitors remained within the visual acuity of the rat (Gaffan & Eacott, 1995). The arms of the maze were 22 cm high and cut from aluminium that had been painted black. A perspex lid, cut into 4 sections, covered the maze; the middle section was removed to place rats inside.

The ends of the arms of the maze held two monchromatic display monitors, with maximum image areas of 18.5 cm x 23.5 cm. The adjacent monitor screens were separated by an automated food well measuring 7 cm in width. Each well had a perspex door covering a food tray (Campden Instruments pellet trough), which animals had to push open to collect 45 mg food reward pellets (Bioserve). A dispenser (Campden Instruments) containing food pellets was situated above each food well. The dispenser released pellets into the food trough via a plastic tube encased in black aluminium. When a food pellet was dispensed, the food tray became illuminated by a 3W, 24V bulb. The opening and closure of the food well door was sensed by a microswitch that signalled collection of the pellet and ended the illumination of the food well.

It was possible to vary the number of pellets to be dispensed and the time interval between dispension. When more than one pellet was

dispensed collection of the first pellet prompted dispension of the second and so on. During the interpellet interval the food well remained illuminated and the stimuli remained on the screen whilst the animal collected its reward, during this time the computer generated stimuli for the next trial (Gaffan & Eacott, 1995). Following an intertrial interval a new trial began. If the animal left the arm of the maze within this interval then he was required to return before the new trial could commence. The length of the intertrial interval could vary, for the purposes of magazine training it was set at 1 second.

Photodetector beams (RS components) that signalled when an animal had entered an arm of the maze detected the rats' movements around the maze. Each arm contained 2 horizontal beams, situated 23 cm and 30 cm away from the monitor screens and 3.5 cm above the floor of the maze. The stimuli used in each study are described in detail in the corresponding experimental chapters. However, all stimuli were drawn onto the monitors in low resolution VGA mode (640 horizontal, 200 vertical) with 16 grey levels. In order to remain within both the rats' mesopic and scotopic range, the maximum luminance of grey level 16 was 16 cd/m^2. Stimuli could be presented in mirror images across adjacent monitor screens or only one monitor screen.

The maze was housed in a purpose built room lit by a partially covered 40W bulb placed 197 cm above the floor. Activity within the maze was viewed in an adjacent room, via a video camera (JVC TK5300, sens 0.3 lux) suspended 160 cm above the floor of the maze. The image

from the video camera provided a clear view of the animals' movements within the maze and of the stimuli displayed on the monitor screens. The computer controlling the maze was also situated in the adjacent room. Each programme used on the maze monitored the animals' reaction times to stimuli onset and reward collection, the number of trials and errors made in each session and length of session. In order to provide a constant level of background noise and to mask extraneous noise all testing in the maze was accompanied by white noise.

Each maze was controlled by a 486 DX, 66HZ Viglen computer, with 4 MB ram, 2 x 325 MB hard disks and 8 full length expansion slots. A locally built interface operating at 24 V DC, fed information to the computer regarding the status of the photodetector beams and foodtray flaps and sent signals to the traylights and feeders. The monitors in the maze were 6 monochrome Viglen monitors with 300mm diagonal screens. The monitors were driven by 3 dual VGA plus cards, each with 2 x 512 kybyte video RAM. When experimental programmes were run the graphics were sent to the maze monitors and a text display was provided on a standard Brother monitor attached to the computer for the experimenters use. All experimental programmes were written in-house in Turbo Pascal V 6.0.

In a simple two choice visual discrimination programme two different stimuli appear in different arms of the maze, approach to only one of which will elicit a food reward. An approach to the monitors displaying the rewarding stimuli was detected by the photodetector beams which

cross the arms of the maze. If a correct approach is detected, the food-well became illuminated and a pellet dispensed. When the pellet was retrieved, the stimuli presentation ended and a new trial began. If the animal approached the non-rewarded stimulus, it was detected by the photodetector beams and the stimuli presentation ended to begin a new trial. In each task described in this thesis the intertrial interval was set at 1 second, and a correct response was rewarded with one 45mg pellet (Bioserve). In all tasks described in the following experimental chapters, response to a correct stimulus resulted in the stimulus remaining on the screen until the food pellet had been collected. During this time the other non-rewarded stimulus was removed from the screen. Throughout the tasks described in the following chapters an incorrect response resulted in the stimuli presentation ending and was followed by the start of a new trial. The only exception to this is in the correction trials described in chapter 7.2.

The computer operated testing apparatus was used in order to minimise the number of tactile and olfactory cues available to animals performing visual discrimination tasks, thereby increasing animals dependence on visual cues. It has been suggested that rats will perform object discrimination tasks on the basis of tactile, olfactory and visual cues provided by 3 dimensional objects used in hand operated testing apparatus (Houston & Aggleton, 1987). Therefore, presenting 2 dimensional visual stimuli on the monitor screens in the maze was designed to eliminate olfactory and tactile cues associated with each visual stimulus. The

availability of nonvisual cues in visual discrimination tasks may be reduced further by presenting the visual stimuli distally, rather than proximally (see Gaffan & Eacott, 1995). Therefore, animals tested in the Y - maze viewed the choice of stimuli and decided which stimuli to approach from a distance. Compared to hand testing apparatus, the automated apparatus also reduced the amount of rat handling, increased the number of trials completed each day by each rat and allowed for the simultaneous testing of 2 rats in different mazes (Gaffan & Eacott, 1995).

A detailed analysis of Dark Agouti rats performances in visual discrimination tasks has been completed in a replica version of the automated Y- maze used throughout this thesis (Simpson & Gaffan, 1999). A series of experiments evaluated which aspects of the visual stimuli presented on the monitor screens in the Y - maze were encoded by rats performing a constant negative visual discrimination task, a task akin to non-match to sample. The stimuli used were computer generated spatial scenes that contained a number of discrete visual objects. The monitor screens were divided into hypothetical quadrants in which the objects within a scene could appear. The results showed that Dark Agouti rats discriminated visual scenes more easily if they contained 4 objects, rather than 6 and showed an attentional bias to the lower half of the monitor screens, whereas discrimination levels were the same for stimuli presented in the lateral and medial quadrants. However, presenting objects in the same spatial positions within the scenes, i.e. in the same quadrants, removed the attentional bias to the lower quadrants, as rats had to

distinguish the form of the objects presented in each position. It was shown that rats could perform the discrimination task when the objects presented in each scene were very similar in terms of position, luminance and area. Animals also encoded shapes with differing areas, but the same geometric form as being more alike than shapes differing in geometric form. These findings suggest animals use cues regarding the form of individual objects and not area or luminance cues to perform visual discrimination tasks in the automated Y- maze apparatus. The authors argue that animals learn to rely on form cues when performing visual discrimination tasks, as they are more reliable than the lower order cues of luminance and area (Simpson & Gaffan, 1999). These findings suggest that Dark Agouti rats are capable of utilising visual cues presented in the automated apparatus in order to perform a visual discrimination task. Therefore, rats appear to be capable of discriminating the shape and stimuli class of an object and its spatial location on the monitor screens on the basis of 2 dimensional visual cues. Consequently, the automated Y - maze is considered the most suitable apparatus to test a number of complex visual discrimination tasks in the rat.

2.3 Pre-Training

All animals underwent initial training in the maze in order to learn to approach and collect food rewards from the illuminated food wells and respond to changes in visual stimuli on the monitor screens. Thereafter they underwent training specific to the various experimental tasks. This further training will be described in the appropriate experimental chapters.

Initial exploration of the maze was designed to encourage naïve animals to approach the illuminated food wells to collect a food pellet and habituate the rats to the testing apparatus. First, the food well doors were fixed open and illuminated, with pellets placed both within and outside the food well. Over several sessions the food well doors were gradually closed and pellets placed only inside the food trough, until the animals could open the covering perspex door to retrieve the pellets. This stage of training was completed in a mean of 10 sessions, (range 9 to 12).

The next stage of training was to teach animals that only illuminated food wells would dispense reward pellets. Therefore, only one food well at a time was illuminated and would dispense pellets when approached. At this stage only one photodetector beam in the arm of the illuminated food well was active, so that an error approach to an unlit arm did not end the trial. The food well remained illuminated until the pellets had been collected, after which a new trial began in another arm of the maze. The mean number of sessions to complete this stage of training was 2.35, range 2-3. When animals performed consistently well at this stage, visual stimuli were introduced to train the animals to attend to stimuli on the monitor screens. Initially a simple rewarded stimulus (S+) resembling a white bar (1.5 cm deep, 23.5 cm wide, and 7 cm above the bottom edge of the monitor screen) on a black background, appeared across both monitor screens in one arm of the maze. An approach to the S+ resulted in dispension of a reward pellet and its collection signalled a new trial to begin in another arm of the maze.

At this stage animals were required to complete up to a maximum of 50 trials a day. When animals were performing well at this stage, the task was changed so that an error ended the trial, therefore, an approach to the arms of the maze not displaying the S+ ended the stimuli presentation and a new trial was started. The mean number of sessions to complete this stage of training was 6.4, range 5-9. When animals were consistently making 80% correct choices at this stage, a non-rewarded stimulus (S-) was introduced, comprising small white dots spread over a black background. The new stimuli contained the same array of grey level pixels as the original stimuli distributed at random across the entire screen, thereby maintaining an equal luminance level between the two stimuli. The S+ and S- were presented concurrently, thereby training animals' to discriminate between visual stimuli on the basis of reward. Animals remained at this stage of training until they were consistently performing at levels of 80% correct responses or above. The mean number of sessions to complete this stage of training was 3.7, range 3-5.

The final stage of training involved gradually introducing a number of different rewarded stimuli. The aim was to ensure that animals responded to stimuli placed in any part of the screen. To this end the new stimuli introduced were white lines of varying width, but equal depth, presented in varying horizontal positions on the monitor screens. Therefore stimuli were presented above, below or to the left or right of the centre of the monitor screens. The new S+'s were always presented with the original S-. Magazine training was complete when animals

consistently performed at levels of 80% correct responses in the final stage of training. The mean number of sessions to complete the final stage of training was 5.5 sessions, range 3-7. The mean number of sessions to complete all stages of pre-training, including initial maze exploration was 29 sessions, range 25-38, all sessions were usually completed within 15 minutes with a range 10-20 minutes. Rats were food deprived from the beginning of magazine training.

2.4 Surgery

Surgery was performed on all animals, either bilateral perirhinal lesion by aspiration or a sham control surgery. The site and extent of the perirhinal lesions followed the boundaries of perirhinal cortex defined by the brain atlas of Paxinos and Watson (Paxinos & Watson, 1986). Each rat was anaesthetised using halothane; its head shaved and positioned in a stereotaxic headholder which allowed rotation of the head. An incision was made in the skin, the temporal muscle retracted and an area of the skull was removed over the rhinal sulcus, approximately 4-7 mm posterior to bregma. In the perirhinal group of animals the dura was cut to allow access to the underlying cortex and a lesion was made by aspiration with the aid of an operating microscope. The aspiration was performed with a 0.6mm x 25mm flat ended needle at an approximate vacuum level of 200 mm Hg (0.25 bar) vacuum. For both perirhinal and sham animals the temporal muscle was returned to place and the procedure performed contralaterally. The scalp was then closed using wound clips and antibacterial wound powder was applied. Each animal received 5 ml of

saline, 0.05 ml of respiratory stimulant (milophyline) and 0.03 ml of analgesic (vetergesic) subcutaneously. Post-operative administration of analgesic was provided as and when necessary.

Overall thirty nine animals underwent surgery. Post-surgical recovery was normal for all but four animals that developed fatal respiratory infections in the days following surgery. All animals had a 14 day rest period following surgery before post-operative testing began; during which time their post-operative recoveries were monitored.

2.5 Histology

For histological purposes, at the end of testing the rats were perfused intracardially with a 5% formal saline solution, their brains were removed, embedded in wax and coronally sectioned into 10 μm slices, every 10th section was mounted and stained with Cresyl violet (Nissl stain). The extent of the intended perirhinal lesions is shown in figures 2.2 and 2.3. The results of detailed histological analysis will be included in the relevant experimental chapters.

Figure 2.2. The lateral surface of the rodent brain, with the extent of the intended perirhinal cortical lesion shaded in black, adapted from Burwell et al. (1995).

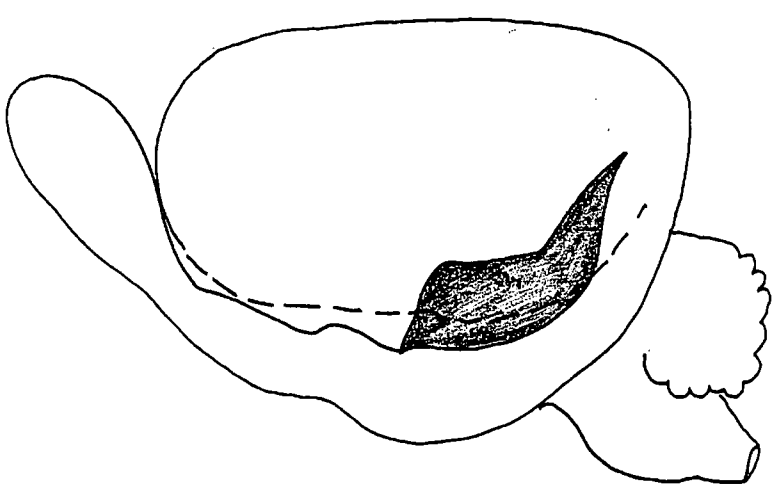
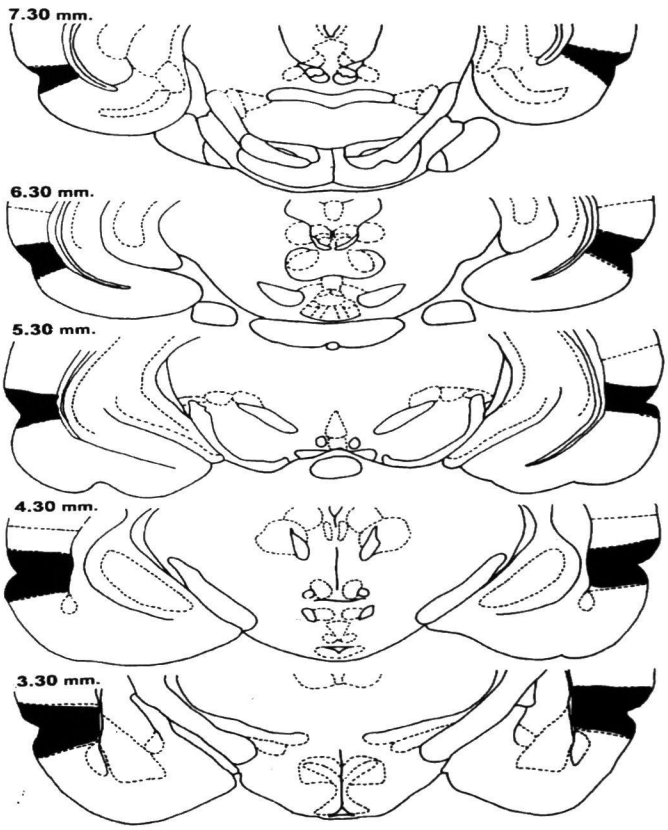


Figure 2.3. Several ventral views of the rodent brain marked with their approximate distances from Bregma, the extent of the intended perirhinal lesion is shaded in black. Figure adapted from Paxinos & Watson (1986).



Chapter 3: The Effects of Perirhinal Ablation on Post-Operative Reacquisition of Visual Discrimination Learning in the Rat

3.1 Introduction

The role of the perirhinal cortex in visual associative memory tasks is of great interest, as not only are medial temporal amnesics impaired in such tasks (Gaffan et al., 1990; Oscar-Berman & Zola Morgan, 1980; Squire, Zola Morgan & Chen, 1988), but they are considered valid means of assessment in animal models of amnesia (Squire & Zola Morgan, 1983). A useful test of visual associative memory in amnesic patients (Gaffan et al., 1990), primates (Buffalo et al., 1998) and rodents (Eacott, 1998) alike is the concurrent visual discrimination task. In this task subjects learn to discriminate between pairs of visual stimuli presented concurrently in order to gain reward (Aggleton et al., 1988; Kessler, Irle & Markowitsch, 1986). Patients with amnesia following Korsakoff's syndrome or anoxic episodes are impaired in learning an 8 pair concurrent visual discrimination task, in which the stimuli are 3 dimensional junk objects and money is given as the reward (Squire, Zola Morgan & Chen, 1988). Impairments in 2 and 10 pair concurrent visual discrimination tasks are also evident in Korsakoff's syndrome amnesic patients (Gaffan et al., 1990).

Whilst both electrophysiological and behavioural studies suggest that mechanisms within the rhinal cortex contribute to visual recognition memory (Fahy Riches & Brown, 1993; Gaffan & Murray, 1992; Meunier et al, 1993; Miller and Desimone, 1993; Mumby & Pinel, 1994), the

behavioural effects of perirhinal ablation on visual associative memory tasks are less certain. There are reports of impaired performances in post-operative recall of concurrent visual discrimination tasks that were acquired prior to rhinal (Gaffan & Murray, 1992; Thornton, Rothblat & Murray, 1997) or perirhinal ablation (Buckley & Gaffan, 1997) in the primate. Furthermore, there are reports of impaired acquisition of concurrent visual discrimination tasks following lesions to the perirhinal cortex (Gaffan, 1994) and perirhinal and parahippocampal cortices (Zola Morgan et al., 1989) in the primate. However, there are reports that perirhinal ablation in the primate impairs retention of concurrent visual discrimination tasks acquired prior to surgery, whereas post-operative acquisition remains intact (Gaffan & Murray, 1992; Thornton et al., 1997).

Studies in the rat have also produced contradictory findings. There are reports of intact post-operative acquisition and retention of object discriminations acquired prior to surgery following perirhinal ablation in the rat (Astur, Mumby & Sutherland, 1995). In contrast there are reports of impaired post-operative acquisition of an 8 pair concurrent object discrimination task and a simple object discrimination task following perirhinal ablation (Kornecook et al., 1995). A further study found impairments in post-operative retention of object discriminations acquired prior to surgery, yet post-operative acquisition of new discriminations remained normal (Wiig, Cooper & Bear, 1996).

A more recent study, designed to clarify the nature of perirhinal involvement in visual associative memory, found perirhinal ablation in the

rat produces a deficit in retention of concurrent visual discriminations acquired prior to surgery (Eacott, 1998). However, the same animals then went on to learn a new set of discriminations at a rate comparable to control animals, suggesting a dissociation exists between anterograde and retrograde visual associative memory processes following perirhinal ablation. Similar patterns of impairments and sparing of function following rhinal (Gaffan & Murray, 1992; Thornton, Rothblat & Murray, 1997) or perirhinal (Buckley & Gaffan, 1997) lesions in the primate support this suggestion. However, Buckley and Gaffan (1997) suggest that in monkeys perirhinal cortex ablation impairs both the retention of old discriminations and the ability to acquire new visual discrimination learning. In this study the impairment in new learning was revealed by increasing the number of stimuli in the discrimination task during acquisition (Buckley & Gaffan, 1997). This finding is reminiscent of the report that performance of delayed match to sample in the monkey is only impaired by rhinal cortex ablation when the size of the stimuli set used is relatively large (Eacott, Gaffan & Murray, 1994). Likewise, lesions to the rhinal, presubicular and parasubicular cortices in rats disrupt learning of a 4 pair concurrent discrimination task using real objects, but spare acquisition of a two choice visual discrimination between two simple stimuli (Rothblat et al., 1993). Furthermore, perirhinal lesions in primates disrupt performance in learning a concurrent visual discrimination task with 320 complex scenes (Gaffan, 1994), whereas acquisition of a 20 pair concurrent visual discrimination task remains intact (Gaffan & Murray, 1992).

This pattern of impairments has led to the suggestion that loss of accurate object identification disrupts performance of both recognition and associative memory tasks following perirhinal ablation in the monkey (Buckley & Gaffan, 1997; Eacott and Heywood, 1995). Therefore, increasing stimuli set sizes in a visual discrimination or recognition memory task increases the demands on the processes of stimulus identification and categorisation. Whilst it is possible that perirhinal ablation affects new learning in monkeys and rats differently, it is also possible that the rat post-operative learning capacity has not been sufficiently taxed to reveal a similar deficit following perirhinal lesions. Thus, the existing rat literature is not extensive enough to reveal the exact nature of impairments in visual associative memory tasks following perirhinal ablation. In particular, it is unclear whether perirhinal ablation produces a deficit in retention of visual associative information acquired prior to surgery, whilst leaving new learning intact.

It has been suggested that the perirhinal cortex may contribute to the consolidation of visual associative memories by virtue of its extensive cortical and subcortical connections, (Squire & Zola-Morgan, 1991). Squire and Alvarez (1995) propose that the hippocampal formation acts as a temporary store for information that is eventually consolidated in neocortex, therefore consolidation is maintained by the gradual binding of multiple storage sites in neocortex. One assumption of this view is that damage to any component of the hippocampal formation will result in a temporally graded retrieval deficit. If this is the case, it may be expected

that any retrograde memory impairments following ablation of structures within the hippocampal formation are temporally graded, as in human amnesic patients (Warrington & McCarthy, 1988). There is evidence to suggest that hippocampal ablation in rats (Winocour, 1990) and rabbits (Kim, Clark & Thompson, 1995) or entorhinal cortex ablation in rats (Cho, Kesner & Brodale, 1995) produce temporally graded retrograde memory deficits in a variety of behavioural tasks.

However, behavioural evidence to ascertain the role of the perirhinal cortex in consolidation processes has so far proved inconclusive. There are reports of combined lesions to the hippocampus and rhinal cortex in the monkey resulting in a temporally graded retrograde amnesia for 5 sets of 20 object discriminations learnt prior to surgery (Zola Morgan & Squire, 1990). Post-operative retention was best for items learnt 16 week's prior to surgery relative to items learnt 1 week prior. Subsequent studies with rats in spatial memory (Weisand, Astur & Sutherland, 1996), object place memory (Koerner et al., 1996) and object discrimination tasks (Astur et al., 1994), all fail to replicate these findings with lesions restricted to the hippocampus, suggesting that the deficit is dependent upon the rhinal cortex ablation.

However, studies focusing on the rhinal cortex itself have produced contradictory results. There is evidence that perirhinal ablation, fornix transection or both combined in the rat, results in a temporally graded retrograde amnesia, with better retention of visual discriminations learnt 6-8 weeks prior to surgery than discriminations learnt 1-3 weeks

prior (Wiig, Cooper & Bear, 1996). In this study animals learnt 5 pairs of two-choice visual discriminations with real objects. There are further reports that rhinal ablation in the rat results in a temporally graded retrograde amnesia, with better retention of visual discriminations learnt 56, 37 or 16 days prior to surgery than discriminations learnt 9 and 2 days prior (Kornecook et al., 1997). However, a similar study in rats, that tested post-operative reacquisition of 5 pairs of two-choice object discriminations failed to find a temporally graded retrograde effect following perirhinal ablation (Astur, Mumby & Sutherland, 1995). Furthermore, a study in primates found that rhinal lesions did not result in a temporally graded retrieval deficit for 2 sets of concurrent object discriminations learnt 16 and 1 week prior to surgery (Thornton, Rothblat & Murray, 1997). Thus the retrograde effects of perirhinal cortex lesions are unclear. It is possible that differences in the tasks or time intervals used in these studies may account for the apparent differences in their results.

Therefore, the aim of the current study was to further investigate the effects of perirhinal cortex ablation on pre-operatively learned visual discrimination tasks in the rat. As it has been suggested that perirhinal ablation disrupts object identification processes (Buckley & Gaffan, 1997), a difficult version of the concurrent visual discrimination task was used in which any S+ can be presented with any S-, rather than stimuli always being presented in fixed pairings. With constant pairings one salient feature of the S+ or S- may be sufficient to discriminate between the two stimuli. Thus, an animal may adopt a strategy of using a single feature of

the stimuli pairs to perform the discrimination task. However, with a variety of S+/S- pairings, the animal has to distinguish the S+ from a number of S-'s with which it may be paired. A single feature which is sufficient to distinguish between the S+ and S-, may be insufficient when there are multiple S-'s. This version of the task therefore assumes more demands on visual identification processes than a two choice discrimination with constant pairings, and thus may be more likely to reveal a post-operative deficit.

In the current experiment we asked whether perirhinal cortex ablation in the rat produces a retrograde amnesia for visual associative information and whether this deficit is temporally graded. Thus the animals learnt two sets of concurrent visual discriminations at different time intervals (approximately 8 and 3 weeks) prior to either a bilateral perirhinal lesion or sham surgery. The order of testing post-operative reacquisition of the two sets of discriminations was balanced to control for any transience in post-operative deficits. The testing took place in a computer-controlled Y-maze to minimise testing variances associated with traditional testing apparatus.

3.2 Method

3.2. i Subjects

Twenty male Dark Agouti rats (Bantin & Kingman, Hull, UK) were used in this experiment. Ten animals were aged approximately ten months at the start of the study and were already pre-trained to use the testing apparatus, a further ten animals were experimentally naïve and

were aged approximately five months at the start of the study. Two rats failed to reach criterion on the tests used and were removed from the study, another two died of respiratory infection in the days following surgery. Overall sixteen rats completed experiment 1, seven had bilateral sham surgery, nine bilateral perirhinal lesions. A detailed description of the subjects used is provided in chapter 2.1.

3.2. ii Apparatus

The apparatus used was a computer-operated Y-maze designed by Gaffan & Eacott (1995), and described fully in chapter 2.2.

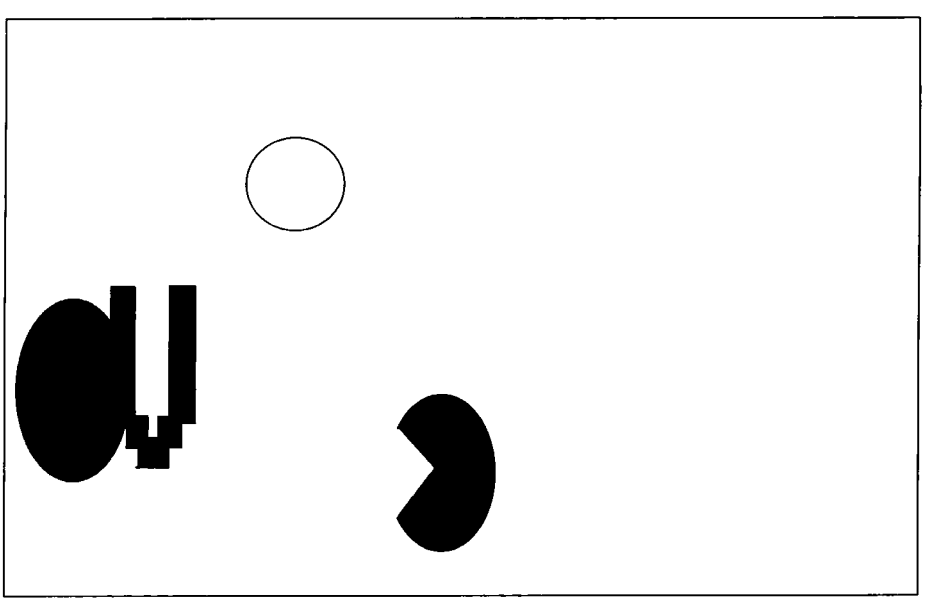
3.2. iii Pre-Operative Training

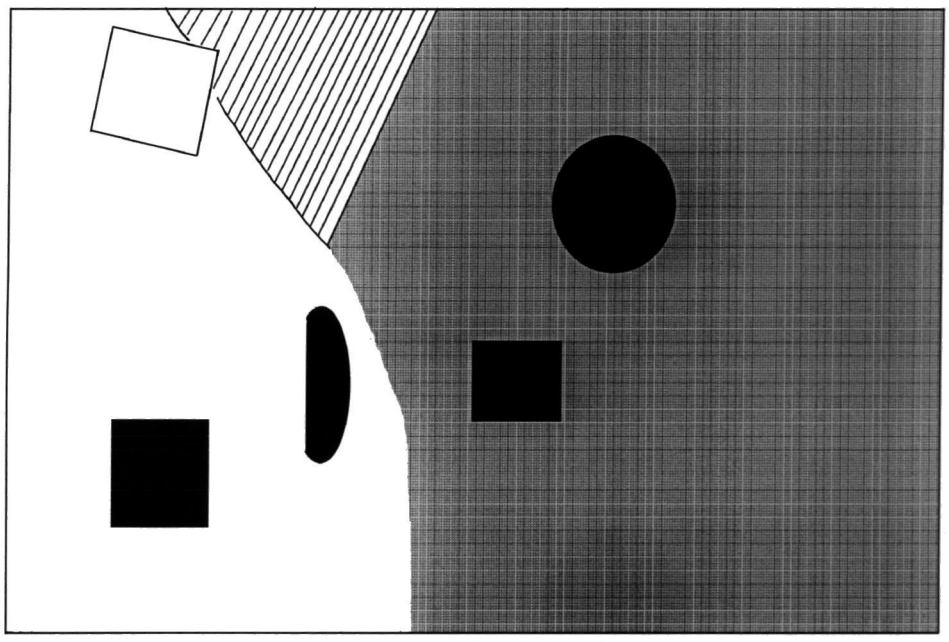
Initial training involved approaching simple stimuli presented in the maze for food rewards, as described in detail in chapter 2.5. When this was accomplished training in the concurrent visual discrimination task began. The rats learned two sets of discriminations; both comprised of five pairs of stimuli. The stimuli used in this task were comprised of a number of common elements, arranged to resemble junk scenes. The background of each scene contained 0 – 3 large ellipses, presented in varying positions, orientations and degrees of overlap. The foreground of each scene contained 1-8 smaller figures, such as polygons and rectangles; these too were presented in various positions and orientations, but with little overlap. The large background ellipses ranged in size from approximately 2 to 4cm^2, whereas the larger background elements ranged from 4 to 9cm^2. The scenes were presented in mirror images across the two monchromatic

display monitors in each arm of the maze. Figure 3.1 shows two typical scenes from the discrimination task.

Definition of the elements within the scenes was achieved by two subsets of grey levels, i.e. dark and light, when the foreground objects were presented in the light grey levels (16 to 4.9 cd/m^2) then the background objects were presented in the dark (3.1 to 0.04cd/m^2) and vice versa. The grey levels used are described in detail in chapter 2.2. The contrast between objects in the scenes remained high, as objects were never presented in sequential grey levels.

Figure 3.1. Two sample scenes from the concurrent discrimination task.





Variability within the scenes was increased by randomly presenting one third of all background ellipses in horizontal stripes at 1.33 cycles per degree. The scenes were also randomly assigned to move or remain still; movement was achieved by presenting 3 successive versions of each scene in either vertical or horizontal displacement. The left and right halves of the monitors moved sequentially from one half to the next in either a zigzag or a saw-tooth movement. The rate of movement was 2.5 cycles/s for a sawtooth movement or 1.7 cycles/s for a zigzag movement. The stimuli were assigned movement to increase variability within the scenes created.

An original stimuli set of 525 scenes was created by the stimuli generating algorithm, from these scenes two sets of five pairs of stimuli

were created. The stimuli generating algorithm used is described in Gaffan and Eacott (1995). Each stimulus was used only once and was randomly assigned to rewarded or non-rewarded status. Within each pair of stimuli there was a rewarded stimulus (S+) and an un-rewarded foil (S-). The stimuli in the task covered all of the screen area. First, the animals were presented with just one pair of stimuli. When they reached a criterion of 80% correct within a single session, another pair of stimuli was introduced. When two pairs of stimuli were being tested animals had to attain a criterion of 75% correct responses for each pair of stimuli and for the total trials completed in the session. Subsequent pairs were then introduced in the same way, until the animals were discriminating between five pairs of stimuli to a criterion of 75% correct. At all stages of training, stimuli presentations were not confined to the initial pairings, so that a given S+ could be presented with any one of the currently used S-s. All animals completed up to 100 trials a day, five days a week. Animals that had not achieved criterion after completing 50 sessions of 100 trials in either set were removed from the study.

Animals' reaction times in the maze were recorded throughout each training session. The computer programme used throughout the task calculated the mean number of seconds taken to respond to stimuli following its onset and the time taken to collect the reward pellets following delivery into the food tray. Animals' mean reaction times were calculated for the last 10 sessions that they completed in each set of discriminations.

A two week rest period was introduced between reaching criterion on set one and beginning training on set two. Therefore set one was learnt approximately 8 weeks prior to surgery, and set two at approximately 3 weeks prior to surgery. Animals were then pseudorandomly assigned to experimental or control groups and given a three week rest period before surgery.

3.2. iv Surgery

All animals underwent surgery, a detailed description of the surgical methods can be found in chapter 2.4.

3.2. v Post-Operative Testing

All animals had a two week rest period after surgery prior to post-operative testing. They were then pseudorandomly assigned to two groups for testing post-operative retention of sets one and two. Animals in sequence A were tested for reacquisition of set one, followed by set two, whereas animals in sequence B were tested in the reverse order. Performance in post-operative retention was assessed by calculating the number of trials and errors accumulated in reattaining a criterion of 75% correct choices made in a single session of up to 100 trials. All animals completed up to 100 trials a day, five days a week, until criterion was met. Reacquisition rates were used to assess retention, as a major determinant of the rate of reacquisition is the degree of retention of information acquired prior to surgery, along with the ability to perform non-mnemonic demands of the task and relearn what has been forgotten. Animals' reaction times to

stimuli onset and time taken to collect reward were calculated for each post-operative training session.

3.2. vi Histology

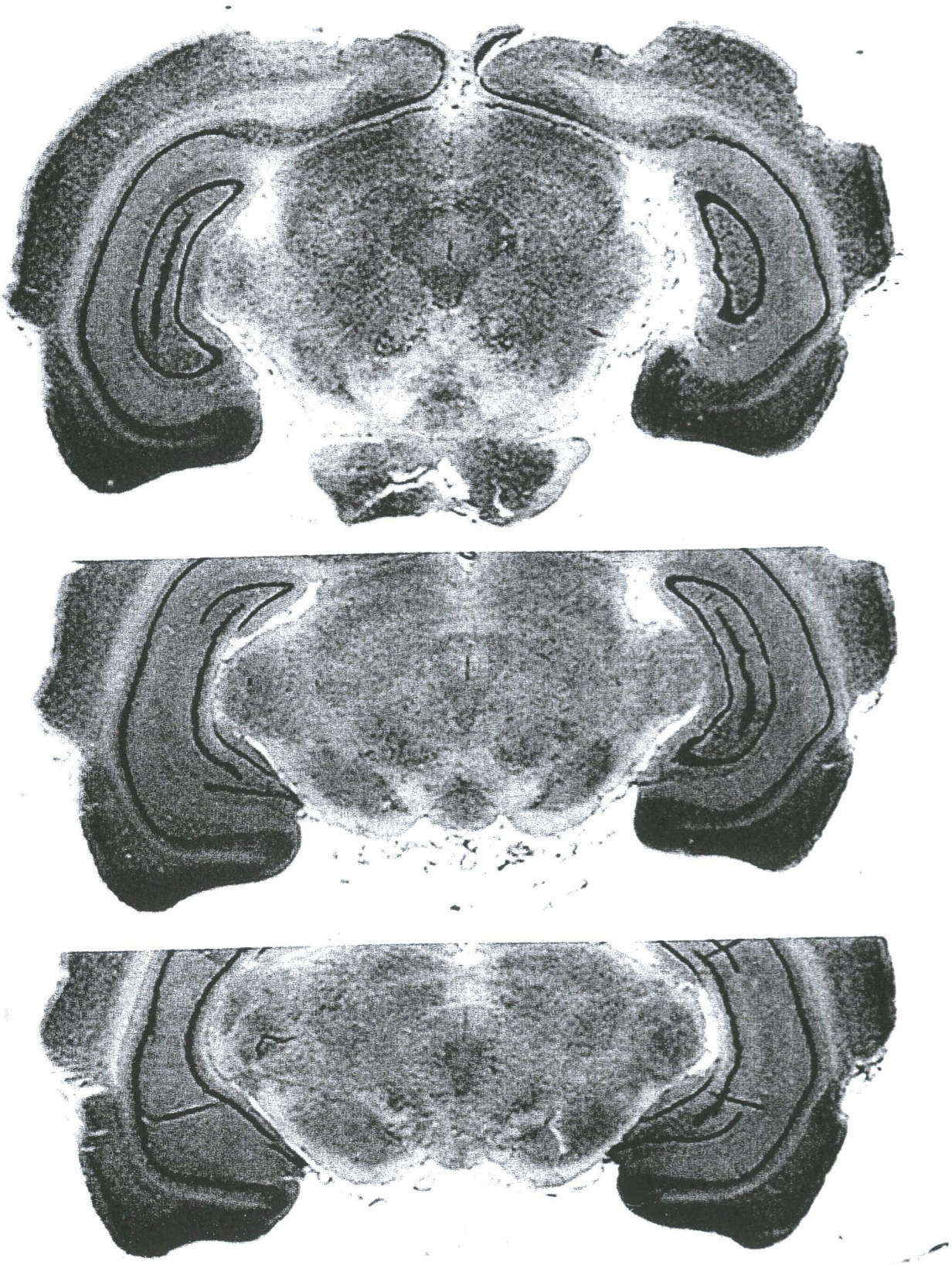
A detailed description of histological methods is described in chapter 2.5. Following histological processing the percentage of tissue loss in the perirhinal cortex and area TE were calculated. The percentages of cortical damage were estimated by analysing the extent of damage within the boundaries of the perirhinal cortex and area TE in every other section of histological processing. i.e. one in every twenty 10 μm section. The percentage of tissue damage was calculated by dividing the intended lesion into 10 sections, these sections were then divided into quadrants. The amount of damage to each quadrant was then estimated and the overall percentage of the size of each lesion was calculated.

3.3 Results

3.3. i Histological Results

Histological analysis revealed that in all cases the perirhinal lesions were essentially as intended, extending approximately 4mm to 7mm posterior to Bregma. Figure 3.2. shows three representative sections from animal R5.

Figure 3.2. Three representative sections of a bilateral perirhinal lesion from animal R5.

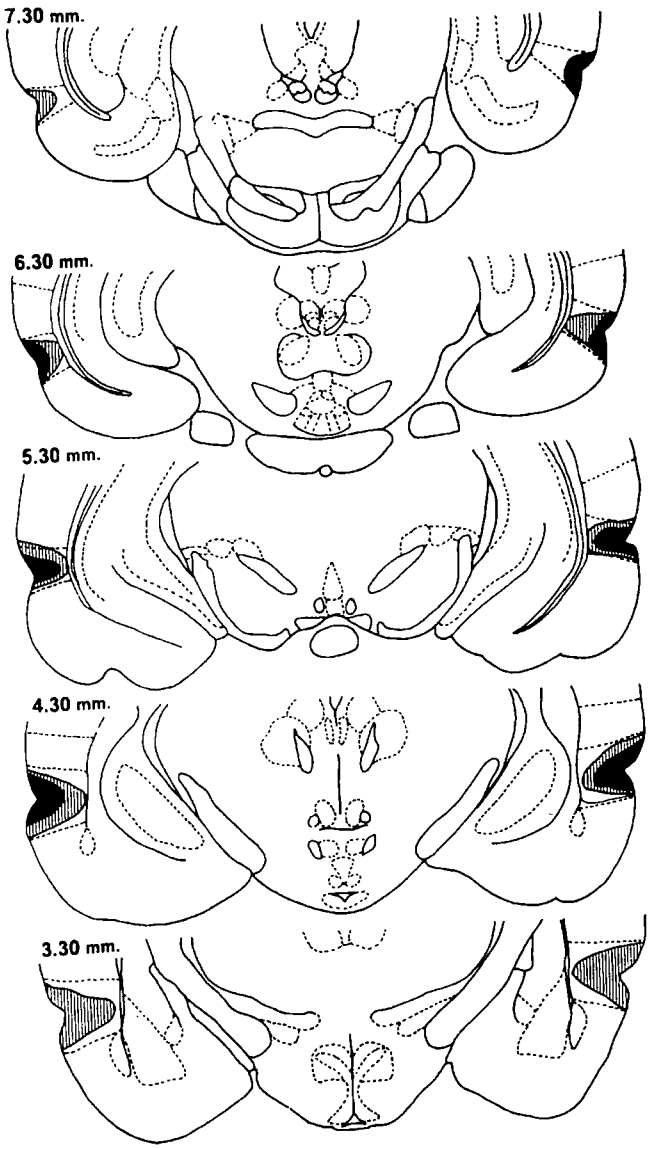


As shown in table 3.1, the mean estimated damage to the perirhinal cortex was 60% of the total extent of the perirhinal cortex. The perirhinal cortex was clearly lesioned in all cases, in some animals there was a small degree of intact tissue toward the extreme dorsal extent of the intended lesion. There was no evidence of damage to the neighbouring entorhinal cortex, although in some cases there was slight intrusion into adjacent area TE of inferotemporal cortex. Table 3.1 shows that the mean estimated extent of damage for each animal. Overall the mean extent of damage to TE was 10% of its total area. In all cases there was some intact tissue toward the extreme caudal extent of the lesion, thereby excluding the possibility of unintended damage extending into postrhinal cortex. Figure 2.3 shows a representative section from a relatively large lesion, (R8), and figure 2.4 a relatively small lesion, (R45).

Table 3.1 Estimated damage to the perirhinal cortex and area TE, as shown in percentage of overall area.

RAT	**Perirhinal Lesion Size**			**TE Lesion Size**		
	Left	**Right**	**Total**	**Left**	**Right**	**Total**
R51	72	66	69	14	8	10
R1	69	66	67	14	11	12
R8	69	66	68	16	12	14
R50	65	57	61	12	7	9.5
R48	58	61	59	9	15	12
R53	60	58	59	10	6	8
R5	56	58	57	20	18	19
R3	56	55	56	7	2	5
R45	47	43	45	0	0	0
Mean	**61**	**58**	**60**	**11**	**8**	**10**

Figure 3.3. The extent of a relatively small (R45, black) and a relatively large (R8, vertical stripes) lesion drawn onto standard sections taken from Paxinos and Watson (1986).



3.3. ii Pre-Operative Learning

The two groups formed, the perirhinal and sham groups, did not differ significantly in the number of trials (Set One: $t = < 1$; Set Two: $t = 1.02$) or errors (Set One: $t = < 1$; Set Two: $t = <1$) made in attaining criterion pre-operatively. Both groups found set one significantly more

difficult to learn than set two (Trials: $t = 12.63$, $df = 15$, $p = <0.001$; Errors: $t = 10.89$, $df = 15$, $p = <0.001$). Although this disparity has also been found in an earlier study (Eacott, 1998), it was unclear then whether set 1 was actually more difficult to acquire or whether differences in acquisition were due to the animals' previous experience in another visual learning task. However, the animals in the current study had no prior experience in visual discrimination learning, suggesting set 1 was more difficult to learn. All animals' trials and errors accumulated in pre-operative acquisition of the two discrimination sets are shown in table 3.2.

Table 3.2 Pre-Operative Acquisition of Two Sets of Concurrent Object Discriminations

	Set One		Set Two			Set One		Set Two	
PRh	**Trials**	**Errors**	**Trials**	**Errors**	**Sham**	**Trials**	**Errors**	**Trials**	**Errors**
R45	1153	304	502	95	R46	1151	168	537	114
R48	1543	427	413	95	R47	1137	295	568	140
R50	1484	398	588	151	R49	1165	288	553	129
R51	961	254	385	82	R52	1444	414	431	83
R53	1106	281	576	117	R4	1567	456	316	70
R1	990	282	424	99	R9	1388	336	283	46
R3	1432	289	492	46	R11	1105	286	279	47
R5	1890	433	476	98					
R8	1390	298	428	106					
Mean	**1327**	**329**	**476**	**98**		**1279**	**320**	**423**	**89**

Pre-operative reaction times to stimuli onset and reward collection were compared between surgical groups, for these analyses reaction time data for each animal were collated from the last 10 sessions in each set and compared in a series of one way ANOVA's. There were no statistically significant differences between the perirhinal and sham animals pre-

operative reaction times to stimuli onset (Set 1: F = 1.14; Set 2: F = < 1), or reward collection (Set 1: F = 3.14; Set 2: F = <1) for either stimuli set.

3.3. iv Post-Operative Reacquisition

The perirhinal and sham animals were pseudorandomly subdivided for post-operative testing: those in sequence A were tested for retention in the order the sets were learnt, whereas animals in sequence B were tested in the reverse order. Post-operative retention was assessed by comparing the number of trials and errors accumulated in reacquisition of the 2 sets of discriminations to criterion. The number of trials and errors accumulated by each animal in post-operative acquisition of two sets of discriminations are shown in table 3.3. It is interesting to note that the scores for animals R45 and R8, with the smallest and largest perirhinal lesions, were similar to the other perirhinal animals scores in the reacquisition task.

Table 3.3 Post-Operative Reacquisition of Two Sets of Concurrent Object Discriminations

					Sequence A				
	Set One		**Set Two**			**Set One**		**Set Two**	
PRh	**Trials**	**Errors**	**Trials**	**Errors**	**Sham**	**Trials**	**Errors**	**Trials**	**Errors**
R45	313	48	60	9	R46	97	21	93	19
R48	537	147	146	34	R47	231	51	267	56
R1	100	19	132	31	R9	134	38	154	29
R8	209	59	114	31					
Mean	**289**	**68**	**113**	**26**		**154**	**36**	**171**	**34**
					Sequence B				
	Set Two		**Set One**			**Set Two**		**Set One**	
PRh	**Trials**	**Errors**	**Trials**	**Errors**	**Sham**	**Trials**	**Errors**	**Trials**	**Errors**
R50	285	44	205	44	R49	127	27	137	24
R51	115	25	43	4	R52	176	32	323	86
R53	341	59	149	26	R11	159	28	188	43
R5	134	21	47	7	R4	181	54	266	85
R3	176	26	128	19					
Mean	**210**	**35**	**114**	**20**		**160**	**35**	**228**	**59**

The effect of group, set and sequence on the number of trials taken to reattain criterion for both sets of discriminations is shown in Figure 3.4. The number of trials to criterion were analysed by a 2 x 2 x 2 (Group x Set x Sequence) ANOVA with 1 repeated measure. Overall there was no significant difference between reacquisition of set 1, learnt approximately 8 weeks prior to surgery, and set 2, learnt approximately 3 weeks prior (Trials: F= < 1; Errors: F = < 1). There was also no significant interaction between group and set (Trials:F = < 1; Errors: F = < 1). The mean number of trials to reach criterion on both sets of discriminations was 179 for the perirhinal group and 180 for the control group, therefore there was no significant difference between the two groups in terms of overall performance (Trials: F = < 1; Errors: F = < 1). The main effect of sequence was not statistically significant (Trials: F = 3.22; Errors: F = 1.31), nor was the interaction between set and sequence (Trials: F= <1; Errors: F= <1). However, the interaction between group and sequence was significant (Trials:F=11.73, df = 1, 12, p=0.005; Errors: F= 6.84, df=1, 12, p = 0.023).

As figure 3.4 illustrates, the sequence of testing affected the two groups in opposing ways: the perirhinal animals demonstrated a marked improvement in performance in the second set they were tested in relative to the first (Trials: t = 3.114, df = 8, p=0.014; Errors: t = 3.184, df = 8 p = 0.013), whereas the performance of the sham animals declined (Trials: t = -2.435, df = 6, p=0.05; Errors: t = -1.277, df = 6, p = 0.249).

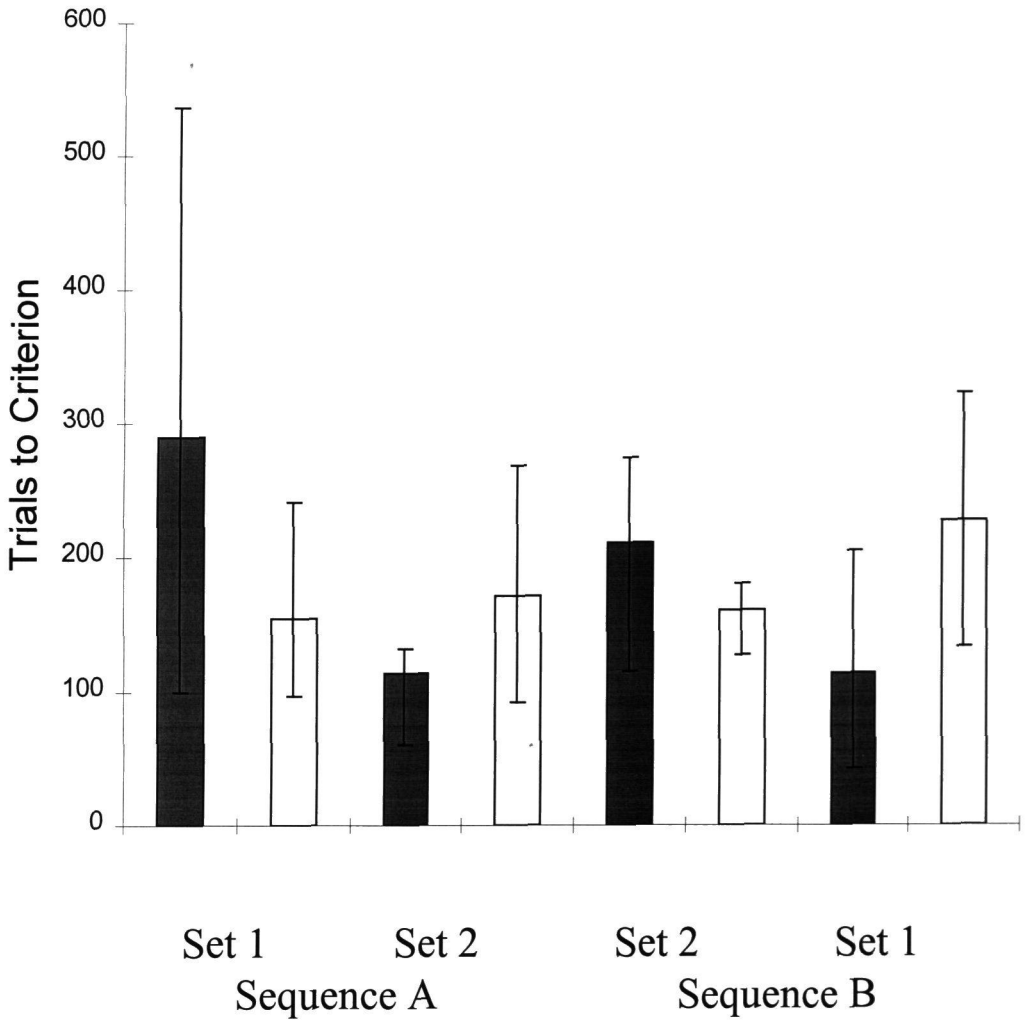


Figure 3.4. The mean post-operative number of trials to criterion in retention of two sets of pre-operatively learned discriminations for both the perirhinal (shaded bars) and the sham (open bars) animals. The error bars show the range of scores.

To investigate this effect further, a percent savings score was calculated for each rat, in order to measure post-operative reacquisition of the first set tested post-operatively relative to reacquisition of the second set tested. It was calculated on the basis of (T1 -T2) / (T1 + T2) x 100, where T1 and T2 represented the number of trials or errors accumulated in reattaining criterion of the first set tested and the second set tested respectively. The saving score percentage reflects the magnitude of the

difference between T1 and T2 scores, ranging from 100 % to -100%. A positive saving score reveals that the number of trials accumulated in reattaining criterion in T1 is higher than for T2. A negative saving score reveals that the number of trials accumulated in reattaining criterion in T1 is lower than for T2. A savings score of 0 reveals no difference between the trials accumulated in T1 and T2. The saving scores analysis for the perirhinal and sham animals are shown in figure 3.5.

The savings score analysis revealed that the perirhinal animals pattern of reacquisition was significantly different to that of the sham animals. A 2 x 2 (Group x Sequence) ANOVA on the percent savings of both the total trials and errors to criterion for the first set tested relative to the second set tested, revealed a significant difference between the perirhinal and sham groups (Trials: $F = 16.297$, $df = 1, 2$, $p=0.002$; Errors: $F = 8.941$, $df = 1, 2$, $p= 0.013$). In contrast there was no effect of sequence (Trials: $F = < 1$; Errors: $F = < 1$), nor any interaction between sequence and group (Trials: $F = <1$; Errors: $F = <1$).

Further analysis revealed that, overall, the saving scores of the perirhinal animals were significantly greater than zero (Trials: $t = 4.104$, $df = 8$, $p = 0.003$; Errors: $t=3.183$, $df = 8$, $p=0.013$), while the saving scores of the sham operated animals were significantly smaller than zero (Trials: $t = -2.455$, $df = 6$, $p=0.049$; Errors: $t =-1.277$, $df=6$, $p = 0.249$). Therefore, the perirhinal animals demonstrated a significant improvement in reacquisition of the second set tested post-operatively relative to the first set tested, whereas the sham animals demonstrated the opposite pattern.

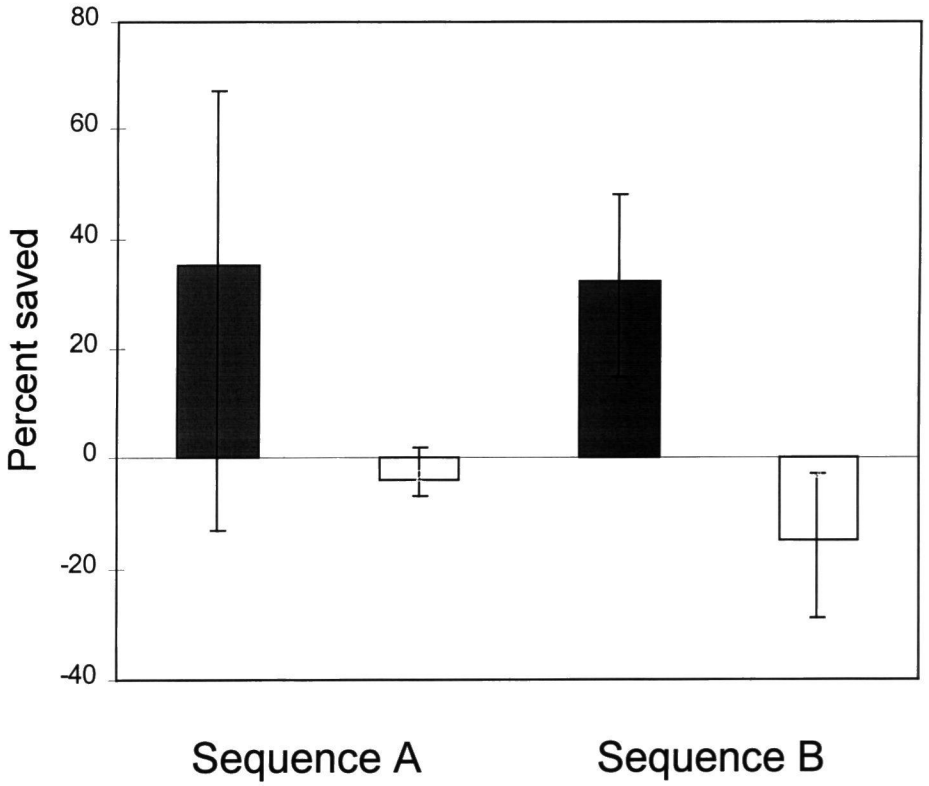


Figure 3.5. The mean percent savings score of post-operative trials to criterion for two sets of pre-operatively learned discriminations for both the perirhinal (shaded bars) and the sham (open bars) animals. The error bars show the range of scores.

Because the above analysis suggests that the perirhinal group may have had a deficit confined to the first tested set, we reconsidered earlier analysis of retrograde effects that included both first and second sets tested. Therefore a between-subjects comparison of reacquisition rates for set 1 from sequence A and set 2 from sequence B was conducted for both perirhinal and sham animals in a 2 x 2 (Group x Set) ANOVA, thereby comparing immediate post-operative performances only. As before, however, there was no effect of set (Trials: $F = <1$; Errors: $F = 1.2$) nor any interaction between set and group (Trials:$F= 1.5$; Errors: $F=1$). In this

analysis, the effect of group did not reach significance (Trials: F =5.581, df = 2, 1, p=0.13; Errors: F= 1.028, df = 2,1,p = 0.331).

In order to test for any possible nonmnemonic effects of perirhinal lesions on performance in the concurrent discrimination task, reaction times to stimuli onset and reward collection were compared between surgical groups. Post-operative reaction times to stimuli presentation were examined in a 2 x 2 x 2 (Group x Sequence x Set) ANOVA with 1 repeated measure. No statistically significant differences were found for any of the main effects (Group: F = <1; Sequence: F = <1; Set: F = < 1) nor for any of the interactions (Surgery x Sequence: F= 1.2; Surgery x Set: F = <1; Sequence x Set: F = <1; Set x Sequence x Surgery: F = < 1). Post-operative reaction times to reward collection were examined in a 2 x 2 x 2 (Group x Sequence x Set) ANOVA with 1 repeated measure. No statistically significant differences were found for any of the main effects Group: F = < 1; Sequence: F = < 1; Set: F = <1;), nor any of the interactions (Surgery x sequence: F = 1.02; Surgery x Set: F = < 1; Sequence x Set: F = <1; Sets x Sequence x Surgery: F = 1.27). Therefore, it appears that perirhinal lesions did not affect animals' reaction times to stimuli presentation or reward collection.

To determine whether a relationship exists between lesion size and post-operative performance, the total number of trials taken to reattain criterion in the two sets of discriminations were correlated with the size of the lesions to the perirhinal cortex and area TE. The correlation analyses revealed no significant relationship between lesion size and post-operative

performance (Perirhinal Lesion: r = -0.272, p = 0.479; TE Lesion: r = -0.201, p = 0.605). Moreover, perirhinal animal R45, with the smallest estimated lesion accumulated more trials overall in the reacquisition task than perirhinal animal R8, with the largest perirhinal lesion.

3.4 Discussion

The present study examined the behavioural effects of perirhinal ablation in the rat. All animals learnt 2 sets of concurrent visual discriminations prior to bilateral perirhinal ablation or control surgery. For both groups of animals there was no significant difference between reacquisition of set 1, learnt approximately 8 weeks prior to surgery and set 2, learnt approximately 3 weeks prior, whether tested on all data, or more conservatively using data from the first tested set only. However, regardless of the order of the sets tested, there was evidence that the perirhinal group were impaired in reacquisition of the first set tested, regardless of when this set was learnt prior to surgery. In contrast, reacquisition of the following set tested was consistently as good as that of the control animals. Together these results suggest that perirhinal ablation in the rat leads to a reacquisition deficit limited to immediate post-operative performance.

The question of whether perirhinal cortex ablation results in a temporally graded reacquisition deficit is complicated by the unexpected finding that prior to surgery set 1 was more difficult to learn than set 2. As a result, all animals in the current study had substantially more experience of the stimuli and contingencies used in set 1 than in set 2. It is possible

that increased exposure to set 1 aided subsequent retention and thus reacquisition. On the basis of previous findings it was predicted that for the perirhinal group retention of the first-learned set 1 would be better than that of set 2 (Wiig et al., 1996). Had this prediction been fulfilled, it may have been argued that the result may have been in part attributed to the increased exposure to set 1 during pre-operative learning. However, in fact, we found equivalent performance with sets 1 and 2 in both the sham and perirhinal groups. If increased exposure to set 1 had enhanced performance with this set, this would suggest an underlying reverse temporal gradient in the perirhinal group. As this seems unlikely, our results suggest that, although set 1 was more difficult to learn, this did not substantially affect its subsequent retention for either group.

However, the finding that there was a deficit limited to the first tested discrimination must also be considered here. Is it possible that this effect could have prevented a retrograde effect being observed? This suggestion would imply that any within-animal comparison of performance of set 1 and set 2 is flawed as testing on the second tested set followed behavioural recovery from the deficit. However a between-animal comparison of the performance on set 1 and set 2 when each was tested first could still reveal a greater impairment on set 2 than set 1 in the perirhinal group. However, there was no indication that this was the case. Thus we conclude that there is no evidence of a temporal gradient to the retrograde effect we observed.

These findings are consistent with previous studies that failed to find a temporally graded retrograde deficit following perirhinal ablation in both the rat (Astur, Mumby & Sutherland, 1995) and the monkey (Thornton, Rothblat & Murray, 1997). Contradictory reports citing a temporally graded retrograde deficit in the rat (Kornecook et al., 1997; Wiig, Cooper & Bear, 1996) tested post-operative reacquisition of two choice object discriminations learnt at 5 different time intervals prior to surgery. It could be argued that this testing procedure was not as demanding as that of the present study, which requires discrimination between a larger number of stimuli presented in pseudorandomly assigned pairings, thereby making greater demands on the processes of visual identification. It is possible that, at the pre-operative learning stage of the discrimination task used in our study, internal representations of each stimuli were formed under different levels of encoding than those formed under the fixed pairs version of the task. Alternatively, a greater range in the timing of pre-operative learning may be necessary to reveal a temporally graded deficit. However, this seems unlikely, as a similar study using more varied time intervals also found a flat retrograde deficit in rats (Astur, Mumby & Sutherland, 1995).

The findings reported here question the role of the perirhinal cortex in a time limited consolidation process for visual associative learning. It has been suggested that lesions to any component of the hippocampal formation will disrupt the consolidation of information in sites in neocortex, producing a temporally graded retrograde deficit (Squire &

Alvarez, 1995; Wiig, Cooper & Bear, 1996). This assumption is not supported by the results of this study or by reports of flat retrograde deficits in spatial tasks (Rat: Bohbot et al., 1996; Bolhius, Stewart & Forrest, 1994) and object discrimination tasks (Primate: Salmon, Zola Morgan & Squire, 1985) following hippocampal ablation. The hippocampal formation is deemed to initiate gradual representations of associative information in cortex that eventually no longer require activation of the hippocampal formation for retrieval (Squire & Alvarez, 1995). However, evidence from primates suggests feedback from the perirhinal cortex modulates cortical representations of stimulus-stimulus associations in inferotemporal area TE at the time of learning and is continually required for their successful retrieval (Higushi & Miyashita, 1996). Likewise, hippocampal lesions rarely produce temporally graded retrieval deficits in spatial memory tasks, suggesting retrieval of spatial information may remain continually dependent upon the hippocampus (Nadel & Moscovitch, 1997). Therefore it is possible that retrieval of some forms of associative learning may remain dependent upon structures within the hippocampal formation.

The present experiment has demonstrated that perirhinal ablation in the rat produces a deficit in reacquisition limited to immediate post-operative performance. This finding is consistent with previous reports of a limited degree of behavioural recovery in animals with perirhinal lesions. Rats with perirhinal lesions make significantly more errors in the first 10 trials in a test of post-operative retention of 3 object discriminations learnt

prior surgery. However, perirhinal animals were not impaired in subsequent retention trials, suggesting a degree of behavioural recovery (Francis, Glenn & Mumby, 1996). Following perirhinal ablation, rats also fail to discriminate between novel and familiar objects in an object discrimination task. However, the animals' performance improves substantially with increased exposure to the stimuli and length of the post-operative recovery period (Ennaceur & Aggleton, 1997). Therefore, behavioural recovery may be due to the animal learning to compensate for difficulties experienced in the initial post-operative testing. For example, animals may increase stimulus viewing time or focus on relearning aspects of the task. The concurrent discrimination task used in the present study consisted of random pairings of the S+ and S-, in order to perform this version of the task the animals may have had to encode more salient features of each S+ or S-, so as to distinguish them from a random S-/S+ pairing. The behavioural recovery documented may be due to the animal incorporating components of a potentially richer representation of each S+ or S- into its performance strategy.

Although our results are consistent with previous reports of impaired retention of discrimination learning in the rat (Astur, Mumby & Sutherland, 1995; Eacott, 1998; Wiig, Cooper & Bear, 1996), they question whether the deficit is enduring in nature and whether it is due to impairments in mnemonic or nonmnemonic processes. Perirhinal ablation may disrupt a number of possible nonmnemonic processes that underlie normal performance in reacquisition of a concurrent visual discrimination

task. No differences were found between sham and perirhinal operated animals in reaction times to stimuli and reward collection. Therefore, whilst not all possible nonmnemonic deficits were tested for, the crucial motivational processes underlying response rates to the discrimination stimuli and reward are intact following perirhinal ablation. It is possible previous studies did not test post-operative reacquisition to such an extent as to reveal a degree of behavioural recovery. In addition, reports that perirhinal ablation in the rat affects acquisition and retention of visual discriminations differentially (Eacott, 1998) may be due to the order of testing post-operatively. New learning following perirhinal ablation may also be detrimentally affected by an initial post-operative behavioural deficit in discrimination learning.

It is possible that behavioural recovery was due to accessing learning via an alternative learning system that was engaged during initial pre-operative learning. Eacott (1998) tentatively suggested such an explanation as the reason for the impaired retention of post-operatively learned discriminations in the absence of a deficit in post-operative discrimination learning. There, it was suggested that the discriminations could be learned in alternative forms, and an impairment would only be apparent if a system was used for learning that was unavailable at the retention test. However, this explanation is questioned by our current findings that retention of a pre-operatively learnt task may be unimpaired, if it is not tested as the first post-operative test. Our results are more consistent with the view that the animals had an impairment from which

they recovered. However, the mechanisms of behavioural recovery are not well understood. It is possible that parallel learning systems were active at the pre-operative learning stage and that behavioural recovery reflected a shift in the post-operative system used to perform the retention task.

It has been suggested that associative learning can be accessed by two systems, a declarative learning system that allows for the relational or flexible expression of associative information, and a habit learning system that allows for the rigid expression of associative information that has been accumulated over many trials (Reber, Knowlton & Squire,1996). In rats, the hippocampus is considered to sustain declarative memory, whereas the dorsal striatum sustains non-declarative habit learning (Packard, Hirsch & White, 1989; Packard & McGaugh, 1992). Deficits in the acquisition of memory tasks that require flexible expression of learnt associations are evident following hippocampal lesions in the rat, yet incremental learning of associations over many trials remains intact (Packard, Hirsh & White, 1989). In contrast lesions to the dorsal striatum are seen to have the opposite effect (Packard, Hirsh & White, 1989). These findings are supported by reports that medial temporal lobe amnesics can learn a probabilistic classification task over many trials, yet have no recollection of the testing items or procedures. Parkinson's disease sufferers, with neuronal degeneration in the substantia nigra and loss of cortical inputs to the neostriatum, demonstrate the opposite pattern of behaviour (Knowlton, Mangels & Squire, 1996). It has been suggested that concurrent discrimination learning can be performed by a nondeclarative habit

learning system not reliant upon the perirhinal cortex (Buffalo et al., 1998; Phillips & Mishkin, 1984; Zola Morgan et al., 1994). Therefore, the presence of retrograde deficits in visual associate learning following perirhinal lesions may depend upon whether the tasks used can be solved by a habit learning system. Thus, the behavioural recovery reported in the current study may reflect a shift in the animals behavioural strategy, from reliance on a declarative system to a habit learning system.

However, this view does not account for consistent reports of impairments in retrieval of concurrent visual discrimination learning following perirhinal ablation in the monkey (Buckley & Gaffan, 1997; Murray & Gaffan, 1992; Thornton, Rothblat & Murray, 1997) and the rat (Eacott, 1998). It would be expected that retrieval deficits would be less severe if a habit learning system was capable of eventually sustaining retrieval. Moreover, the effects of lesions to the structures proposed to sustain habit learning, i.e. the dorsal striatium, on the retention of visual associative learning acquired prior to surgery are not known. It could be argued that the task used in our study could not be solved exclusively by a habit learning system, due to the constantly random S+/S- pairings. However, further studies could test the notion of dissociable declarative and nondeclarative learning systems by directly comparing perirhinal and striatal lesions on a range of associative tasks.

Behavioural evidence suggests that the perirhinal cortex contributes to visual stimulus-reward associations by virtue of its subcortical connections to the amygdala (Spiegler & Mishkin, 1981). The finding of

an initial retrieval deficit reported in the present study support this suggestion. However, the degree of behavioural recovery also reported suggests stimulus-reward associations are not exclusively dependent upon cortico-limbic interactions via the perirhinal cortex. It is possible that the amygdala modulates stimulus-reward associations acquired via the suggested cortico-striatal habit learning system, as the amygdala is deemed to influence learning in both systems (Packard & Teather, 1998; Packard, Cahill, McGaugh, 1994).

However, alternative explanations of our results are possible. Although histology revealed that all animals had substantial damage to the perirhinal cortex, the lesions in most cases were not complete and portions of perirhinal cortex remained intact. Therefore, one explanation is that an incomplete lesion had temporarily disrupted perirhinal function but did not destroy it, resulting in a transitory behavioural effect. However, while this view is difficult to disprove without testing much more extensive lesions, it seems unlikely that the remaining tissue could sustain retrieval to the limits of normal rats, evident in the retrieval rates of the perirhinal animals for the second set they were tested in post-operatively. Furthermore, there was no significant relationship between lesion size and post-operative performance.

It is possible that the task we used did not tax the central function of the perirhinal cortex, although perirhinal cortex clearly contributed to performance in the task. Although our discriminative stimuli were intended to mimic junk objects they were more akin to junk scenes. Thus

the stimuli contained a number of broadly similar components which had different spatial arrangements, orientations and patterns of contrast. In retrospect, this may have enabled the animals to solve the discrimination task other than as an object discrimination task, perhaps using spatial cues. It has been suggested that the perirhinal cortex contributes to stimulus identification by means of a perceptual learning process. In primates and rodents, cells within and surrounding the perirhinal cortex have been shown to finely tune their response properties upon repeat presentation of visual stimuli (Primates: Sakai & Miyashita, 1991; Sakai & Miyashita, 1994; Tanaka, 1993; Rodents: Zhu et al., 1995). Disruption to this process was thought to result in retrieval deficits in discrimination learning following perirhinal ablation, as the cells with response properties tuned to the task stimuli would be lost. Alternatively, if the task can be solved by means of the arrangement of components within a complex scene (Gaffan, 1994), the role of the perirhinal cortex may be less critical and therefore the effects of the lesion may be transitory. The discrimination in the current study may have been performed on the basis of the spatial arrangement of the objects within a scene, without in-depth processing or recognition of the objects themselves. It has been suggested that perirhinal ablation only impairs spatial scene discriminations when the subject has to correctly identify objects within a scenes (Murray, Baxter & Gaffan, 1998); yet there is evidence that perirhinal ablation in the monkey impairs acquisition of a concurrent visual discrimination task with complex naturalistic scenes as the stimuli (Gaffan, 1994). Therefore, it is possible

that a test of post-operative retention of visual discrimination tasks containing discrete visual objects as the stimuli may produce more severe or enduring retrieval deficits following perirhinal ablation.

In summary, therefore, our results suggest that the perirhinal ablation in the rat does not produce a temporally graded retrieval deficit for visual associative information, but a deficit limited to initial post-operative performance.

Chapter 4: The Effects of Perirhinal Ablation on Post-Operative Acquisition of Visual Discrimination Learning in the Rat

4.1 Introduction

The findings from experiment 1 (chapter 3), suggest that perirhinal ablation impairs post-operative retention of visual discrimination learning in the rat. However, there are contradictory accounts of the effects of perirhinal ablation on post-operative acquisition of visual stimulus-reward associative learning (Buckley & Gaffan, 1997; Eacott, 1998). In the visual modality there are reports that perirhinal ablation impairs both post-operative acquisition and retrieval of visual stimulus-stimulus associations in the primate (Murray, Gaffan & Mishkin, 1993). However, there is evidence that perirhinal ablation in the rat (Eacott, 1998; Kornecook, Anzaret & Pinel, 1997; Kornecook et al., 1995; Wiig, Cooper & Bear, 1995) and the primate (Gaffan & Murray, 1992; Thornton, Rothblat & Murray, 1997) impairs retrieval of visual associative learning acquired prior to surgery, whilst new post-operative learning remains intact. Moreover, there are reports that perirhinal ablation in the rat produces a similar pattern of impairments in associative learning between an auditory stimulus and an aversive event in fear conditioning (Romanski & LeDoux, 1992). Following perirhinal ablation rats acquire fear conditioning normally, however post-operative retrieval of fear conditioning learnt prior to surgery is impaired.

Therefore, it is possible that perirhinal ablation impairs retrieval of visual discrimination tasks acquired prior to surgery, yet the ability to

acquire new visual discrimination tasks remains intact. Thus, a dissociation between anterograde and retrograde visual associative processes may be apparent following perirhinal ablation. Dissociations between anterograde and retrograde memory processes are evident in medial temporal lobe amnesic patients. Human amnesia is typically characterised by deficits in anterograde learning, accompanied by retrograde deficits of varying severity (Zola Morgan, Squire & Amaral, 1986). However, two new classifications of amnesia have recently emerged, Focal Retrograde Amnesia, characterised by severe retrograde, but only minimal anterograde deficits (Kapur, 1992; Parkin, 1996) and Visual Deficit Amnesia, characterised by severe retrograde deficits, minimal anterograde deficits and an object recognition deficit in the form of associative agnosia (Rubin & Greenberg, 1998). Patients diagnosed with focal retrograde amnesia usually display multifocal lesions in either the temporal or frontal lobes following traumatic brain injury or herpes simplex encephalitis (Levine et al., 1998; Parkin, 1996). Although these new classifications of amnesia are still in their formative stages, the pattern of impairments they describe are consistent with the effects of perirhinal ablation on visual associative learning in primates (Gaffan & Murray, 1992) and rodents (Eacott, 1998).

The mechanisms of memory consolidation and retrieval are complex and not yet fully understood. According to one theory, memories are represented in the sensory cortical areas that originally processed the information to be remembered. Storage sites in neocortex are bound together by a convergence zone to enable both consolidation and

recollection of sensory information (Damasio & Damasio, 1993). It has been suggested that the perirhinal cortex contributes to the consolidation of associative information in neocortex by virtue of its extensive cortical and subcortical connections (Squire & Zola Morgan, 1991). Therefore, perirhinal ablation may disrupt the processes of converging and binding together information in neocortex, resulting in impairments in retrieval or acquisition of associative information. It is possible that dissociations between the processes of retrieval and acquisition are evident following perirhinal ablation as other structures within the hippocampal formation may sustain new learning.

However, at present there is no clear indication that perirhinal ablation produces a dissociation between retrograde and anterograde associative processes. Moreover, the role of the perirhinal cortex in visual associative learning remains unclear. In contrast to reports of impaired post-operative retrieval and intact acquisition of visual associative learning (Eacott, 1998), there are conflicting reports of intact retrieval and acquisition of visual discrimination learning following perirhinal ablation in the rat (Astur, Mumby & Sutherland, 1995). Furthermore, there are reports of impaired acquisition of a 4 pair concurrent visual discrimination task, with real objects following lesions to the rhinal, presubicular and parasubicular cortices in the rat (Rothblat et al., 1993). There are also reports of impaired post-operative acquisition of visual discrimination learning following perirhinal ablation in the primate (Buckley & Gaffan, 1997; Gaffan, 1994). One difference between the discrimination tasks in

which a deficit in post-operative acquisition is reported (Buckley & Gaffan, 1997; Gaffan, 1994) and those in which no deficit is seen (Eacott, 1998; Murray & Gaffan, 1992; Thornton, Rothblat & Murray, 1997), is the number of pairs of discriminations to be learnt. In the studies reporting a deficit, the number of stimuli in the discrimination task is increased to 160 pairs (Buckley and Gaffan, 1997; Gaffan, 1994), whereas previous studies tested stimuli sets containing only 20 (Murray and Gaffan, 1992) or 10 pairs (Thornton, Rothblat & Murray, 1997) of discriminations. Therefore it has been suggested that perirhinal ablation impairs new learning when increased demands are placed on the processes of object identification (Buckley & Gaffan, 1997). This view is supported by electrophysiological evidence suggesting that the perirhinal cortex contributes to object recognition processes (Primates: Gross et al., 1972; Lueschow, Miller & Desimone, 1994; Nakumura, Mikami & Kubota, 1992; Rodents: Zhu, Brown & Aggleton, 1995).

The notion that perirhinal ablation disrupts the ability to correctly identify a large number of visual stimuli for mnemonic purposes has been suggested previously on the basis of findings from visual recognition memory tasks (Eacott, Gaffan & Murray, 1994; Gaffan, 1994; Horel et al., 1987; Meunier et al., 1993,) and visual discrimination learning tasks (Buckley & Gaffan, 1998a,b, 1997). These findings suggest that increasing demands on the perceptual processes of object identification may reveal deficits in visual discrimination learning in the primate.

Therefore, the role of the perirhinal cortex in visual associative memory processes is unclear. It is possible that a dissociation between anterograde and retrograde visual associative processes exists following perirhinal ablation in the monkey (Thornton, Rothblat & Murray, 1997) and the rat (Eacott, 1998). Evidence of a dissociation would suggest that the processes of acquisition and retrieval are served by distinct neuronal mechanisms that are not equally reliant on the perirhinal cortex. Alternatively, perirhinal ablation may disrupt the perceptual processes of object identification to such an extent as to produce deficits in visual associative learning and visual recognition memory tasks. It is possible that processes of retrieval and acquisition of visual associative learning place different demands on object identification processes, thus producing the apparent dissociation between retrieval and new learning following perirhinal ablation in the rat (Eacott, 1998). Thus, reports of intact new learning following perirhinal ablation have not placed enough demands on the processes of acquisition to reveal a deficit.

Therefore, this experiment was designed to place increased demands on the processes of visual discrimination learning in the rat, to determine whether a deficit in new learning can be revealed following perirhinal ablation. Accordingly, all animals learnt a new set of concurrent visual discriminations, in which the number of stimuli increased gradually up to 15 pairs

4.2 Method

4.2. i Subjects

Sixteen male Dark Agouti rats were used in this experiment, all had undergone surgery, either sham operated or bilateral perirhinal ablation and had successfully completed experiment 1 described in chapter 3. One rat from the perirhinal group was removed from the study after reaching criterion on five pairs of stimuli, due to developing a tumour. The results of this rat are reported only up to five pairs. Therefore, only fifteen rats completed the study, seven sham animals and eight perirhinal operated. A detailed description of the animals used in this study is provided in chapter 2.1.

4.2. ii Apparatus

The same computer operated Y - maze was used as in experiment 1, as described in chapter 3; a full description of the apparatus is given in chapter 2.2. A detailed description of the discrimination task and generation of the stimuli used is provided in chapter 3. 2.iii.

4.2. iii Surgery

A detailed description of the surgical procedures used is provided in chapter 2.4.

4.2. iv Post-Operative Training

All animals learned a new set of concurrent visual discriminations, composed of 15 pairs of stimuli. As in experiment 1, described in chapter 3, in each pair of stimuli there was a rewarded stimulus, S+, and an un-rewarded foil, S-. Acquisition of the new discrimination progressed in an

almost identical manner to pre-operative learning described in chapter 3.2 iii. As before, the animals were initially presented with just one pair of stimuli. When they reached criterion of 80% correct in any given session of up to 100 trials, a new pair of stimuli was introduced, providing the subject had not accumulated more than 1000 trials before reaching criterion in the last-learned pair. One perirhinal animal (R11) failed to attain criterion at 14 pairs, therefore 1000 trials was added to his score for the final pair of stimuli that he did not complete. Animals R50, R9,and R49 all attained criterion at 14 pairs of stimuli and completed 1000 trials at 15 pairs of stimuli before being removed from the study. As before, the stimulus pairings were not confined to initial pairings so that any S+ could be paired with any current S-.

4.2. v Histology

The methods of histological analysis performed on all animals in the current study are described in chapters 2.5 and 3.2 vi.

4.3 Results

4.3. ii Histology

Chapter 3.3 i describes the results of the histological analysis of the animals in the current study.

4.3. iii Post-Operative Testing

The rate of acquiring the new set of discriminations post-operatively is shown in Table 4.1 and Figure 4.1 for both the perirhinal and

sham animals. Overall three sham animals and one perirhinal animal failed to attain criterion for all 15 pairs of stimuli, (Sham: R11, R9, R49; Perirhinal: R50). Animal R11 completed 1000 trials at 14 pairs of stimuli, but failed to attain criterion at this point, likewise animals R9, R49 and R50 all completed 1000 trials at 15 pairs of stimuli, yet failed to attain criterion. Animals performances in the task with 14 pairs of stimuli were compared, as this was the final stage which all animals completed.

Table 4.1. Cumulative trials to criterion in post-operative acquisition of a new set of concurrent visual discriminations.

					Perirhinal Animals						
Pairs	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**
RAT											
R45	1097	1451	1517	1596	1673	1805	1961	2947	3125	3526	3732
R48	880	960	1009	1059	1128	1272	1588	1945	2037	2091	2896
R50	1168	1270	1333	1427	1471	1590	1630	2052	2252	2438	
R53	1420	1465	1607	1680	1818	1919	2058	2102	2612	2662	3625
R51	1062										
R3	646	695	730	942	986	1210	1341	1461	2344	2827	3132
R5	1148	1266	1399	1535	1690	2214	2388	2626	3118	3802	4132
R8	959	998	1139	1185	1241	1470	1502	1745	1846	2019	2385
R1	1178	1365	1376	1421	1520	1755	1766	1805	2062	2157	2380
Mean	**1062**	**1183**	**1263**	**1355**	**1440**	**1654**	**1779**	**2082**	**2424**	**2690**	**3183**
					Sham Animals						
R46	1083	1319	1376	1483	1543	1645	1698	1950	2529	2744	3448
R52	1078	1117	1163	1308	1352	1447	1543	1738	2254	2750	2843
R4	790	872	909	1063	1093	1217	1310	1618	1967	2051	2648
R9	970	1067	1190	1278	1321	1574	1675	2477	2713	3067	
R11	1219	1373	2084	2152	2351	2883	3170	3320	4327		
R47	1410	1619	1820	1868	1918	2360	2414	2509	4133	4477	4616
R49	1953	2459	2504	2784	2904	3030	3254	4477	4540	4690	
Mean	**1214**	**1403**	**1578**	**1705**	**1783**	**2022**	**2152**	**2584**	**3209**	**3296**	**3388**

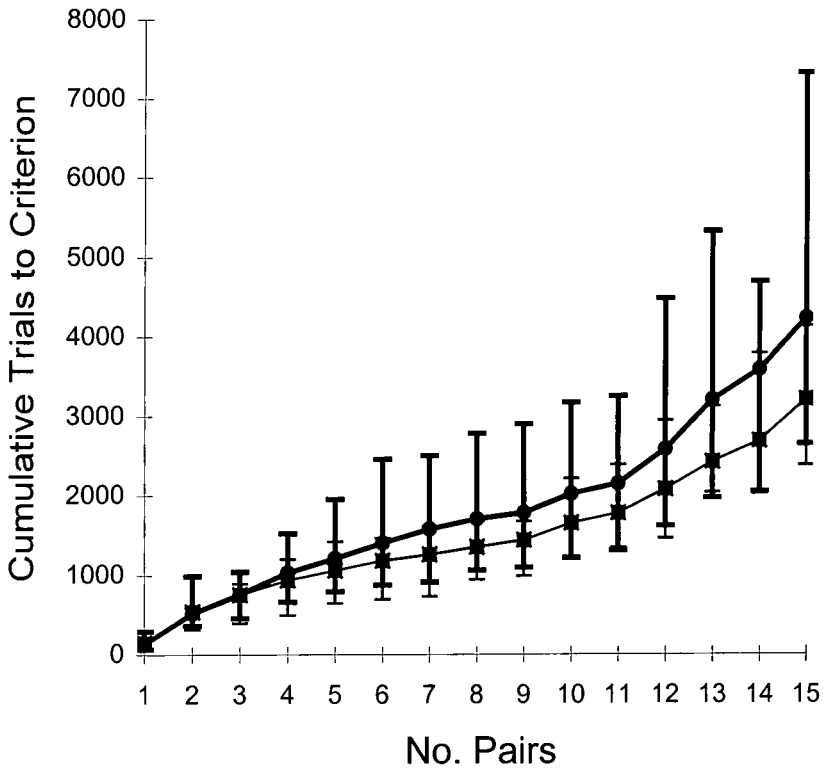


Figure 4.1. The number of trials to criterion in post-operative acquisition of a new set of discriminations for both the sham, (dots, thick lines) and the perirhinal (squares, thin lines) animals. For the animals that failed to attain criterion in pairs 14 and 15 1000 trials were added to their final scores for the pairs they could not complete. The error bars show the range of scores.

The acquisition rates of the sham and perirhinal animals were compared for each pair of stimuli between 5 and 14 in a 2 (Surgical Group) x 10 (No.of Pairs, 5-14) ANOVA with 1 repeated measure. The number of trials accumulated in attaining criterion at 5 pairs of stimuli and then additional trials for each pair of stimuli were compared. As expected, the number of pairs of stimuli in the discrimination task had a significant effect on the number of trials taken to attain criterion ($F = 71.5$, $df = 8$, 104, $p = <0.001$). The main effect of surgical group did not have a significant effect on performance ($F = 2.031$, $df = 1, 13$, $p = 0.178$), the interaction between surgical group and the number of pairs of stimuli was

not statistically significant ($F = 2.042$, $df = 8, 104$, $p = 0.51$). Table 4.1 and figure 4.1 show how the perirhinal animals actually accumulated fewer trials to criterion than the sham animals.

4.3. iv Lesion Size and Performance

Table 3.1 in chapter 3, shows the relative lesion sizes of the animals in the current study. Correlation analyses were performed to determine whether lesion size had a significant effect on post-operative acquisition performance. There was no significant correlation between the number of trials to criterion for 5 pairs of stimuli and the extent of damage to the perirhinal cortex ($r = 0.061$, $p = 0.875$) or area TE ($r = 0.132$, $p = 0.735$). There was no significant correlation between the number of trials to criterion in 15 pairs of stimuli and the extent of damage to area TE ($r = -0.115$, $p = 0.787$). However, there was a significant negative correlation between the extent of damage to the perirhinal cortex and the number of trials to criterion in 15 pairs of stimuli ($r =- 0.709$, $p = 0.049$). This finding suggests that the number of trials to criterion decreased along with increases in lesion size, suggesting that the perirhinal animals' performances actually improved with increases in lesion size. Therefore, the extent of damage to area TE did not have a significant effect on performance, whereas more extensive damage to the perirhinal cortex appears to actually facilitate learning the task with 15 pairs of stimuli.

4.4 Discussion

All animals in the present study learnt a new set of concurrent visual discriminations following either bilateral perirhinal ablation or sham

surgery. The animals had successfully completed experiment 1, described in chapter 3. The number of pairs of stimuli in the concurrent discrimination task was increased from the usual 5 pairs to 15 pairs, to determine whether this would have a detrimental effect on the animals' ability to acquire the discrimination task. The sham-operated animals amassed slightly more trials to attain criterion for 15 pairs of stimuli than the perirhinal group, however this difference was not statistically significant. It appears that increasing the number of stimuli in a concurrent visual discrimination task, thereby increasing the demands on object identification does not have a detrimental effect on acquisition following perirhinal ablation.

Our results are inconsistent with previous reports indicating that increasing the number of stimuli to be learnt in a concurrent visual discrimination task has a greater detrimental effect on learning following perirhinal ablation in the monkey (Buckley & Gaffan, 1997; Gaffan, 1994). It is possible that ablation of the perirhinal cortex affects acquisition of visual associative information in primates and rodents differently. However, our results are consistent with reports of intact new learning of visual associative tasks containing 10 (Murray & Gaffan, 1992), 20 (Thornton, Rothblat & Murray, 1997), or 60 (Thornton, Malkova & Murray, 1997) pairs of discriminations following rhinal cortex ablation in the monkey. Our results are also consistent with previous reports of normal acquisition of a 5 pair concurrent visual discrimination learning task (Eacott, 1998) and a 2 choice visual discrimination learning task

(Astur, Sutherland & Mumby, 1995; Wiig, Cooper & Bear, 1996) following perirhinal ablation in the rat. It is possible previous reports of intact new learning following perirhinal ablation (Eacott, 1998), did not tax the processes of acquisition to such an extent as to reveal a deficit. However, the results of the current study suggest new learning remains intact when increased demands are made on the processes of visual associative learning. These findings suggest structures other than the perirhinal cortex are capable of sustaining the acquisition of visual associative learning.

There are reports that retrieval of visual discrimination learning is impaired following perirhinal ablation in the rat (Eacott, 1998; Wiig, Cooper & Bear, 1996) and the monkey (Gaffan & Murray, 1992; Thornton, Rothblat & Murray, 1997). However, our results suggest new learning remains intact following perirhinal ablation in the rat. Therefore, it is possible that acquisition and retention of visual discrimination learning are dissociable following perirhinal ablation. There is evidence to suggest that perirhinal ablation in the rat produces a similar pattern of impairments in associative learning in other modalities (Corodimas & LeDoux, 1995; Romanski & LeDoux, 1992; Rosen et al., 1992). Therefore it is possible that the perirhinal cortex plays a general role in the retrieval of associative learning, while acquisition of associative learning may be sustained by other structures within the hippocampal formation.

There is evidence that increasing the number of stimuli in a discrimination learning task, thereby increasing the demands made on

object identification, reveals an impairment in new learning (Buckley & Gaffan, 1997). However, it has been argued that the previous study does not show a clear relationship between set size and the degree of impairment in new learning (Thornton, Rothblat & Murray, 1997). Although Buckley & Gaffan (1997) demonstrate impaired acquisition of a concurrent visual discrimination task containing 40 pairs of stimuli, when all sets of stimuli learnt are combined to make a set of 160 pairs the perirhinal animals are not significantly impaired. In addition, acquisition deficits are evident in the perirhinal animals when the rewarded stimuli in a 40 pair discrimination task are presented with 7 extra foil stimuli. However, this deficit is no longer seen when the number of foils are increased to 14 (Buckley & Gaffan, 1997). These discrepancies raise the possibility that deficits in new learning following perirhinal ablation may not be directly related to the number of stimuli in the learning task (Thornton, Rothblat & Murray, 1997). Nevertheless, there are reports of deficits in learning a concurrent discrimination task, containing 160 pairs of stimuli, following perirhinal ablation in the monkey (Gaffan, 1994). It has been suggested that animals may perform the concurrent discrimination task at different levels of encoding at different levels of training (Gaffan et al., 1990). Therefore the results of the Buckley & Gaffan (1997) study may reflect the over-learnt nature of the task, as animals learnt the discriminations in individual sets before they were combined to make one set of 160 pairs of stimuli. Alternatively,

impairments in new learning may be due to the complexity of the visual stimuli used, not the number.

There are reports of impaired acquisition of concurrent visual discrimination learning in medial temporal lobe amnesic patients (Aggleton et al., 1988; Gaffan et al., 1990; Oscar-Berman & Zola Morgan, 1980; Squire, Zola Morgan & Chen, 1998). Although amnesic patients demonstrate impaired new learning relative to control subjects, patients' performances do improve with successive trials and most patients consistently perform above chance (Aggleton et al., 1988; Oscar Berman & Zola Morgan, 1980). Furthermore, there are reports that amnesic patients can learn a 6 pair concurrent visual discrimination task at the same rate as control subjects, yet are impaired in learning 2 and 10 pair concurrent discriminations (Gaffan et al., 1990). Therefore, medial temporal lobe amnesics appear to learn some aspects of the concurrent visual discrimination task. However, in the current study perirhinal ablation did not impair acquisition of a concurrent discrimination task. Therefore, the areas within the medial temporal lobe crucial to normal concurrent discrimination learning may lie outside the perirhinal cortex. Alternatively, the apparent discrepancies between reports of impaired new learning in amnesic patients and intact new learning following perirhinal ablation in animal studies may reflect differences in the strategies used by humans and animals to perform the tasks (Buffalo et al., 1998). It has been suggested that humans form an explicit memory for each stimulus in the discrimination task, which is then assigned to a group of rewarding or non-

rewarding stimuli (Zola Morgan et al., 1994). Whereas animals may form less explicit memories of each stimuli, and rely more heavily on the processes of skill and habit learning (Buffalo et al., 1998; Zola Morgan et al., 1994). Although it is difficult to determine how animals and humans formulate behavioural strategies, this view supposes that concurrent visual discrimination learning can be solved by a non-declarative habit learning memory system. If this were the case it would be expected that amnesic patients could acquire the task without any deficits as amnesic patients can acquire skill or habit learning tasks (Corkin, 1984).

Alternatively, it is possible that the deficit experienced by amnesic patients (Aggleton et al., 1988; Gaffan et al., 1990), is due to the extent of damage both within and outside the medial temporal lobe. The amnesic subjects used in the patient studies suffered from Korsakoff's syndrome, typically resulting in diffuse cell loss in both the medial temporal lobe, and also diencephalic structures (Ellis & Young, 1991; Gaffan et al., 1990). Therefore, the extent of damage within these areas may have a cumulative effect on the severity of impairments in anterograde memory processes.

The results of the current study suggest that perirhinal ablation has distinct effects on the processes of visual recognition memory and visual associative memory. Rhinal ablation in the rat (Mumby & Pinel, 1994) and perirhinal ablation in the monkey (Meunier et al., 1993) impairs performance in visual recognition memory tasks. However, our results suggest that acquisition of visual associative memory tasks remains intact following perirhinal ablation in the rat. There are reports that rhinal cortex

ablation in the primate impairs performance in the recognition memory task, delayed match to sample, providing a large number of visual stimuli are used, rendering each stimulus trial unique (Eacott, Murray & Gaffan, 1994). This deficit is evident when there is no delay interval between stimulus presentations, suggesting a perceptual impairment in recognising a large number of complex visual stimuli. It is possible that recognition memory tasks and associative memory tasks place different demands on the processes of object recognition. In a recognition memory task a large number of visual stimuli are presented for a short period of time, whereas in concurrent discrimination learning the stimuli are presented repeatedly, thus providing more time for the subject to form representations of each stimulus.

There is behavioural evidence to suggest that perirhinal ablation impairs the ability to discriminate between large numbers of complex visual stimuli (Buckley & Gaffan, 1997, 1998a, b). However, the results of the current study suggest that the identification of all types of visual stimuli is not exclusively dependent upon the perirhinal cortex in the rat. Electrophysiological evidence suggests that cells in the perirhinal cortex fine tune their response properties (Primates: Sakai et al., 1994; Tanaka, 1993) and signal the familiarity and recency of presentation of complex visual stimuli (Rodents: Zhu Brown & Aggleton, 1995; Primates: Riches et al., 1991;). However, although the majority of such cells are distributed throughout the rhinal cortex, they are also evident in anterior inferotemporal area TE in both rats (Zhu, Brown & Aggleton, 1995) and

monkeys (Brown, 1996; Sakai et al., 1994; Tanaka, 1993). Therefore, it is possible that structures outside of the perirhinal cortex sustain visual processing for the purposes of visual discrimination learning.

Both electrophysiological studies in the primate and neuroimaging studies in humans suggest that area TE contributes to the recognition of complex visual stimuli (Tanaka, 1997). Area TE is thought to provide sensory information in the form of higher order visual processing to limbic and striatal structures involved in learning and memory (Buffalo et al., 1998). It has been suggested that impairments in acquisition of concurrent visual discrimination learning are due to lesions to area TE and not the perirhinal cortex in the primate (Buffalo et al., 1998). There are reports that TE lesions in the primate impair acquisition of concurrent visual discrimination learning (Buffalo, Ramus, Zola Morgan & Squire, 1995). A meta-analysis of the results of several studies in the primate, reveals a linear relationship between the severity of the impairment in post-operative acquisition of concurrent visual discrimination learning and the extent of damage to area TE (Buffalo et al., 1998). The analysis did not find a relationship between the severity of the impairment in visual associative learning and the extent of the lesion to the perirhinal cortex. Therefore, it has been argued that impaired acquisition of concurrent discrimination learning following perirhinal ablation in the primate (Buckley & Gaffan, 1997), may be due to perirhinal lesions extending into area TE (Buffalo et al., 1998). However, there is evidence of impaired acquisition of concurrent discrimination learning following perirhinal ablation in the

monkey, in which there is no indication of damage to area TE (Gaffan, 1994). Furthermore, there are reports of intact new discrimination learning in the primate following lesions to the perirhinal cortex that did include damage to area TE (Thornton, Rothblat & Murray, 1997). In the current study the extent of unintended damage to area TE did not affect animals' post-operative performance in the discrimination learning task. However, the mean extent of unintended damage to area TE in the present study was 10% of its overall area. It is probable that more extensive lesions to TE may produce deficits in concurrent visual discrimination learning (Buffalo et al., 1998).

Whilst it is possible that area TE sustains new visual associative learning following perirhinal ablation, the effects of TE lesions on the retention of associative learning acquired prior to surgery is not known. The notion that TE sustains visual associative learning does not account for the findings of deficits in post-operative retention of concurrent discrimination learning following perirhinal ablation in the monkey (Murray & Gaffan, 1992) and the rat (Chapter 3; Eacott, 1998). Furthermore, deficits are evident in retention of associative learning in non-visual modalities following perirhinal ablation (Parker & Gaffan, 1998; Romanski & LeDoux, 1992). These findings suggest that, although area TE may contribute to new learning following perirhinal ablation, the perirhinal cortex may be necessary for the retention of multimodal associative learning.

The results reported here suggest new visual discrimination learning remains intact following perirhinal ablation in the rat, even when increased demands are made on the processes of visual object identification. One possible explanation of our results is that we did not tax the rats' discriminative ability enough to reveal a deficit in new learning. By increasing the number of stimuli in the concurrent discrimination task further to 20 pairs, or by introducing more distracting stimuli, it may have been possible to reveal a deficit. However, even with a set size of 15 pairs, the sham animals in the present study were beginning to fail to learn efficiently, with 3 animals failing to attain criterion. Therefore, it may prove unrealistic to increase the number of stimuli further. In addition it suggests that the discriminative abilities were sufficiently taxed.

The current study was designed to increase demands on the perceptual processes of visual object identification. However, as previously suggested, in retrospect the stimuli used in the current study were more akin to junk scenes than objects. This may have enabled the animals to solve the discrimination task by relying on spatial cues within the stimuli. Therefore, a test of post-operative acquisition of visual discrimination learning tasks containing more discrete visual objects may reveal a deficit in discrimination learning following perirhinal ablation. However, reports of impaired acquisition of a concurrent visual discrimination task containing 2 dimensional complex naturalistic scenes

following perirhinal ablation in the monkey argue against this possibility (Gaffan, 1994).

As previously stated in chapter 3, although the histology revealed that all animals in the current study sustained substantial damage to the perirhinal cortex, the lesions in most cases were incomplete and portions of the perirhinal cortex remained intact. It is possible that the remaining perirhinal tissue was sufficient to sustain new learning. However, while this view is difficult to disprove without testing more extensive lesions, it seems unlikely that the remaining tissue could sustain new learning to the limits of normal rats, evident in the perirhinal animals' acquisition rates. Furthermore, the extent of damage to the perirhinal cortex did not have any affect on animals' performance in the task with 5 pairs of stimuli and at 15 pairs more extensive lesions appeared to actually facilitate performance in the task. However, it should be noted that the behavioural effects of varying the extent of the perirhinal lesions was not a primary aim of the current study. Therefore, due to the relatively small differences in lesion sizes found for the majority of animals in the current study it is uncertain whether the facilitation reported here is a true reflection of lesion size. This issue could be addressed more systematically by directly comparing the behavioural effects of a number of different sized perirhinal lesions.

In conclusion, our results suggest that following perirhinal ablation in the rat, acquisition of a new concurrent visual discrimination task is unimpaired even when the demands on the processes of identification are increased. Further studies are needed to measure more discretely how

visual discrimination tasks are affected by perirhinal ablation in the rat, to determine to what extent the perirhinal cortex is critical for the accurate identification of large numbers of complex visual stimuli.

Chapter 5: The Effects of Perirhinal Ablation on Acquisition and Retention of a Visual Generalisation Task

5.1 Introduction to Experiment 3a

The findings from experiment 2, described in chapter 4, suggest that increasing demands on the processes of visual object recognition has no effect on post-operative acquisition of a concurrent visual discrimination task following perirhinal ablation. However, there is increasing evidence to suggest that the perirhinal cortex in the primate (Nakumura & Kubota, 1996) and the rat (Ennaceur et al., 1996; Zhu, Brown & Aggleton, 1995,) contributes to visual object recognition processes.

There is electrophysiological evidence to support the view that the perirhinal cortex contributes to visual object recognition (Primates: Baylis & Rolls, 1987; Gross et al., 1972; Rodents: Zhu, Brown & Aggleton, 1995). Single cell recording studies in primates have revealed cells within the perirhinal cortex that finely tune their response properties to familiar visual stimuli (Sakai, Naya & Miyashita, 1994; Sakai & Miyashita, 1991, 1994). Further studies suggest perirhinal neurons sustain recognition of familiar visual objects presented in various situations, by modifying response rates to transformations in stimuli form, but not to transformations in stimuli size, location or definition cues such as luminance, texture or motion (Nakumura & Kubota, 1996; Miyashita & Chang, 1988; Sato et al., 1980; Sary et al., 1993). Cells within the perirhinal cortex also encode the relative familiarity and recency of occurrence of visual stimuli (Primates: Brown, Wilson & Riches, 1987;

Fahy et al., 1993; Li et al., 1993; Miller et al., 1991; Rodents: Zhu, Brown & Aggleton, 1995). These findings suggest that neuronal mechanisms within the perirhinal cortex not only encode mnemonic information, but contribute to the perceptual process of object recognition (Brown, 1996; Riches et al., 1991; Zhu, Brown & Aggleton, 1995).

The suggestion that the perirhinal cortex contributes to visual object recognition is supported by findings from behavioural studies. Bilateral rhinal cortex ablation in primates results in an impairment in the visual recognition memory task, Delayed Match to Sample, when a relatively large stimuli set is used, rendering each stimulus trial unique (Eacott et al., 1994). Increasing the stimuli set size in a simultaneous matching task, in which there is no delay period, also reveals a deficit, suggesting a disruption of perceptual rather than mnemonic processes (Eacott et al., 1994).

Similar findings have been reported in tests of visual associative memory. Following perirhinal ablation primates (Gaffan & Murray, 1992) and rodents (Eacott, 1998) are impaired in retention of visual discriminations learnt prior to surgery, whereas post-operative acquisition of a new set of discriminations remains intact. However, increasing the demands on object recognition processes, by increasing the number of stimuli in the post-operative acquisition task, has a detrimental affect on performance in primates (Buckley & Gaffan, 1997). Furthermore, increasing demands on stimuli identification by presenting familiar stimuli within visual scenes or in novel orientations has a detrimental effect on

primates' performances in visual discrimination tasks with only small numbers of stimuli (Buckley & Gaffan, 1998a, 1998b). However, the results of chapter 4 suggest that increasing demands on the processes of visual stimuli recognition in a concurrent discrimination task has no effect on acquisition performance following perirhinal ablation in the rat.

Disruption to the perceptual process of object identification may contribute to the visual mnemonic deficits associated with perirhinal ablation. However, evidence suggesting the perirhinal cortex contributes to visual object identification in the rat remains inconclusive, it is necessary to measure further the effects of perirhinal ablation on visual perceptual processes. Therefore, the aim of the following experiment, 3a, was to determine whether perirhinal cortex in the rat contributes to the process of visual object identification, by signalling variations in stimuli form, but not stimuli size. In experiment 3a we measured the effects of perirhinal ablation on acquisition of a simple two choice visual discrimination task and generalisation of the discrimination, in order to observe the effects of bilateral perirhinal ablation on visual perceptual learning processes. Therefore, perirhinal and unoperated animals learnt a two choice visual discrimination task and were then tested for generalisation of the learning task which used size and form transformations of the nonrewarded stimuli, S-, used in the original discrimination. It was then possible to measure the generalisation gradients for the new S- `s and S+'s.

Generalisation to the new stimuli in the current task is thought to occur as these stimuli share common elements with the stimuli in the original discrimination (Mackintosh, 1974). As the original and the transformed stimuli in the current task do not share common elements equally, it would be expected that animals' correct response rates decrease with increasing transformations of the S- or S+, producing a sloping gradient. A flat generalisation gradient or a gradient that is broader or narrower than normal would suggest an impaired ability to distinguish the different transformed stimuli from the original stimuli. However, it has been suggested that a flat generalisation gradient may actually reflect increased discrimination between the original stimuli and its subsequent transformations (Mackintosh, 1983). Thus, if animals recognise that the transformed stimuli are different to the original stimuli then they will respond equally to each transformed stimulus, regardless of the extent of transformation. Although generalisation gradients are open to different interpretations, the effect of perirhinal ablation on animals generalisation performances is still of interest.

5.2 Experiment 3a: Method

5.2. i Subjects

Twenty-one male Dark Agouti rats were used in this experiment; they were aged approximately 4 months at the start of testing. Chapter 2.1 provides a detailed description of the subjects used.

5.2. ii Apparatus

The apparatus used was a computer operated Y - maze, as described in chapter 2.2.

5.2 iii Surgery

Bilateral perirhinal ablation was performed on 7 animals; a detailed description of the surgical methods used is given in chapter 2.4.

5.2 iv Behavioural Training

Initial pre-operative training involved responding to simple stimuli in the maze for food reward, as described in chapte r 2.3. Once this was accomplished animals were assigned to 2 groups. Group 1 contained seven animals who underwent bilateral perirhinal ablation, prior to continuing behavioural testing and group 2 contained fourteen animals that remained unoperated throughout behavioural training. The perirhinal animals had a two-week rest period following surgery before they began post-operative training in a two choice visual discrimination task and 2 visual generalisation tasks.

Initially all animals learnt a two choice visual discrimination between two geometric shapes of equal area. The rewarded stimulus, S+,

was a square, measuring 6cm² and the nonrewarded stimulus, S-, a rectangle, measuring 2.4cm x 15cm. The S+ and S- were therefore of equal area and the width of the rectangle equalled 40% of the width of the square. The S+ and S- were presented in different arms of the Y-maze and animals learnt to approach the S+ to collect a food reward (45mg pellet, Bioserve). Throughout this task the stimuli were randomly presented in a central location across only one monitor screen in two different arms of the maze. The stimuli could appear on either monitor screen in each arm of the maze. The stimuli were defined by presenting the background in a dark grey level and the stimuli in a light grey level.

The brightness and location of the test stimuli on the monitor screens remained constant, until a criterion of 80% correct responses over 2 consecutive sessions was reached. The test stimuli were then presented in five different degrees of brightness, when the same criterion was reached at this stage the stimuli were presented in random locations on the monitor screens. The only limit was that the whole stimulus had to appear within the area visible on the screen. The stimuli were presented in the following levels of brightness, 12.4, 6.9, 3.1, 1 and 0.21 cd/m². The brightness of the background monitor screen remained at 0.01cd/m² throughout the task. The location and brightness of the stimuli were varied in order to increase animal's reliance on cues regarding the form of the stimuli to perform the discrimination task, over spatial or luminance cues. All animals were tested five days a week and completed up to 100 trials a day. Throughout the task the intertrial interval was 1 second and the

reward for a correct response was one 45mg reward pellet (Bioserve). Animals attained a criterion of 80% correct responses over two consecutive sessions in the final stage of testing, before training began on the two visual generalisation tasks.

The two visual generalisation tasks included the discrimination between the square S+ and the rectangular S- that formed the two choice visual discrimination task. However, 6 more S-'s were added that varied in terms of size or form from the original S- and 3 more S+'s were added that varied in size. In generalisation task 1 the transformations in form were as follows. The width of the original S- was 40% of the square S+, whereas the widths of the new foil stimuli were 60%, 75% and 90% of the square. As the same overall area was retained, the new foil stimuli increasingly resembled the square S+. These new transformations in form of the S- were always presented with the original S+. The new transformations in size of the S- retained their rectangular form, but were reduced to 50%, 40% and 30% of the area of the original stimuli. The new transformations in size of the S- were always presented with a size matched S+. Figures 5.1 and 5.2 show the dimensions of the stimuli used in generalisation tasks 1 and 2.

Figure 5.1 Reproductions of the stimuli used in the base discrimination and the variations in stimuli size used in generalisation tasks 1 and 2 (the actual dimensions of the stimuli used are described in section 5.2. iv).

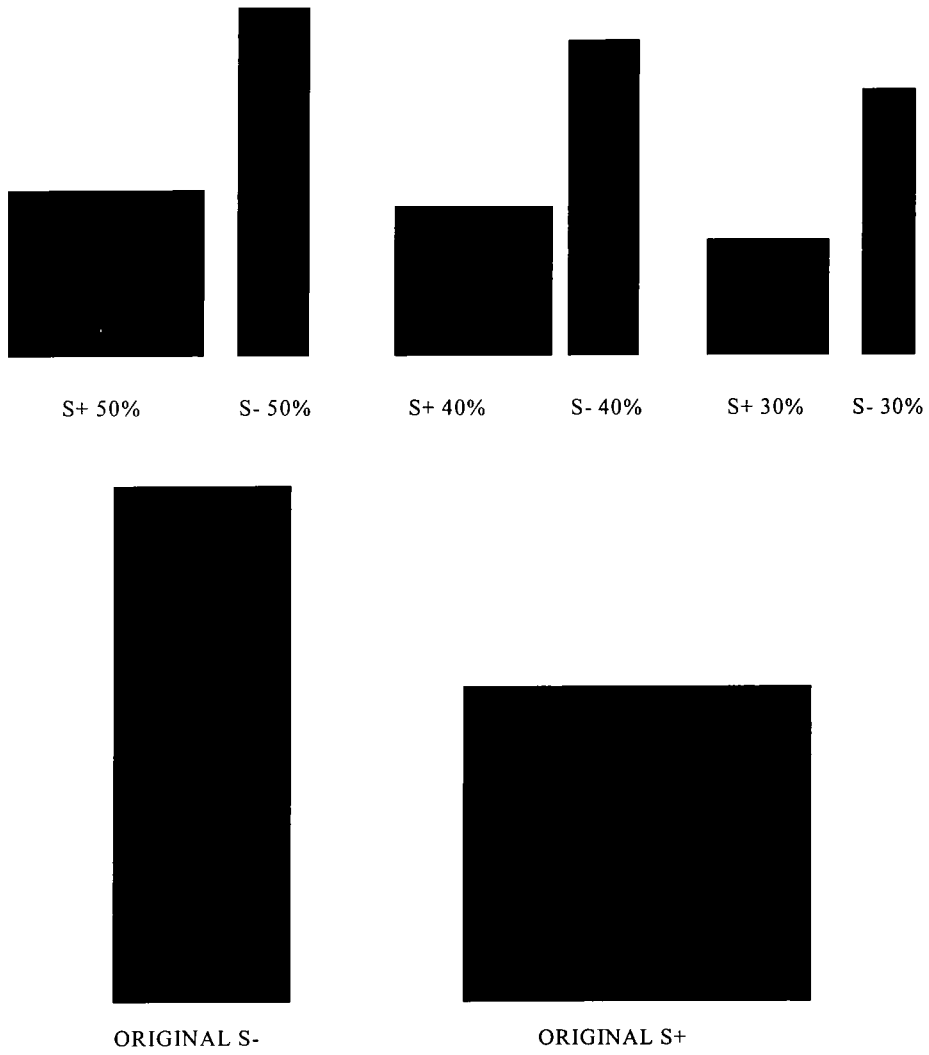
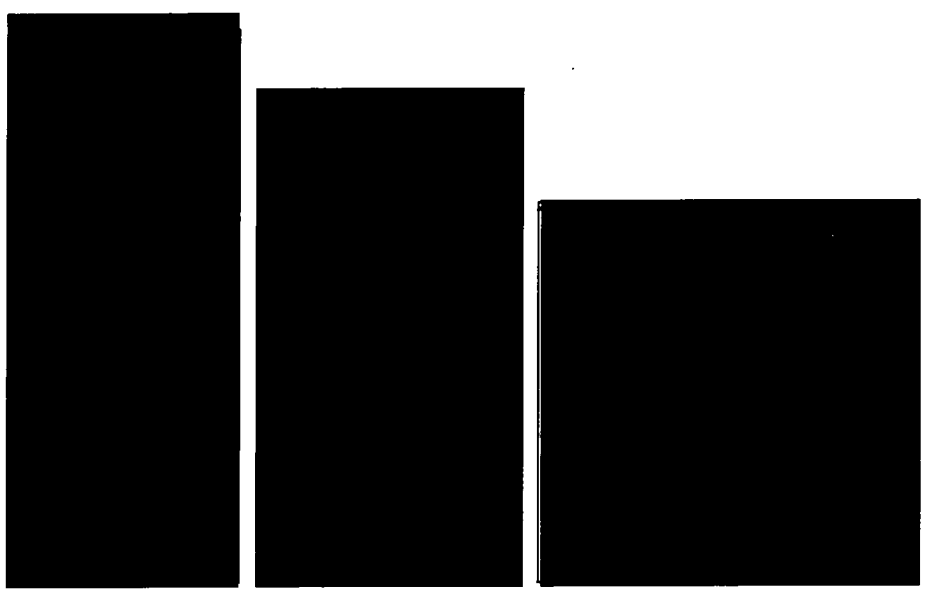


Figure 5.2 Reproductions of the form transformed stimuli used in generalisation tasks 1 and 2 (the actual dimensions of the stimuli used are described in section 5.2.iv).

55% OF ORIGINAL S+ 65% OF ORIGINAL S+ 75% OF ORIGINAL S+
FORM STIMULI USED IN GENERALISATION TASK 2



60 % OF ORIGINAL S+ 75 % OF ORIGINAL S+ 90% OF ORIGINAL S+
FORM STIMULI USED IN GENERALISATION TASK 1

Generalisation task 1 was presented in blocks of 20 trials. Each block contained 8 trials of the original S+/S- pairings, along with 2 trials of each of the form and size transformations. The brightness and location of the stimuli on the monitor screens were randomly selected, so that the S+ and S- could vary in both brightness and location across trials. There were five possible variations in brightness and location that were the same as those used in the original two choice discrimination. In each block of trials animals had to attain a criterion of 6 correct responses out of the 8 trials containing the original S+/S- pairing, for the scores from that block to be counted. This criterion was introduced to ensure that animals generalisation performances were only counted in the blocks of trials in which the animals were performing reasonably well in the base discrimination. All animals performed up to 100 trials a day until they had successfully completed 10 blocks of 20 trials to criterion. The percentage of correct responses for the base discrimination and for each of the size and form transformed stimuli were then calculated. When animals had completed 10 blocks of generalisation task 1 they began training in the second generalisation task.

Generalisation task 2 introduced a different range of transformed stimuli, as the extreme form stimuli (90%) used in generalisation task 1 proved to be relatively difficult to distinguish from the S+ for both perirhinal and unoperated animals. In this task the new measurements of the transformations in form of the S- measured 55%, 65% and 75% of the width of the S+, the transformations in stimuli size remained the same.

These values were chosen after examination of animals' performances in generalisation task 1. Testing in generalisation task 2 was performed in exactly the same manner as that described for the first generalisation task, except animals completed 40 blocks of generalisation task 2. For both generalisation tasks the number of blocks rejected for failing to attain criterion on the original base discrimination were calculated for each animal. Performance in the generalisation tasks was assessed by calculating the overall percentage of correct responses for each stimulus in each task. All animals completed up to 100 trials a day, five days a week in all stages of behavioural testing.

5.2 v Histology

Chapter 2.4 describes the method of histological analysis used for all animals and the extent of the intended perirhinal lesions.

5.3 Results

5.3 i Histology

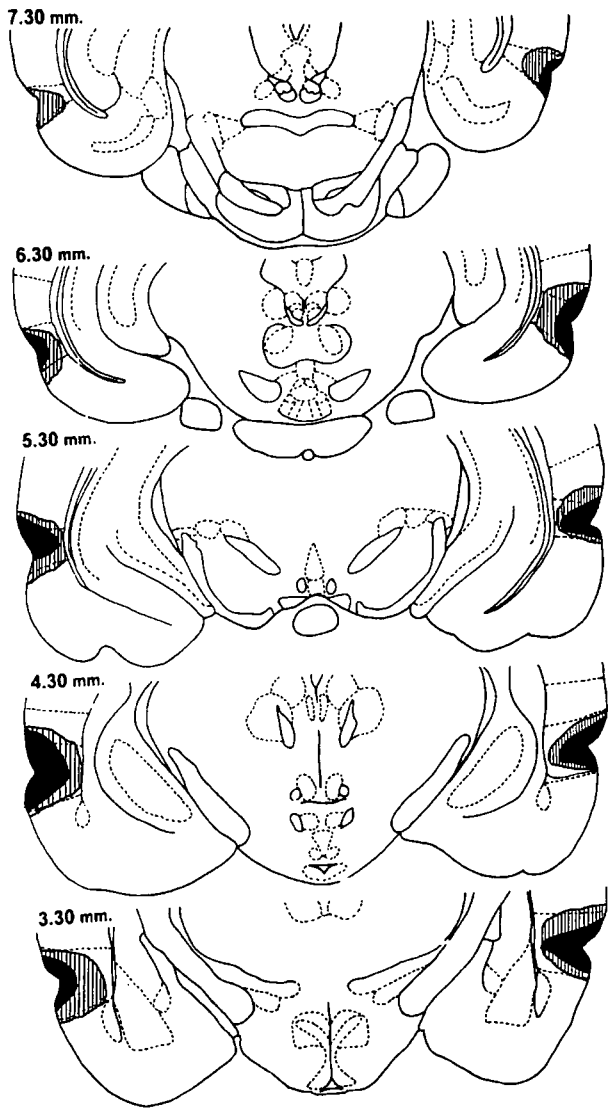
A detailed description of the methods of histological analysis and the extent of the intended perirhinal lesions are given in chapters 3.2 vi and 2.5. Histological analysis revealed that all lesions were essentially as intended, extending approximately 3mm to 7mm posterior to Bregma. The analysis of animal R019 was only approximate as a proportion of sections from this animal were damaged in the process of preparing the histology. As shown in table 5.1 the mean estimated extent of damage to the perirhinal cortex was 69.39%.

Table 5.1 Estimated damage to the perirhinal lesion as shown in percentage of overall area

	Perirhinal Lesion Size		
RAT	**Left Hemisphere**	**Right Hemisphere**	**Total**
	Animals that completed Expt. 3A & 3B		
R01	79%	82%	81%
R06	56%	55%	55.5%
R04	67%	66%	66.5%
R07	78%	75%	76.5%
R08	72%	75%	73.5%
R010	78%	76%	77%
R014	76%	74%	75%
MEAN	**72.2%**	**71.8%**	**72%**
	Animals that completed Expt. 3A		
R015	75%	75%	75%
R016	73%	72%	72.5%
R017	55%	55%	55%
R018	72%	70%	71%
R019	65%	65%	65%
R020	60%	60%	60%
R021	67%	68%	67.5%
MEAN	**67%**	**66.4%**	**67%**

There was some evidence of slight intrusion into the neighbouring entorhinal cortex and inferotemporal area TE. In all cases there was some intact tissue towards the extreme caudal extent of the lesion, thereby excluding the possibility of unintended damage to postrhinal cortex. Figure 5.3 shows representative sections from a relatively large (R01) and relatively small lesion (R06).

Figure 5.4. The extent of a relatively large (R01, vertical stripes) and relatively small (R06, black) perirhinal lesion drawn onto standard sections taken from Paxinos and Watson (1986).



5.3 ii Post-Operative Learning

Acquisition of the Two Choice Visual Discrimination

Acquisition of the two choice visual discrimination was compared between the perirhinal and unoperated animals. Two one way ANOVA'S found no statistically significant differences between the two groups in the

number of trials (F= <1) or errors (F= <1) accumulated in attaining criterion in the task, as shown in table 5.2.

Table 5.2. Unoperated and perirhinal lesioned animals acquisition of a two choice visual discrimination

Rat	Trials to Criterion	Errors to Criterion	Rat	Trials to Criterion	Errors to Criterion
	Unoperated Animals			**Perirhinal Animals**	
R01	1733	600	R015	1350	485
R02	1248	369	R016	1423	489
R03	1780	699	R017	1674	570
R04	1735	582	R018	1557	532
R05	1789	559	R019	2192	692
R06	1261	389	R020	1200	426
R07	1893	574	R021	1503	545
R08	941	291			
R09	1213	331			
R010	1550	505			
R011	1223	350			
R012	2132	634			
R013	1898	642			
R014	1614	549			
Mean	**1572.14**	**505.28**	**Mean**	**1557**	**535.14**

Acquisition of Generalisation Task 1

All animals attained criterion in 10 blocks of generalisation task 1. The percentage of correct responses for each of the form and size transformed stimuli are shown in table 5.3, along with the number of blocks rejected for failing to attain criterion in the base discrimination. Animals performances in each of the form and size transformed stimuli were compared separately without the base discrimination trials, so as to compare generalisation abilities and performance in the original discrimination separately. An independent samples t test found no significant differences between the perirhinal and sham animals performances in the base discrimination trials in 10 blocks of generalisation task 1 (t = < 1). This was expected as scores were taken

from the blocks of trials in which animals attained >75% correct in the base discrimination trials.

The numbers of blocks of trials rejected due to failing to attain criterion in the base discrimination were not significantly different between groups (t = <1). The perirhinal and unoperated animals rejected a mean of 28 and 24 blocks respectively.

Generalisation to Transformations in Stimuli Form

The percentage of correct responses for each of the stimuli that varied in form were compared between surgical groups in a 2 (Surgical Group) x 3 (Form Stimuli) ANOVA with 1 repeated measure. The main within subject effect of variation in stimuli form was statistically significant (df = 2, 38, F= 6.240, p=0.005), whereas the main between subject effect of surgery (F= < 1) and the interaction between form and surgery (F= <1) did not attain statistical significance. Therefore all animals displayed significantly different responses to the transformations in form of the S-. Figure 5.4 and table 5.3 show how both the perirhinal and unoperated animals correct responses generally decreased with increased transformation in form of the S-. However, the percentages of correct responses to transformations in form did not differ statistically between the perirhinal and unoperated animals, suggesting perirhinal ablation had no effect on generalisation performance.

Table 5.3 Unoperated and perirhinal animals' acquisition of 10 blocks of generalisation task 1

RAT	BASE STIMULI	FORM STIMULI 60%	75 %	90 %	SIZE STIMULI 50%	40%	30%	REJECT BLOCKS
				Unoperated Animals				
R01	92	55	70	50	70	70	60	30
R02	91	55	70	50	70	70	60	30
R03	91	70	55	60	60	60	80	8
R04	92	80	55	65	65	80	70	25
R05	89	70	60	40	75	60	50	20
R06	91	55	50	45	45	65	65	14
R07	91	70	30	65	60	70	70	47
R08	91	75	55	45	80	65	80	14
R09	89	65	35	45	65	55	80	20
R010	90	60	65	80	80	65	75	45
R011	89	70	70	30	60	50	50	29
R012	91	55	70	25	65	80	75	11
R013	92	45	50	55	85	45	60	23
R014	91	70	65	60	80	90	80	26
Mean	**90.71**	**63.92**	**57.14**	**51.07**	**68.57**	**66.07**	**68.21**	**24**
				Perirhinal Animals				
R015	91	65	65	50	85	60	65	10
R016	94	50	65	35	75	65	50	41
R017	90	60	55	55	70	45	60	32
R018	89	65	55	45	65	60	60	19
R019	89	45	60	45	70	55	35	38
R020	89	55	65	60	80	65	55	25
R021	91	70	60	25	85	50	65	31
Mean	**90.42**	**58.57**	**60.71**	**45**	**75.71**	**57.14**	**55.71**	**28**

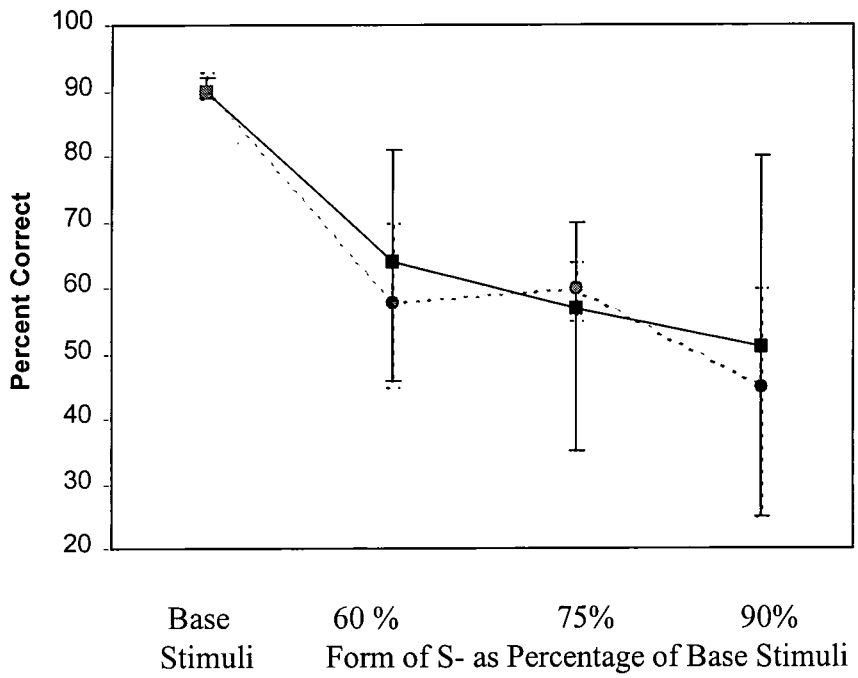


Figure 5.4. The mean percentage of correct responses in the base discrimination and each transformation in form of the S- in 10 blocks of generalisation task one for both the perirhinal (broken lines & dots) and unoperated animals (squares). The error bars show the range of scores.

Generalisation to Transformations in Stimuli Size

The percentage of correct responses for each of the stimuli that varied in size were compared between surgical groups in a 2 (Surgical Group) x 3 (Size Stimuli) ANOVA with 1 repeated measure. The main between subject effect of surgery was not significant ($df = 1, 19$, $F=2.175$, $p = 0.157$), whereas the main within subject effect of transformation in size ($df = 2, 38$, $F=7.106$, $p = 0.002$) and the interaction between surgery and size ($df = 2, 38$, $F= 5.434$, $p = 0.008$) were statistically significant.

A post hoc comparison of the groups performance for each transformation in size of the S- found performances in the smallest sized stimuli, 30%, and 40% were significantly different between groups (Newman Keuls, alpha = 0.05, r = 2, df = 19, Wr = 7.77; 30%: 13 > 7.77; 40%: 9> 7.77;). Performances in the largest sized stimuli 50% (7 < 7.77) were not significantly different between groups. The differences between the perirhinal and unoperated animals generalisation gradients for the transformations in stimulus size are shown in Figure 5.5. Transformations in stimuli size affected performance of all animals. However, the perirhinal animals typically demonstrated a sharper generalisation gradient, as their performance typically worsened with decreases in the stimulus size.

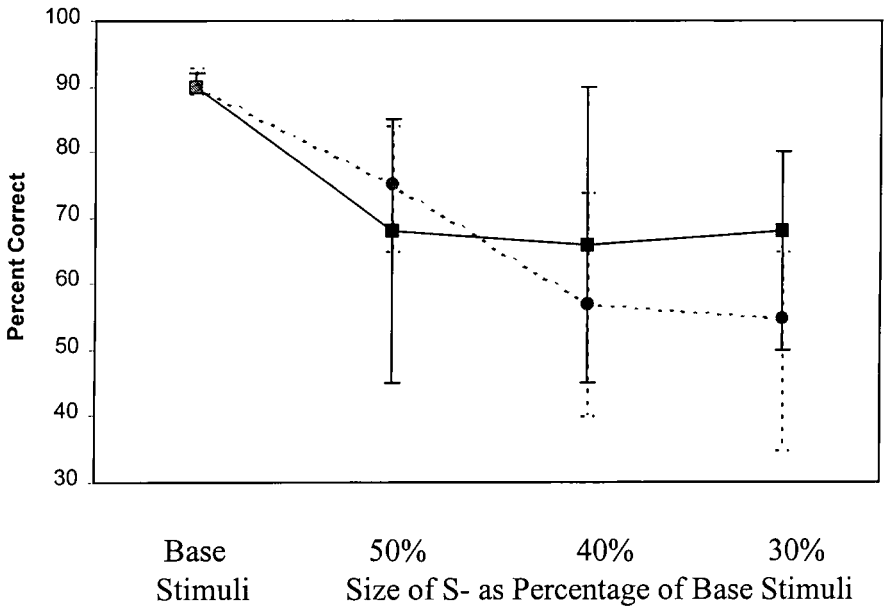


Figure 5.5. The mean percentage of correct responses for the base discrimination and each transformation in stimuli size in 10 blocks of generalisation task one for both the perirhinal (broken lines & dots) and unoperated animals (squares). The error bars show the range of scores.

Acquisition of Generalisation Task 2

The percentages of correct responses for the perirhinal and unoperated animals for all stimuli in 40 blocks of generalisation task 2 are shown in table 5.4. An independent samples t test found no significant differences between the perirhinal and sham animals' performances in the base discrimination trials in 40 blocks of generalisation task 2 ($t = <1$). The numbers of blocks of trials rejected due to failing to attain criterion in the base discrimination were significantly different between groups in an independent samples t test ($df = 19$, $t = 2.890$, $p = 0.009$). These findings suggest that the perirhinal animals' performance in the base discrimination trials was impaired, as they rejected a mean of 28 blocks each, compared to 17 for the unoperated animals.

Table 5.4. Unoperated and perirhinal animals acquisition of 40 blocks of generalisation task 2

RAT	BASE STIMULI	FORM STIMULI 55%	65%	75%	SIZE STIMULI 50%	40%	30%	REJECT BLOCKS
				Unoperated Animals				
R01	85	58	57	57	59	67	69	21
R02	91	68	63	52	85	65	72	7
R03	81	64	52	64	64	69	60	29
R04	84	61	65	59	69	77	58	16
R05	88	71	74	59	77	64	69	12
R06	87	72	45	50	68	58	60	15
R07	81	71	50	53	69	61	58	18
R08	85	68	64	57	76	76	73	6
R09	84	61	61	57	73	69	67	32
R010	85	64	49	61	65	74	57	14
R011	82	63	65	54	73	65	64	16
R012	87	72	58	60	75	65	62	7
R013	84	63	67	55	68	76	67	23
R014	85	74	60	52	69	57	60	19
Mean	**85.9**	**66.5**	**59.28**	**56.42**	**70.71**	**67.35**	**64**	**17**
				Perirhinal Animals				
R015	82	58	59	61	61	68	60	43
R016	85	71	65	67	76	63	59	18
R017	85	68	58	57	83	71	63	27
R018	83	67	59	59	80	60	65	36
R019	84	61	68	52	73	68	63	17
R020	87	63	63	55	68	65	50	28
R021	85	58	61	61	73	67	70	26
Mean	**84.4**	**63.7**	**61.85**	**58.85**	**73.42**	**66**	**61.42**	**28**

Generalisation to Transformations in Stimuli Form

The percentage of correct responses for each of the stimuli that varied in form were compared between surgical groups in a 2 (Surgical Group) x 3 (Form Stimuli) ANOVA with 1 repeated measure. The main within subject effect of variation in stimuli form was significant ($df = 2, 38$, $F=8.00$, $p = < 0.001$), whereas the effect of surgery ($F= < 1$) and the interaction between variation in form and surgery ($F= 1.29$) did not attain statistical significance. Therefore the perirhinal and sham animals

demonstrate remarkably similar generalisation gradients, as shown in Figure 5.6.

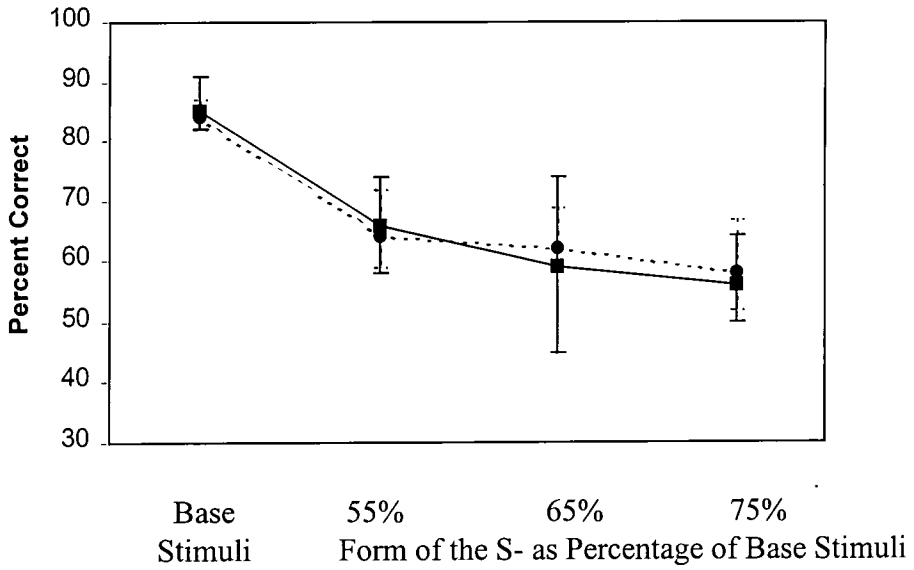


Figure 5.6. The mean percentage of correct responses in the base discrimination and each transformation in stimuli form in 40 blocks of generalisation task two for both the perirhinal (broken lines & dots) and unoperated animals (squares). The error bars show the range of scores.

Generalisation to Transformations in Stimuli Size

The overall percentages of correct responses for each of the transformations in stimuli size were compared between surgical groups in a 2 (Surgical Group) x 3 (Size Stimuli) ANOVA with 1 repeated measure. The main within subject effect of variation in stimulus size was significant ($df = 2, 38$, $F=13.386$, $p = <0.01$), whereas the effect of surgery ($F= < 1$) and the interaction between surgery and size ($F=1.163$) did not attain statistical significance. Figure 5.7 shows the generalisation gradients for the perirhinal and sham animals. Therefore, perirhinal ablation did not have a significant effect on the ability to generalise to transformations in stimuli size in 40 blocks of generalisation task 2.

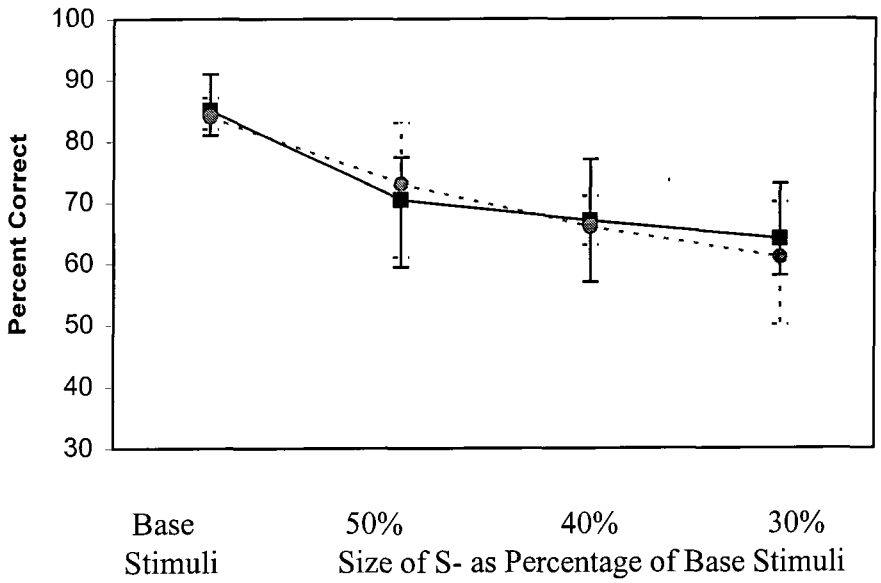


Figure 5.7. The mean percentages of correct responses for the base discrimination and each transformation in stimuli size in 40 blocks of generalisation task two for both the perirhinal (broken lines & dots) and unoperated animals (squares). The error bars show the range of scores.

5.4 Discussion

The present study examined the behavioural effects of perirhinal ablation on generalisation of a simple two choice visual discrimination task in the rat. No significant differences were found between perirhinal and unoperated animals acquisition of the two choice visual discrimination task. In generalisation task 1 there were no significant differences between the perirhinal and unoperated animals' generalisation gradients for the form transformed stimuli. However there was a significant difference between the groups' performances in the size transformed stimuli. The perirhinal animals made more incorrect responses when the stimuli were reduced in size. No significant differences were found in the number of blocks of trials rejected by the two groups due to failing to attain criterion in the base discrimination.

In generalisation task 2 there were no significant differences between the perirhinal and unoperated animals generalisation gradients for either the form or size transformed stimuli. However, the numbers of blocks of trials rejected for failing to attain criterion on the base discrimination were significantly different between the two groups of animals, with the perirhinal animals rejecting a higher number of blocks. The results of generalisation tasks 1 and 2 were not expected. It was anticipated that perirhinal ablation would lead to impairments in the ability to generalise to transformations in stimuli form, leaving generalisations to transformations in stimuli size and performance in the base discrimination intact.

These findings suggest that perirhinal ablation in the rat does not have any effect on the ability to detect changes in stimulus form in a visual generalisation task. However, a deficit in performance in the task is evident as perirhinal animals perform less well in the base discrimination trials in generalisation task 2. Furthermore, the perirhinal animals' generalisation gradient for the size transformed stimuli in generalisation task 1 suggests an impairment in visual discrimination learning when the stimuli are reduced in size. However, this deficit was not enduring as performance in the size-transformed stimuli in generalisation task 2 was the same as that of the unoperated animals, suggesting the perirhinal animals learnt to compensate for initial discrimination difficulties. It is possible the perirhinal animals in this study relied on different visual cues

to perform the base discrimination, that were less reliable when the stimuli were reduced in size, resulting in the initial impairments seen.

In generalisation task 2 the perirhinal animals had a significantly higher number of blocks of trials rejected for failing to attain criterion in the base discrimination. The number of blocks of trials rejected in the first generalisation task was slightly higher for the perirhinal animals, but this difference was not significant. It is possible that the different range of stimuli used in generalisation task 2 made the base discrimination more difficult to perform than in the first generalisation task. Deficits in the relatively simple two choice base discrimination may be due to the increased demands placed on identification of the stimuli when presented in the generalisation task. This finding is supported by reports of impaired acquisition of concurrent visual discrimination learning in the primate when increased demands are made on visual object recognition (Buckley & Gaffan, 1997, 1998a,b).

In the current study the perirhinal animals demonstrated a deficit in performing the base discrimination trials when presented in generalisation task 2. This finding is inconsistent with reports that following perirhinal ablation visual discrimination learning remains intact when increased demands are made on the processes of object identification (Experiment 2, described in Chapter 4, Machin & Eacott, in press). It is possible that experiment 2 failed to reveal a deficit in new learning as the stimuli used were akin to junk scenes, rather than single visual objects, as used in the

current study. However, the discriminations of the simple forms used in the present study were expected to be impaired by perirhinal lesions.

The perirhinal animals acquired the base discrimination normally, yet were impaired in performing the base discrimination trials presented in the second generalisation task. This finding is reminiscent of reports of intact post-operative acquisition of a two choice visual discrimination task, but poor retention of the discrimination over a 15 day period following perirhinal ablation in the rat (Wiig, Cooper & Bear, 1996). It is possible that the perirhinal animals retention of the two choice discrimination was impaired in generalisation task 2, as they began training in this task approximately 2 weeks after attaining criterion in the base discrimination. Alternatively, the perirhinal animals may have used different cues or behavioural strategies to solve the base discrimination that did not transfer well to the generalisation task.

The normal generalisation gradients demonstrated by the perirhinal animals in both visual generalisation tasks suggest intact visual object discrimination abilities. However, as the perirhinal animals rejected a higher number of blocks of trials in the second generalisation task, they also completed more trials in the task overall. Therefore, the normal generalisation gradients of the perirhinal animals may reflect the extra experience they accumulated with the stimuli in this task. It is possible that in the blocks of trials rejected for failing to attain criterion in the base discrimination the perirhinal animals' generalisation abilities were also impaired. Experiment 4, described in chapter 6 addresses this issue by

comparing perirhinal animals performance in a titrating version of the generalisation task that did not contain fixed presentations of the base discrimination.

It has been suggested that the perirhinal cortex sustains visual object recognition by a process of perceptual learning, facilitating fine form discrimination amongst stimulus items within a global form or category (Sakai, Naya & Miyashita, 1994; Sakai & Miyashita, 1991 & 1994). The results of the current study suggest that perceptual learning necessary for the initial acquisition of a simple visual discrimination and generalisation to it are not reliant upon processes within the perirhinal cortex in the rat. Electrophysiological recording studies in the primate have found populations of stimulus selective cells capable of perceptual learning throughout the anterior inferiortemporal cortex, suggesting that anterior portions of area TE may sustain perceptual learning following lesions to the perirhinal cortex (Eacott & Heywood, 1995; Tanaka, 1993; Sakai, Naya & Miyashita, 1994). However, although the perirhinal animals in the current study acquired the base discrimination task normally, they were impaired in performing the base discrimination when it was presented in the second generalisation task. Therefore, the consolidation of relatively simple visual perceptual learning or identification of familiar stimuli when increased demands are made on identification may depend upon the perirhinal cortex.

In summary, the perirhinal animals generalised normally to transformations in the form and size of familiar visual stimuli, yet

demonstrated an initial impairment in generalising to transformations in stimuli size in generalisation to task 1 and made significantly more errors in the base discrimination trials in generalisation task 2. These results suggest that the ability to form reliable or enduring representations of visual objects may be impaired following perirhinal ablation. However, in the blocks of trials in which the perirhinal animals perform over 75% correct in the base discrimination the ability to generalise to the discrimination remains intact.

5.5 Introduction to Experiment 3b

The results of experiments 1 and 2, described in chapters 3 and 4, suggest that perirhinal ablation impairs retention of visual associative information acquired prior to surgery, whereas post-operative learning remained intact. Therefore it is possible that perirhinal ablation affects retention and acquisition of visual associative learning differently. The previous study, experiment 3a, measured the effects of perirhinal ablation on post-operative acquisition of a visual discrimination task and generalisation to this discrimination. It was found that perirhinal ablation resulted in a moderate deficit in the ability to recognise familiar visual stimuli in the task, whereas generalisation abilities remained intact. If perirhinal ablation affects retention and acquisition of visual discrimination learning differently, it is possible that generalisation to visual stimuli learnt prior to surgery will be more severely impaired following perirhinal ablation. Therefore, the aim of experiment 3b was to

evaluate the effects of perirhinal ablation on generalisation of a visual discrimination task learnt prior to surgery.

It has been suggested that cells within perirhinal cortex sustain visual object recognition by modifying their response properties upon repeat presentation of visual stimuli (Primates: Sakai & Miyashita, 1991; Sakai, Naya & Miyashita, 1994; Rodents: Zhu, Brown & Aggleton, 1995). This proposed perceptual learning process enables cells to finely tune their response properties to familiar stimuli (Eacott & Heywood, 1995). Therefore, post-operative retrieval deficits in visual associative learning following perirhinal ablation (Primates: Thornton, Rothblat & Murray, 1997; Rodents: Eacott, 1998), may be due to the loss of fine-tuning to the stimuli used in the learning tasks. If access to perceptual information regarding visual stimuli is dependent upon cells in perirhinal cortex, a deficit in generalisation performance would be expected following perirhinal ablation.

All animals in experiment 3b completed 40 blocks of generalisation task 2 (as part of previously reported experiment 3a) prior to bilateral perirhinal ablation or sham surgery and their post-operative performances in the task compared. In addition, prior to surgery the perirhinal and sham animals head scanning behaviours were observed, to determine whether animals perform the generalisation task by comparing the cues available in the stimuli presented, or by matching only one stimulus to an internal representation. Animals' head scanning behaviour may influence the level of learning regarding the stimuli in the

discrimination, which may influence post-operative performance in the task.

5.6 Method

5.6 i Subjects

The fourteen unoperated animals that had successfully completed experiment 3a were used in this study. Two animals (R02 & R012) died from respiratory infections in the days following surgery, so that five sham operated and seven perirhinal lesioned animals completed the study. A detailed description of the subjects used is provided in chapter 2.1.

5.6 ii Apparatus

The apparatus used in this study was a computer operated Y - maze, as described in chapter 2.2.

5.6 iii Pre-Operative Behavioural Training

All animals had attained criterion in the base discrimination, 10 blocks of generalisation task 1 and 40 blocks of generalisation task 2, as described in experiment 3a. All animals were pseudorandomly assigned to two groups for surgery, either sham surgery or bilateral perirhinal ablation. Animals' pre-operative head scanning behaviour was measured by recording animals head movements in their last 120 trials prior to surgery. Animals' head scanning behaviour was divided into the following 3 categories, no comparison between the S+ and S- before stimulus approach (0), one comparison between the S+ and S- prior to approach (1), and more than one comparison made prior to stimulus approach (2). The numbers of responses made within each behavioural category were calculated and

animals assigned to the head-scanning group in which they had amassed the highest number of responses.

5.6 v Surgery

Surgery was performed on all animals, either bilateral perirhinal ablation by aspiration or sham control surgery. A detailed description of surgical methods is given in chapter 2.4.

5.6 vi Post-Operative Behavioural Training

All animals had a two-week rest period following surgery before post-operative testing began. Post-operative training assessed animals performance in 40 blocks of generalisation task 2 that had been learnt prior to surgery. A detailed description of the generalisation task is given in chapter 5.2 iv. The overall percentage of correct responses for each stimulus used in the generalisation task were then calculated for each animal. The numbers of blocks of trials rejected for failing to attain criterion in the base discrimination were recorded.

5.6 vii Histology

The methods of histological analysis are described in chapter 2.5,

5.7 Results

5.7. i Histology

The results of the histological analysis of the animals used in the current study are provided in chapter 5.3 i.

5.7 ii Behavioural

Animals' pre and post-operative performances in 40 blocks of generalisation task 2 were compared between surgical groups and head scanning groups.

Pre-Operative Performances in Generalisation Task 2

Pre-operative performances in 40 blocks of generalisation task 2 were compared between the perirhinal and sham animals to determine whether there were any differences between the two groups. A series of independent samples t tests found performances in the base discrimination trials ($t = <1$) and the number of blocks of trials rejected for failing to attain criterion in the base discrimination ($t = 1.785$) were not significantly different between groups.

Pre-operative generalisation performances in the form and size transformed stimuli were compared between groups in a 2 (Surgical Group) x 3 (Stimulus Form) ANOVA with 1 repeated measure. Variation in stimulus form had a statistically significant effect on performance ($F = 6.162$, $df = 2, 20$, $p = 0.008$), whereas surgical group ($F = 2.121$) and the interaction between surgical group and stimulus form ($F = 2.082$) did not attain statistical significance.

Pre-operative generalisation performances in the size transformed stimuli were compared between groups in a 2 (Surgical Group) x 3 (Stimulus Size) ANOVA with 1 repeated measure. The effect of stimulus size was approaching statistical significance ($F = 3.238$, $df = 2, 20$, $p = 0.060$), whereas surgical group ($F = 1.295$) and the interaction between

surgical group and stimulus size (F = 2.963) did not attain statistical significance. Therefore, the perirhinal and sham animals' pre-operative performances were not significantly different.

Post-Operative Performances in Generalisation Task 2

Table 5.5 and Figure 5.8 show perirhinal and sham animals' pre and post-operative percent correct scores in the base and form stimuli.

Table 5.5. Pre- and post-operative percent correct scores in generalisation task 2 and animals head scanning groups

	Pre-Operative Scores				Post-Operative Scores				
				FORM	STIMULI				Head scan
RAT	**Base**	**55**	**65**	**75**	**Base**	**55**	**65**	**75**	**Group**
				Sham Animals					
R03	81	64	52	64	86	68	65	60	0
R05	88	71	74	59	88	73	59	55	0
R09	84	61	61	57	90	71	73	55	1
R011	82	63	65	54	87	68	60	61	1
R013	84	63	67	55	86	68	69	61	0
Mean	**83.8**	**64.4**	**63.8**	**57.8**	**87**	**69.6**	**65.2**	**58.4**	
				Perirhinal Animals					
R01	85	58	57	57	86	68	65	60	0
R04	84	61	65	59	89	74	55	63	0
R06	87	72	45	50	83	68	55	65	1
R07	81	71	50	53	83	64	57	60	0
R08	85	68	64	57	93	74	58	54	1
R010	85	64	49	61	91	65	54	58	1
R014	85	74	60	52	90	81	65	63	1
Mean	**84.57**	**66.85**	**55.7**	**55.57**	**87.85**	**70.57**	**58.4**	**60.4**	

Animals' performances in each of the form and size transformed stimuli were compared separately without the base discrimination trials, so as to compare generalisation abilities and performance in the base discrimination separately. Post-operative performances in the base discrimination (t = <1) and the number of blocks of trials rejected for

failing to attain criterion in the base discrimination trials (t = <1) were not significantly different between groups.

Generalisation to Transformations in Stimuli Form

The percentage of correct responses for each of the variations in stimulus form were compared between perirhinal and sham operated animals in a 2 (Surgical Group) x 3 (Stimuli Form) ANOVA with 1 repeated measure. The effect of group was not statistically significant (F =<1). However, the effect of stimulus form (F = 19.103, df = 2, 20, p = <0.01) and the interaction between form and group (F = 3.517, df = 2, 20, p = 0.049) were statistically significant. Therefore, the perirhinal and sham animals' generalisation gradients were significantly different. A post hoc comparison of performances in each transformation in form of the S- found performances in the 65% stimulus were significantly different between groups (Newman Keuls, alpha = 0.05, r = 2, df = 20, Wr = 2.95; 55% stimulus, 0.82 = < 2.95; 65% stimulus, 5.7 = > 2.95; 75% stimulus, 1.68 = < 2.95). Figure 5.8 shows how the sham animals' error rate generally increases with increasing transformation of the S-, with most errors being made in the 75% stimulus. However, the perirhinal animals' error rates in the 65% and 75% stimuli are very similar, with the highest number of errors being made in the 65% stimulus.

One possible explanation of a difference at the 75% transform that disappears at 65% and 55% is a floor effect. To examine this all animals' percent correct scores for the 65% and 75% stimuli were compared to 50 % in a series of Bonferroni post hoc tests to determine

whether the animals perform above chance levels with these stimuli. Both the perirhinal (75%: t' (6) = 3.71, p = <0.05; 65%: t' (6) = 2.45, p = <0.05) and the sham (75% :t' (4) = 2.57, p= <0.05: 65%: t' (4) = 2.57, p = <0.05) animals' performances with the two transformations were significantly above chance. These results suggest that animals generalise to the 65 % and 75% stimuli on the basis of their existing knowledge regarding the stimuli in the task and not merely performing at chance.

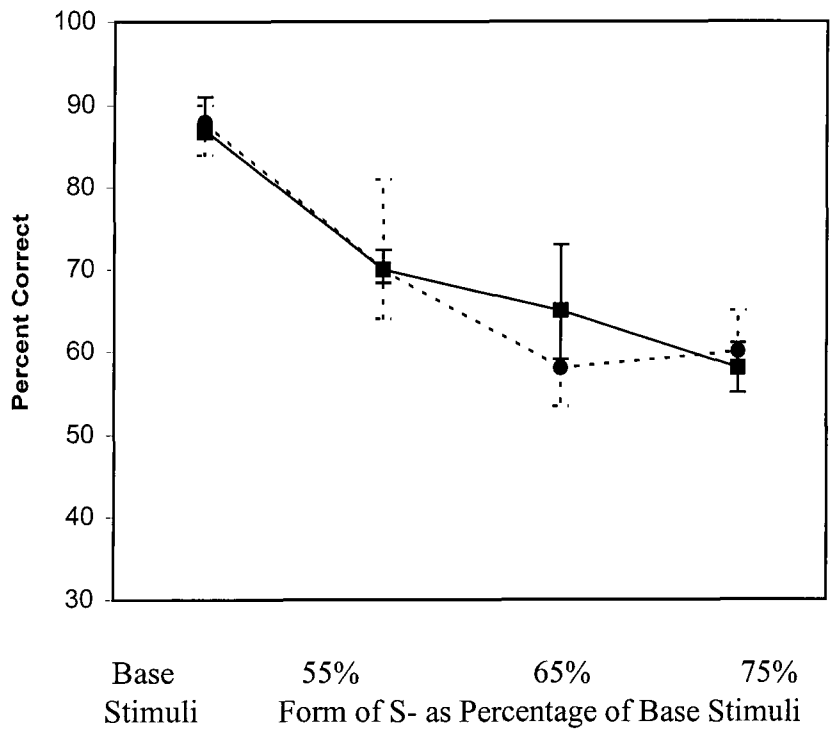


Figure 5.8. Mean post-operative (Perirhinal: broken lines and dots; Sham: squares) scores in the base and form stimuli in generalisation task 2.

Generalisation to Transformations in Stimuli Size

Table 5.6 and Figure 5.9 show perirhinal and sham animals' pre and post-operative percent correct responses for the base and different size stimuli. The generalisation to variations in stimuli size were compared

between perirhinal and sham operated animals in a 2 (Surgical Group) x 3 (Stimuli Size) ANOVA with 1 repeated measure. Stimuli size had a significant effect on generalisation performance ($F = 11.779$, $df = 2, 20$, $p = 0.00$), whereas the effect of group ($F = <1$) and the interaction between form and group ($F = 1.076$) did not attain statistical significance. Therefore, perirhinal ablation did not affect animals' generalisations to transformations in stimuli size.

Table 5.6. Pre and post-operative performances in size transformed stimuli in generalisation task 2

	PRE-OPERATIVE SCORES					POST-OPERATIVE SCORES				
RAT	**Base Stimuli**	**50**	**40**	**30**	**Reject Blocks**	**Base Stimuli**	**50**	**40**	**30**	**Reject Blocks**
					Sham Animals					
R03	81	64	69	60	29	86	75	73	68	5
R05	88	77	64	69	12	88	87	68	64	6
R09	84	73	69	67	32	90	70	77	67	8
R011	82	73	65	64	16	87	73	75	74	12
R013	84	68	76	67	23	86	76	73	57	5
Mean	**83.8**	**71**	**68.6**	**65.4**	**22**	**87.4**	**76.2**	**73.2**	**66**	**7**
					Perirhinal Animals					
R01	85	59	67	69	21	86	75	50	63	12
R04	84	69	77	58	16	89	74	71	61	7
R06	87	68	58	60	15	83	74	65	52	19
R07	81	69	61	58	18	83	76	67	61	8
R08	85	76	76	73	6	93	88	82	83	0
R010	85	65	74	57	14	91	81	61	65	9
R014	85	69	57	60	19	90	82	81	64	0
Mean	**84**	**67**	**67**	**62.1**	**15**	**87.8**	**78.6**	**68**	**64**	**8**

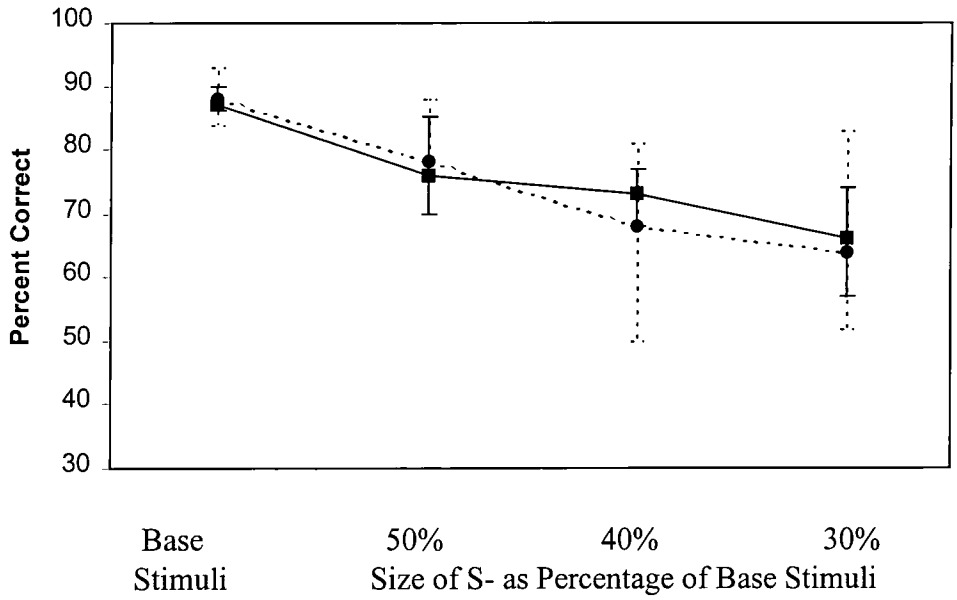


Figure 5.9. Mean post-operative (Perirhinal: broken lines and dots; Sham:squares) scores in the base and size transformed stimuli. The error bars show the range of scores.

Head Scanning Behaviour

To assess the effects of different strategies in this task animals' post-operative performances in generalisation task 2 were compared according to their pre-operative head scanning behaviour. Table 5.5 shows each animal's head scanning categorisation. A series of independent samples t tests found percent correct scores in the base discrimination trials (t = 1.600) and the number of blocks of trials rejected for failing to attain criterion in the base discrimination (t = <1) were not significantly different between head scanning groups.

All animals' generalisations to the variations in stimulus form were compared between head scanning groups in a 2 (Head Scan Group) x 3 (Stimuli Form) ANOVA with 1 repeated measure. The effect of stimulus form was significant (F = 15.447, df = 2, 20, p = <0.001),

whereas the effect of head scanning group (F = <1) and the interaction between form and head scanning group (F = <1) were not statistically significant. Generalisations to variations in stimulus size were compared between groups in a 2 (Head Scan Group) x 3 (Stimuli Size) ANOVA with 1 repeated measure. The effect of stimulus size was significant (F = 12.423, df = 2, 20, p = <0.001) whereas the effect of group (F = 1.688) and the interaction between size and group (F = <1) were not.

These findings suggest that head scanning group did not have a significant effect on overall performance in the task. However, head scanning behaviour may have affected the perirhinal and sham animals' performances differently. Therefore the effect of head scanning behaviour on performance was assessed separately for the perirhinal and sham animals. Head scanning behaviour did not have a significant effect on performance in the base discrimination (t = 1.101) or number of blocks of trials rejected (t = <1) for the sham animals.

The perirhinal animals post-operative performances in the base discrimination trials were not significantly different between head scanning groups (t = 1.299). However, the number of blocks of trials rejected by for failing to attain criterion in the base discrimination was significantly different between head scanning groups for the perirhinal animals (two tailed test: t = 3.008, df = 3, p = 0.057).. The perirhinal animals that scanned the available stimuli before approach rejected a mean of 10 blocks of 20 trials, compared to a mean of 5 blocks rejected by the animals that made an approach after viewing one stimulus. Therefore

animals that learnt the base discrimination by comparing the S- and S+ prior to surgery, made more errors in the discrimination following perirhinal ablation. This difference between perirhinal head scanning groups is not due to pre-operative differences in performance, as prior to surgery the mean number of blocks of trials rejected by the perirhinal animals' that scanned was 13, compared to a mean of 18 rejected by animals that did not scan. This pre-operative difference is not statistically significant ($t = 1.403$).

The effects of head scanning behaviour on generalisations to stimulus form and size were measured for the perirhinal and sham animals separately in a series of 2 (Head Scan Group) x 3 (Stimuli) ANOVA'S with 1 repeated measure. For the perirhinal animals head scanning behaviour did not have a significant effect on generalisations to variations in stimulus form ($F = <1$) or size ($F = 1.489$). As before, the effects of variations in form ($F = 13.910$, $df = 2, 10$, $p = <0.001$) and size ($F= 9.180$, $df = 2, 10$, $p = 0.005$) were significant, whereas the interactions between head scanning group and stimulus form ($F = <1$) and head scanning group and stimulus size ($F = <1$) were not.

For the sham animals head scanning behaviour did not have a significant effect on generalisations to variations in stimulus form ($F = <1$) or size ($F = <1$). The effects of variations in form ($F = 5.982$, $df = 2, 6$, $p = 0.038$) and size ($F= 3.858$, $df = 2, 6$, $p = 0.084$) were significant, whereas the interactions between head scanning group and form stimuli ($F = <1$) and head scanning group and size stimuli ($F = 3$) were not.

Therefore, head scanning group did not have a significant effect on animals generalisation performances overall. However, scanning stimuli prior to approach appears to have a detrimental affect on perirhinal animals' post-operative performances in the base discrimination trials in the generalisation task.

5.8 Discussion

The present study examined the effects of perirhinal ablation on post-operative performance in a visual generalisation task, which measured generalisations to a two choice visual discrimination learnt prior to surgery. The perirhinal animals' post-operative performances in the base discrimination trials in the generalisation task were normal. Perirhinal ablation had no effect on animals' generalisations to the S-'s that varied in size. However, generalisations to each the variations in stimulus form were significantly different to the sham animals. The error rates of the sham animals systematically increased with increasing transformation of the S-, so that they made the highest number of errors in the 75% stimulus. However, the error rates for the perirhinal animals were very similar for the 65% and 75% stimuli, with the highest number of errors being made in the 65% stimulus. Therefore, the perirhinal animals ability to discriminate the 65% stimulus from the S+ was impaired relative to the sham animals.

Prior to surgery the head movements of the animals performing the task were measured to determine whether differences in head scanning behaviour had an effect on post-operative performances in the task. Head scanning behaviour had no effect on either the perirhinal or sham animals

post-operative generalisation gradients. However, the perirhinal animals that pre-operatively scanned the S- and S+ prior to approach made significantly more errors in the base discrimination in post-operative testing. These findings suggest that perirhinal ablation disrupts the performance in the task more severely, if prior to surgery, the discrimination was learnt by relying on comparison of the stimuli presented. However, this view is counter to our hypothesis that the perirhinal cortex contributes to visual discrimination learning by constructing internal representations of visual stimuli. It has been suggested that internal representations are distributed throughout areas in inferotemporal cortex (Murray & Bussey, 1999). It is possible that the perirhinal animals that scanned the stimuli relied on the comparison of cues in the stimuli, following perirhinal ablation these cues may have become less apparent, resulting in their poorer performance rates. Therefore, more robust internal representations may be accessible from other areas following perirhinal ablation. Head scanning behaviour may reflect difficulties in learning the discrimination. However, head scanning behaviour had no effect on pre-operative performances or post-operative performances for the sham animals'. Whilst head scanning behaviours may not reflect changes in behavioural strategy or the formation of internal visual representations, animals' may develop different strategies, of varying efficiency, to perform complex learning tasks.

The perirhinal animals in this study performed the base discrimination that they had learnt approximately 12 weeks prior to

surgery at the same rate as the sham operated animals. This finding is consistent with reports of intact retention of two choice visual discrimination tasks following perirhinal (Wiig, Cooper, Bear, 1996) and rhinal (Kornecook et al., 1997) ablation in the rat. The previous studies found retention of two choice visual discriminations learnt 6-8 weeks (Wiig, Cooper, Bear, 1996) or 56, 37 and 16 days (Kornecook et al., 1997) prior to surgery remained intact, unlike retention of items learnt closer to surgery. Therefore, it is possible that the perirhinal cortex is not necessary for retention of simple visual discrimination learning that is acquired a relatively long time prior to surgery.

However, if visual generalisation abilities are dependent upon pre-operative knowledge regarding the base discrimination stimuli and limited experience of the transformed stimuli in the generalisation task, then the impairments in visual generalisation following perirhinal ablation in the current study suggest retention of the base discrimination may be impaired. This view is consistent with the results of experiment 1, described in chapter 3, that deficits in retention of visual associative learning following perirhinal ablation are not temporally graded.

It has been suggested that cells within perirhinal cortex in the primate sustain object recognition by a perceptual learning process that enables cells to finely tune their response properties to familiar stimuli (Eacott & Heywood, 1995; Sakai, Naya & Miyashita, 1994; Sakai & Miyashita, 1991). It is possible that post-operative retention deficits in visual associative learning following perirhinal ablation (Primates:

Thornton, Rothblat & Murray, 1997; Rodents: Eacott, 1998) are due to the loss of fine-tuning to the stimuli used in the learning tasks. In the current study the perirhinal animals were impaired in generalising to transformations in the form of the S- from the original base discrimination. These findings suggest an impairment in perceptual learning if generalisation performance is reliant upon knowledge regarding the base stimuli and the transformed stimuli in the task.

It should be noted that the deficit in generalisation abilities following perirhinal ablation was not severe and the overall effect of perirhinal ablation was not significant. It is possible that more robust impairments are evident following perirhinal ablation if the visual stimuli used are more complex, thereby increasing demands on object recognition within the perirhinal cortex.

In summary, generalisations to transformations in stimuli size of a simple two choice visual discrimination acquired prior to surgery remain intact following perirhinal ablation in the rat. However, generalisations to transformations in stimuli form were impaired following perirhinal ablation.

5.9 General Discussion

The results of the current study suggest that the perceptual processes of object identification are mildly impaired following perirhinal ablation in the rat. In experiment 3a perirhinal animals' acquisition of the

base discrimination and generalisation gradients were normal, however, identification of the base discrimination was impaired in the second generalisation task. In experiment 3b the ability of the perirhinal animals to generalise to variations in stimuli form were impaired in a post-operative test of generalisation. These findings suggest pre and post training lesions to the perirhinal cortex have different affects on visual generalisation performances.

Experiments 1 and 2, described in chapters 3 and 4, found impaired retention, but intact acquisition of concurrent visual discrimination learning following perirhinal ablation. The findings of experiment 3b suggest that the perirhinal cortex may contribute to the retention of visual perceptual learning. These findings are consistent with reports of impaired retention of concurrent visual discrimination learning in experiment 1, described in chapter 3.

However, in contrast to the findings of experiment 2, experiment 3a found pretraining lesions to the perirhinal cortex impaired performance in the base discrimination trials presented in the second generalisation task. These inconsistencies in results may reflect differences in the stimuli used in the two experiments. The results of experiment 3a suggest that, following perirhinal ablation, less enduring or specific representations of the base discrimination may be formed; resulting in poor recognition of these stimuli when presented in the generalisation task.

Although experiments 3a and 3b found deficits in both acquisition and retention, both deficits were not severe. It is possible that

generalisation to the base discrimination was aided by the repeat presentation of a fixed number of transformed stimuli. It has been suggested that the perirhinal cortex plays a general role in visual object recognition by providing a complete representation of complex visual stimuli (Eacott & Heywood, 1996; Murray & Bussey, 1999). Therefore, lesions to the perirhinal cortex may only disrupt visual object recognition when the stimuli are complex or made up of a large number of overlapping features (Murray & Bussey, 1999). Consequently, the ability to recognise relatively simple visual stimuli remains intact following perirhinal ablation as these processes can be sustained by inferotemporal area TE. One possible explanation of the results of experiment 3a is that the task we used did not tax the object recognition functions of the perirhinal cortex in the rat to reveal a deficit in visual generalisation abilities. The level of object recognition needed to discriminate between the stimuli used in experiment 3a may have been performed by cells in area TE, as the stimuli were relatively simple and did not contain complex configurations of elemental features. However, this view does not account for the deficits in performing the base discrimination in experiment 3a, or the retention deficits in experiment 3b. Although it is difficult to determine the complexity of visual stimuli, these results suggest the perirhinal cortex contributes to the retention of associative information regarding relatively simple visual stimuli and the recognition of familiar visual stimuli when increased demands are made on the processes of recognition. Therefore,

more robust deficits in visual generalisation tasks may become apparent if the stimuli used are more complex.

Therefore, the acquisition and retention of a simple visual discrimination and generalisations to it are affected differently following perirhinal ablation, however, both are mildly impaired. The role of the perirhinal cortex in visual object recognition remains uncertain, it is possible that the relatively simple stimuli in the generalisation task used in the current study did not test generalisation abilities sufficiently to reveal more robust deficits following perirhinal ablation. Experiment 4, described in chapter 6, was designed to test visual generalisation abilities further.

Chapter 6: The effects of perirhinal ablation on acquisition of a titrating visual generalisation task

6.1 Introduction

Despite behavioural evidence to suggest that the perirhinal cortex contributes to the identification of visual objects (Primates: Buckley & Gaffan, 1997, 1998a,b), the results of experiment 2 (chapter 4) suggest acquisition of visual associative learning remains intact following perirhinal ablation, even when increased demands are made on visual object identification. Furthermore, the results of experiments 3a & 3b (chapter 5) suggest that the ability to identify and generalise to visual stimuli is only mildly impaired following perirhinal ablation. It is possible that the previous tests were not demanding enough to reveal more severe deficits in visual object recognition following perirhinal ablation. In generalisation experiments 3a & 3b, described in chapter 5, the presentation of the original base discrimination and repeat presentation of the transformed stimuli may have enhanced the perirhinal animals' performance. Furthermore, it is possible that in the previous generalisation experiments animals may have learnt to respond to each transformation as a separate stimulus, rather than as transformations of the base discrimination.

Therefore, the aim of the current study was to measure the effects of perirhinal ablation in a task that places more demands on the processes of object identification. A titrating version of the generalisation task used in chapter 5 was devised, that compared animals' discrimination abilities

without fixed presentations of the base discrimination or set levels of transformed stimuli. In this task, the performance levels of each animal determined the level of similarity between the S- and S+. Therefore, the results of the task provide an indication as to the minimum difference between stimuli necessary for animals to discriminate between them in the task. In experiment 3a, described in chapter 5, performance in the base discrimination in the generalisation task was impaired in the perirhinal animals that learnt the base discrimination following surgery. It is possible that learning the base discrimination prior to or following perirhinal ablation will affect generalisation performances differently in the current study. Therefore, the current study compares the performances of the perirhinal animals that learnt the base discrimination prior to perirhinal ablation and those animals that learnt the base discrimination post surgery.

6.2 Method

6.2 i Subjects

Nineteen male Dark Agouti rats (Bantin & Kingman, Hull, UK) aged approximately 13 months at the start of the study were used in this experiment. Five sham operated and seven perirhinal lesioned animals (Group 1) had completed generalisation experiments 3a and 3b, described in chapter 5. A further seven perirhinal lesioned animals (Group 2) had only completed generalisation experiment 3a described in chapter 5. A detailed description of the subjects used is provided in chapter 2.1.

6.2 ii Apparatus

A computer operated Y-Maze was used as described in chapter 2.2.

6.2 iii Surgery

All animals underwent surgery, 7 animals sustained bilateral perirhinal ablation and 7 animals sham surgery whilst completing experiment 3b, described in chapter 5. A further 7 perirhinal animals underwent surgery whilst completing experiment 3b (chapter 5). A detailed description of the surgical methods used is provided in chapter 2.4.

6.2 iv Post-Operative Training

All animals were tested on a titrating visual discrimination based on the generalisation tasks described in chapter 5. Prior to learning the new titration task all animals completed up to 100 trials in the original base discrimination. In the titration task the form of the S+ remained constant whereas the transformations in form of the rectangular S- were determined individually by the performance of each animal in the task. To begin the first session, the original S+ and S- were presented (i.e. the width of the S- equalled 40 % of the width of the square, as shown in figure 5.1). Three consecutive correct responses to the S+ resulted in the length/width ratio of the S- changing by 3 % so that it increasingly resembled the square shaped S+. An incorrect response resulted in the S- reversing its length/width ratio by 1 % so that it increasingly resembled its original form. The possible extent of transformation of the length/width ratio of the S- relative to the S+ ranged from 33 % to 99 %. The staircase ratio was choosen so that each increase in length/width ratio of 3% would remain within animals visual acuity. As in the generalisation experiments described in chapter 5, the

stimuli were randomly presented in five different levels of brightness and in random locations across both monitor screens. Therefore, in any given trial the S+ and S- were presented across one monitor screen in different arms of the maze. A correct approach to the S+ resulted in dispension of a food reward (45mg pellet, Bioserve) and its collection signalled onset of the next trial following an intertrial interval of 1 second.

All animals completed up to 100 trials a day, to a maximum of 1000 trials. Each level of transformation of the S- attained was recorded from each session, along with the final level of transformation in the S-, so that the following session started with the S- at that level. The highest transformation of the S- and the means of the highest 50 and 100 transformations reached were calculated for each animal, as were the levels of transformation reached every 10 trials up to 100 and every 100 trials up to 1000. The perirhinal animals were divided into two groups; group 1 had completed experiments 3a and 3b of chapter 5 and therefore learnt the base discrimination in this study prior to perirhinal ablation. The second group of perirhinal animals and the sham animals had completed experiment 3a of chapter 5 and therefore learnt the base discrimination following surgery. Training in the titration task began 2 months following surgery for the first perirhinal group and 6 months following surgery for the second perirhinal group.

6.2 v Histology

The method of histological analysis are described in chapter 2.5.

6.3 Results

6.3 i Histology

The results of the histological analysis of the animals in the current study are described in chapter 5. 3 i.

6.3 ii Behavioural

The highest levels of transformations of the S- attained were compared between the perirhinal and the sham animals. Table 6.1 shows the mean highest levels of transformation and the mean levels of transformation from the highest 50 and 100 levels attained by the perirhinal and sham animals. The highest percentages of transformation of the S- achieved by each animal were compared between the perirhinal and sham animals. A series of independent samples t tests found no statistically significant differences between the perirhinal and sham animals for the highest level of transformations attained overall (Perirhinal Group 1 & 2 Combined: t = <1: Perirhinal Group 1: t = <1; Perirhinal Group 2: t = <1); the mean of the highest 50 transformations (Perirhinal Group 1 & 2 Combined: t=1.295; Perirhinal Group 1: t = <1; Perirhinal Group 2: t = 1.605); or the mean of the highest 100 transformations attained (Perirhinal Group 1 & 2 Combined: t = <1; Perirhinal Group 1: t = <1; Perirhinal Group 2: t = 1.220).

A series of independent samples t tests found no statistically significant differences between the two perirhinal groups for the highest levels of transformation attained (t = 1.094), the mean of the highest 50 transformations (t = 1.111) or the mean of the highest 100 levels of transformations (t = 1.205).

Table 6.1. Post-Operative Scores in Titrating Discrimination Task

Rat	Highest level of transformation reached	Mean of highest 50 levels of transformation	Mean of highest 100 levels of transformation	No. trials to highest level of transformation
		Sham Animals		
R03	76	74	70	195
R05	81	79	72	233
R09	74	70	66	736
R011	75	71	69	384
R013	73	67	63	585
Mean	**76**	**72**	**68**	**426**
		Perirhinal Group 1		
R01	77	72	69	158
R04	75	68	64	958
R06	70	67	62	292
R07	72	68	65	655
R08	78	67	72	261
R010	79	70	67	646
R014	83	80	78	310
Mean	**76**	**70**	**68**	**468**
		Perirhinal Group 2		
R015	63	58	56	709
R016	73	67	66	991
R017	83	76	74	177
R018	76	70	62	728
R019	67	63	62	955
R020	79	71	68	688
R021	69	65	63	865
Mean	**72**	**67**	**64**	**730**
Combined Prh mean	**74**	**68**	**66**	**600**

Therefore, the perirhinal animals achieved the same levels of transformations of the S- as the sham animals. However, it is possible that the perirhinal animals accumulated more trials to achieve their highest levels of transformations. The numbers of trials accumulated by each animal in attaining their highest level of transformation of the S- were compared between surgical groups in a series of independent sample t tests. There were no statistically significant differences between the number of trials accumulated by the sham animals and both groups of

perirhinal animals combined (t = <1) or for the first group of perirhinal animals (t = <1). However, the difference between the number of trials accumulated by the sham animals and the second group of perirhinal animals was approaching significance (Two tailed test: t = 2.022, df = 10, p=0.071). Table 6.1 shows how the second group of perirhinal animals accumulated a mean of 730 trials in attaining their highest level of transformation, compared to a mean of 426 accumulated by the sham animals. Moreover, an independent samples t test found the number of trials accumulated by two groups of perirhinal animals was approaching statistical significance in a one way analysis (Two tailed test: t = 1.744, df = 12, p=0.107). These findings suggest that the perirhinal animals consistently achieve the same high levels of transformation of the S- as the sham animals. However, the second group of perirhinal animals appear to accumulate more trials in attaining their highest levels of transformation of the S-.

Table 6.2 shows the mean level of transformation of the S- attained every 10 trials up to 100 and every 100 trials up to 1000. Examination of these results suggest that animals performances improved rapidly over the first 100 trials completed and plateaued thereafter. To examine this further, the mean levels of transformation of the S- reached every 10 trials up to 100 were compared between all the perirhinal animals and the sham operated animals in a 2 (Surgical Group) x 10 (No. Trials) ANOVA with 1 repeated measure. As expected there was a significant within subject effect of number of trials (F = 48.423, df = 9, 153, p = <0.001). As shown in

figure 6.1, all animals performances in the task quickly improved as more trials were completed. The interaction between surgical group and number of trials was not statistically significant in a one way ANOVA (F= 1.639, df = 9, 153, p = 0.108), nor the main effect of surgical group (F = 2.413, df = 1, 17, p = 1.38). Figure 6.1 shows how the perirhinal animals' levels of transformation of the S- attained every 10 trials up to 100 were generally lower than the levels attained by the sham animals, suggesting that the perirhinal animals performances were impaired.

Table 6.2. Mean levels of transformations reached every 10 trials up to 100 and every 100 trials up to 1000.

No. Trials	Sham	Perirhinal Groups 1 & 2	Perirhinal Group 1	Perirhinal Group 2
10	41	41	41	42
20	46	46	45	47
30	47	48	47	49
40	52	51	51	51
50	58	54	54	53
60	58	55	56	53
70	59	55	55	54
80	58	54	54	54
90	59	55	53	57
100	61	56	57	56
200	64	57	57	57
300	60	58	63	54
400	58	60	64	55
500	54	56	60	52
600	56	56	59	52
700	56	60	58	62
800	61	55	57	53
900	56	56	61	50
1000	52	55	55	56

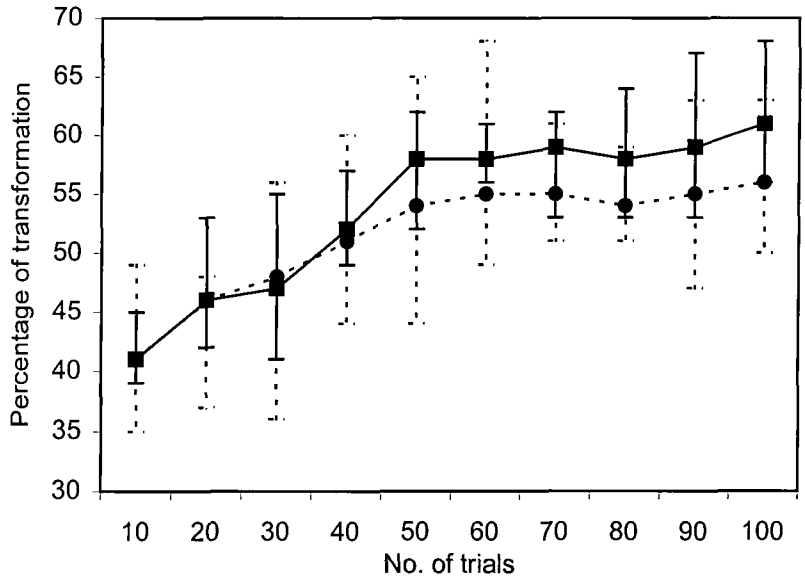


Figure 6.1. The mean level of transformation of the S- at every 10 trials up to 100 for the sham animals (squares) and both groups of perirhinal animals combined (broken lines and dots).

In order to examine whether performances of the two groups of perirhinal animals differ, the mean levels of transformations of the S- attained every 10 trials up to 100 were compared. The performance of two separate groups of perirhinal animals and the sham animals were compared in a 3 (Surgical Group) x 10 (No. Trials) ANOVA with 1 repeated measure. As expected, the within subject effect of the number of trials completed was statistically significant ($F = 53.927$, $df = 4, 18$, $p = <0.001$). Figure 6.2 shows how all three groups quickly attain higher levels of transformation as they complete a higher number of trials. The interaction between group and the number of trials completed was not statistically significant ($F = 1.297$), nor was the main effect of group ($F = 1.151$).

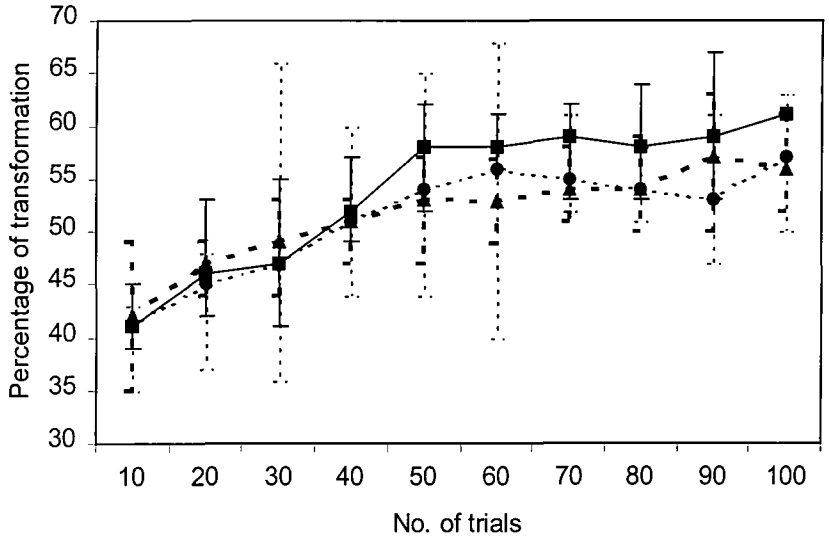


Figure 6.2. The mean levels of transformation of the S- every 10 trials up to 100 for the sham animals (Squares) and perirhinal groups 1 (broken lines, dots) and 2 (thick lines, triangles).

Therefore, the performances of the two groups of perirhinal animals were not significantly different to each other or the sham animals. However, figure 6.2 shows how both groups of perirhinal animals generally attain lower levels of transformations than the sham animals. It is possible that at 100 trials differences between the two perirhinal groups were not evident as animals had not completed enough trials to reveal an impairment. Therefore, the levels of transformations attained every 100 trials up to 1000 were compared between groups.

The mean level of transformation of the S- reached every 100 trials up to 1000 were compared between all the perirhinal animals combined and sham operated animals in a 2 (Surgical Group) x 10 (No. Trials) ANOVA with 1 repeated measure. The main within subject effect of the number of trials completed was not statistically significant ($F = 1.381$). Figure 6.3 shows that performance in the task does not always

improve as more trials are completed. Neither the interaction between the number of trials completed and surgical group (F= 1.019) and the main effect of group (F = <1) were statistically significant. Therefore, the performance of all the perirhinal animals combined and the sham animals were not significantly different every 100 trials up to 1000.

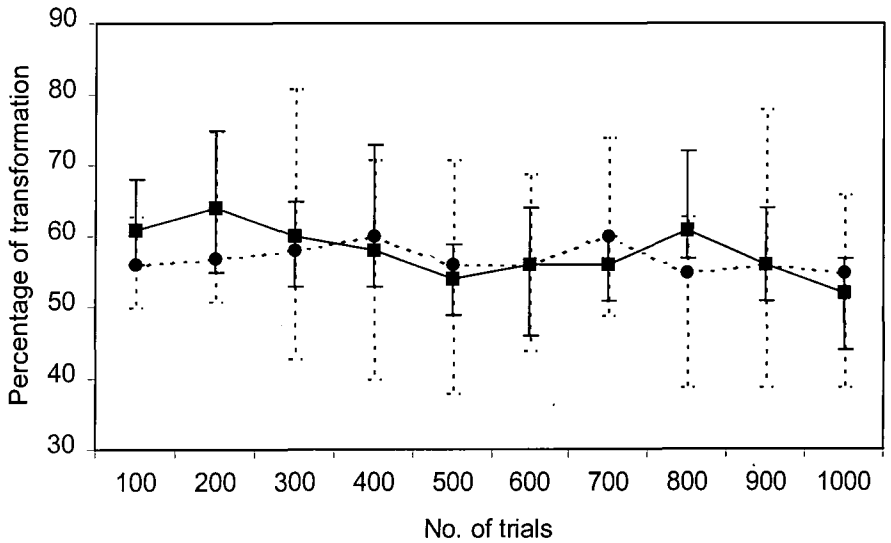


Figure 6.3. The mean levels of transformation of the S- at every 100 trials up to 1000 for the sham animals (squares) and the perirhinal animals combined (broken lines, dots).

The second group of perirhinal animals accumulated more trials to attain their highest levels of transformation of the S- than both the shams and the first group of perirhinal animals. Therefore, although there were no significant differences between the sham animals and the combined group of perirhinal animals the transformations attained every 100 trials to 1000 might have differed between the two perirhinal groups. The mean levels of transformation of the S- attained every 100 trials up to 1000 were compared between the two separate perirhinal groups and the shams in a 3 (Surgical Group) x 10 (No. Trials) ANOVA with 1 repeated measure. The

within subject effect of the number of trials was not statistically significant (F = 1.345). Figure 6.4 shows how the levels of transformations attained do not always improve with the number of trials completed. The interaction between group and the number of trials completed was approaching statistical significance (F = 1.502, df = 18, 144, p = 0.097), as was the main effect of group (F= 3.189, df = 2, 16, p = 0.068). Figure 6.4 shows how performance of the first group of perirhinal animals is generally lower than the shams and second group of perirhinal animals. Therefore, although both groups of perirhinal animals attained lower levels of transformations than the sham animals in the first 100 trials, over 1000 trials the second group of perirhinal animals attained lower levels of transformation compared to both the shams and the first group of perirhinal animals.

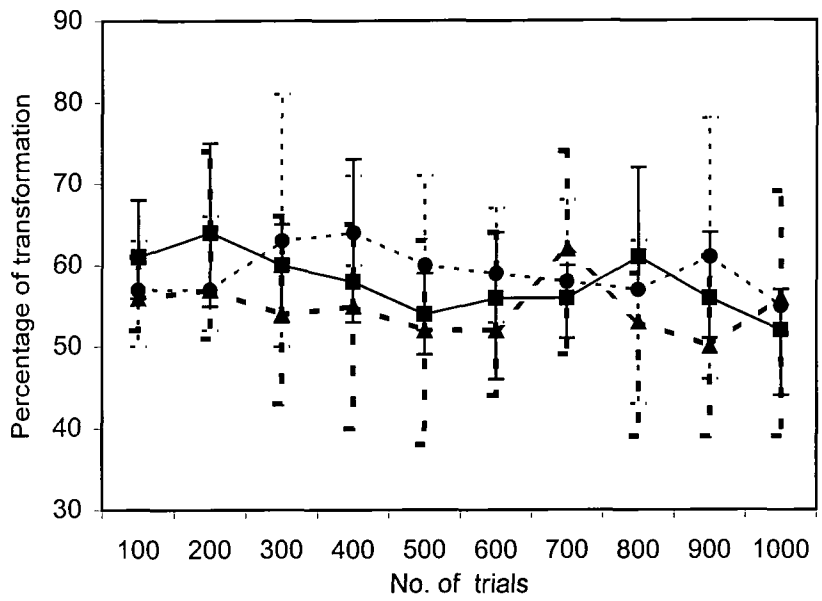


Figure 6.4. The mean level of transformation of the S- every 100 trials up to 1000 for the sham animals (squares) and perirhinal group 1 (broken lines, dots) and 2 (thick broken lines, triangles).

6.4 Discussion

The present study examined the behavioural effects of perirhinal ablation on acquisition of a titrating version of a visual generalisation task in the rat. The task was designed to place more demands on visual identification processes than the generalisation tasks described in chapter 5, as there were no presentations of the base discrimination or fixed levels of transformation of the S-. The perirhinal animals were subdivided into 2 groups, group 1 had completed experiments 3a & 3b, and group 2 had completed experiment 3a, as described in chapter 5.

The highest level of transformation of the S- attained overall and the mean of the highest 50 and 100 transformations of the S- attained did not differ between the perirhinal and sham animals. These findings suggest that the perirhinal animals can actually attain the same levels of transformation of the S- as the sham animals.

However, although the combined group of perirhinal animals attained lower levels of transformations of the S- in the first 10 trials up to 100 compared to the sham animals, there were no statistically significant differences between groups. All animals attained higher levels of transformation of the S- as they completed more trials in the task; however, the perirhinal animals consistently attained lower levels of transformation of the S-. These findings suggest that the perirhinal animals progressed more slowly than the sham animals, yet their performances were not actually impaired. When performances of the two groups of perirhinal animals were compared to the sham animals separately, there

were no significant differences between the groups. This finding suggests differences between the two perirhinal groups had not emerged after completing a relatively small number of trials.

The levels of transformation of the S- attained every 100 trials up to 1000 did not differ between the perirhinal animals combined and the sham animals. However, when performances of the perirhinal groups were compared to the shams separately, the second group of perirhinal animals were impaired relative to both the shams and the first group of perirhinal animals. The second group of perirhinal animals generally attained lower levels of transformations than the other groups of animals and accumulated a significantly higher number of trials to attain their highest level of transformation of the S-. These findings suggest that the second group of perirhinal animals performed the task at a slower rate than the sham animals and the first group of perirhinal animals.

The lower levels of performance of the second group of perirhinal animals may reflect their lower levels of experience in visual discrimination learning, as unlike the other animals they had not had completed experiment 3b, described in chapter 5. However, the second group of perirhinal animals learnt the base discrimination used in the titration task following surgery, whereas the sham animals and other perirhinal animals acquired the base discrimination prior to surgery. It is possible that post-operative acquisition of the base discrimination led to impaired retention and subsequent recognition of the base discrimination in the more demanding titration task.

The results of the current study suggest that performances in the titration task are differently affected by pre or post surgery training in the base discrimination. The more severe impairments demonstrated by the perirhinal animals that learnt the base discrimination following surgery may be attributed to a deficit in perceptual learning, leading to poor identification of the stimuli in the task.

The findings of the current study suggest that perirhinal ablation impairs visual discrimination and identification abilities in those animals that had less experience in the task. Our findings are consistent with the results of chapter 5 that found visual generalisation abilities were mildly impaired following pre or post training perirhinal lesions in the rat. However, it is evident that following perirhinal ablation some aspects of visual object identification may be sustained by structures outside of the perirhinal cortex, as even in the current study animals could eventually attain the same levels of transformation of the S- as the sham animals. It is possible that the task used in the current study did not tax the visual object identification capacities of the perirhinal cortex in the rat sufficiently to reveal a more robust impairment. Therefore, the stimuli used in the task may have been too simplistic to reveal a more severe impairment. It has been suggested that the perirhinal cortex is only crucial for the processing of complex or configural visual stimuli (Murray & Bussey, 1999), a notion that is explored more fully in the following experimental chapters.

The task described in the current study was designed to assess object identification processes and generalisations to familiar stimuli.

Therefore, the task placed further demands on the long-term identification of the stimuli in the base discrimination. Following rhinal ablation primates perform the visual recognition task, delayed-match-to-sample, normally, providing the stimuli sets are small, however, increasing the stimuli set, rendering each stimulus trial unique, produces an impairment (Eacott et al., 1994). The authors argue that rhinal ablation disrupts the ability to identify visual stimuli in the task (Eacott et al., 1994). Therefore, it is possible that the ability to identify visual stimuli is impaired following perirhinal ablation, resulting in impairments in the ability to perform both recognition (Eacott et al., 1994) and associative learning tasks (chapter 5, 6). It has been suggested that object recognition is sustained by a cortical loop from the perirhinal cortex to the orbitofrontal cortex via the magnocellular division of the medial dorsal thalamic nuclei (Aggleton & Brown, 1999; Meunier, Bachevalier & Mishkin, 1997; Parker, Wilding & Akerman, 1998). Visual object recognition memory tasks are impaired following lesions to the orbitofrontal cortex in primates (Meunier, Bachevalier & Mishkin, 1997) and the medial dorsal nucleus of the thalamus in rodents (Hunt & Aggleton, 1991). Furthermore, there is evidence to suggest object recognition is impaired following contralateral lesions to the perirhinal cortex and medial dorsal thalamus and to the perirhinal cortex and prefrontal cortex in primates (Parker, Wilding & Akerman, 1998), thereby suggesting that object recognition is dependent upon within hemisphere interaction between these structures. This proposed system may also contribute to the identification of visual objects

for associative and perceptual learning processes as well as recognition memory. Therefore, more severe deficits in visual object recognition tasks and visual discrimination learning may become evident following more extensive lesions to the proposed system.

In summary, the perirhinal animals attained lower levels of transformations of the S- in the first 100 trials in the task, but there were no statistically significant differences between any of the groups performances at this level. Furthermore, only the perirhinal animals that learnt the base discrimination following perirhinal ablation demonstrated lower levels of transformations of the S- every 100 trials up to 1000. These findings suggest that the performance of the perirhinal animals was impaired in the titrating visual generalisation task. Differences in the performances of the two groups of perirhinal animals suggest retention and acquisition of visual associative learning may be differently affected by perirhinal ablation.

However, the perirhinal animals could eventually attain the same levels of transformation of the S- as the sham operated animals, suggesting some intact object recognition and generalisation abilities. Therefore, further studies are needed to ascertain the effects of perirhinal ablation on acquisition of visual discrimination learning tasks containing more complex or configured visual stimuli.

Chapter 7: The Effects of Perirhinal Ablation on Acquisition of a Complex Visual Discrimination Task

7.1 Introduction

The results of experiments 3a, 3b and 4, described in chapters 5 and 6, found perirhinal ablation in the rat leads to a mild deficit in the ability to recognise and generalise to 2 dimensional visual stimuli. It is possible that perirhinal ablation did not reveal more robust deficits in visual discrimination learning in the previous studies, because the stimuli used in these tasks were not complex enough to tax the visual object recognition functions of the perirhinal cortex in the rat.

It has been suggested that the perirhinal cortex contributes to the processes of identifying complex visual stimuli (Eacott & Heywood, 1995). Furthermore, it has been suggested that anterior inferotemporal cortex is organised in a functional hierarchy; in which the perirhinal cortex contributes to visual object recognition by providing a complete representation of complex visual stimuli and areas TE and TEO sustain recognition of simpler visual stimuli (Murray & Bussey, 1999; Logothetis & Sheinberg, 1996). Therefore, it has been suggested that lesions to the perirhinal cortex disrupt visual object recognition when the stimuli are complex shapes or contain overlapping features (Murray & Bussey, 1999).

The stimuli used in experiments 3a, 3b and 4, described in chapters 5 and 6, were akin to simple or elemental stimuli that could combine to form complex or configured stimuli (Murray & Bussey, 1999). Therefore, a more robust deficit in a visual generalisation abilities may become

evident following perirhinal ablation if the stimuli used are relatively complex. The aim of the current study was to assess discrimination learning with complex visual stimuli following perirhinal ablation in the rat. Therefore, all animals were tested in a version of the visual generalisation task described in chapter 5; however, in this version the stimuli became complex geometric shapes.

7.2 Method

7.2. i Subjects

Eighteen male Dark Agouti rats completed this experiment, they were aged approximately 15 months at the start of testing. Although 19 animals started the study one perirhinal animal became ill partway through testing (R06). Five sham operated animals and thirteen perirhinal operated animals completed the study. All animals had completed the experiments 3a and 4 described in chapter's 5 and 6, 7 perirhinal animals had also completed experiment 3b, described in chapter 5. A detailed description of the subjects used is given in chapter 2.1.

7.2. ii Apparatus

A computer operated Y-maze was used, as described in chapter 2.2.

7.2. iii Surgery

All animals underwent surgery whilst completing the experiments described in chapter 5, 12 animals sustained bilateral perirhinal ablation and 7 animals sham surgery. A detailed description of the surgical methods used is given in chapter 2.4

7.2. iv Behavioural Training

All animals had experience of visual discrimination learning having completed the visual generalisation tasks described in chapters 5 and 6. The discrimination task in the current study was based on the generalisation task described in chapter 5.2 iv. The aim of the task was to teach animals a two choice visual discrimination between complex visual stimuli and then measure animal's generalisation gradients to morphs or transformations of the original stimuli. The visual stimuli in the new task were sets of six polygons, containing 2 extremes (polygons 1 and 6) and 4 morphs (polygons 2 to 5) that were polygons whose shape lay intermediate between polygons 1 and 6.

A set of polygons could have between 4 and 10 sides, each polygon within a set had an equal number of sides. Each polygon within a set also shared maximum and minimum radii (i.e. the distance from the polygon centre to its corners). The level of difference between the corresponding corners of the extreme polygons 1 and 6 and the maximum difference between their corners could vary between sets of polygons. Therefore, it was possible to create sets of polygons with more or less differences between the shapes of the extreme polygons 1 and 6. The computer programme chose a random seed code in order to generate the polygons. The angles of the corners of the polygons all varied by at least 15 degrees and the ratio of the minimum radius to the maximum radius was set in order to define the amount of jaggedness of the extreme polygons. The morphs were created by moving between the corners of the two extreme

polygons in equal steps, so as to gradually move from resembling polygon 1 to polygon 6.

Two sets of polygons were created, figure 7.1 shows polygons 1 and 6 from sets 1 and 2.

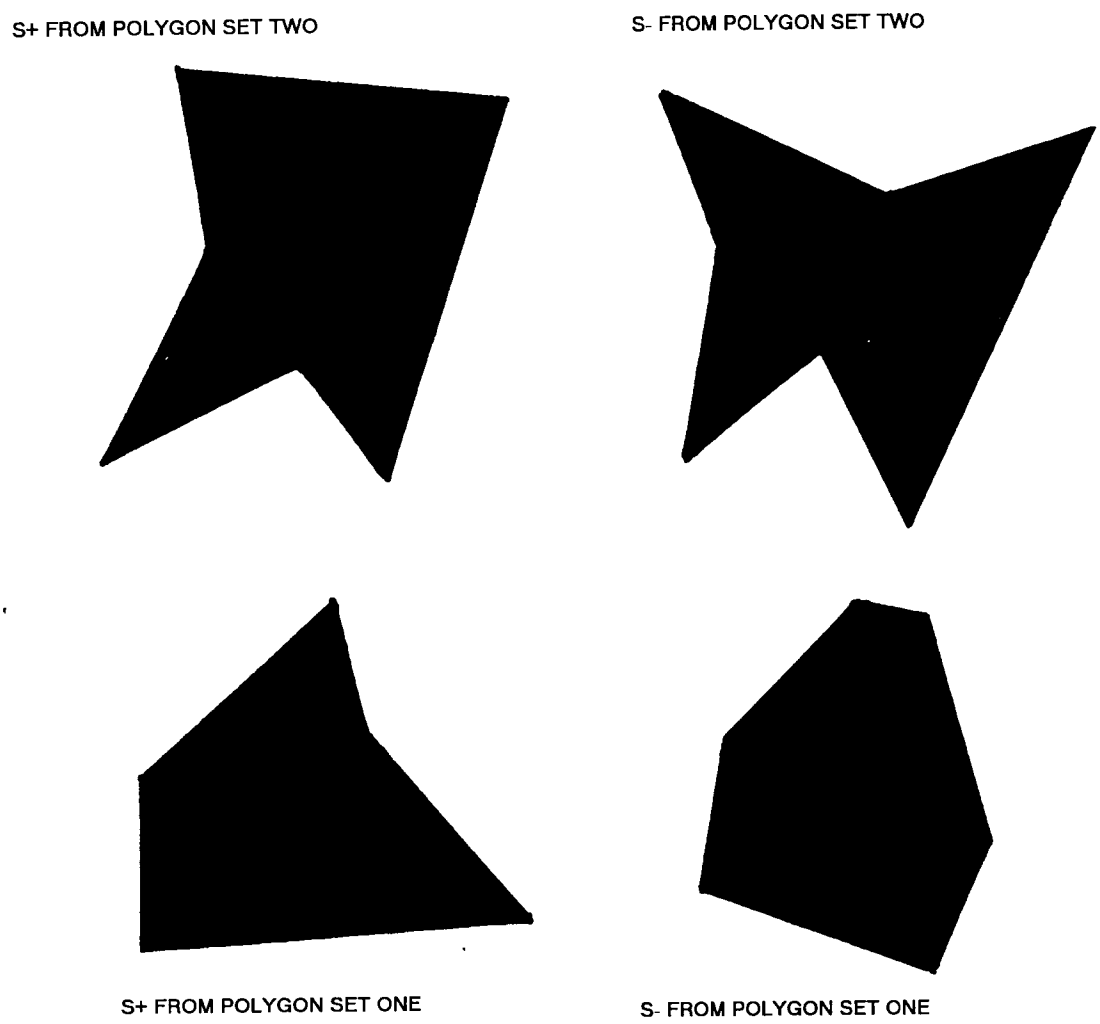


Figure 7.1. Polygons 1 (S+) and 6 (S-) from polygon sets one and two, in the task the stimuli were shown in a light grey level and the background in a dark grey level.

The dimensions of the polygons are described in x units, with one x unit being equivalent to five pixels (2.6 pixels = $1mm^2$) . The first set of polygons had 6 sides, a maximum radius of 90, a minimum radius of 30, the ratio of the minimum to maximum radius was 30 and the maximum difference between the radii of polygon 6 and polygon 1 was 25. For the second set of polygons the number of sides was 7, the maximum radius was 100, the minimum radius was 30, the ratio of the min/max radius was 5 and the maximum difference between the radii of polygon 6 and polygon 1 was 25. For each set of polygons created, the colour of the stimuli and background remained constant. Initially the luminance and location of the stimuli were fixed. Had animals attained criterion at this stage, the stimuli would have been presented in varying location and levels of luminance. The shape of the stimuli used is shown in figure 7.1, in the task the screen background was constant at $0.06cd/m^2$ and the polygons presented in the grey level equivalent to $4.9cd/m^2$.

Initially all animals began training on a two choice discrimination between the extreme polygons in set one. Within the set polygon 1 became the rewarding stimuli, S+, and polygon 6 became the non-rewarded stimulus, S-. The two stimuli were presented concurrently in different arms of the maze. An incorrect approach to the S- ended the trial, whereas an approach to the S+ resulted in dispension of a food pellet; a new trial began when the pellet was collected. A criterion of 80 % correct responses over two consecutive trials was set. All animals completed 4 sessions at this stage and showed no signs of learning the discrimination.

The stimuli in the first stimuli set may have been too similar for the rats to learn the discrimination, therefore the stimuli was changed to that of polygon set 2. All animals completed 4 sessions with stimuli set 2, yet showed no signs of learning the discrimination.

As animals were experiencing difficulty in learning the task, correction trials were introduced. Therefore, when an animal incorrectly approached the S-, its presentation ended, whereas presentation of the S+ remained until approached and the animal had collected its reward. All animals completed up to 4 sessions with correction trials, but were extremely slow to learn the discrimination. At this point animals ended training in the task. All animals completed up to 100 trials a day, five days a week throughout behavioural training.

7.2. v Histology

A detailed description of the methods of histological analysis and the extent of the intended perirhinal lesion are given in chapter 2.5.

7.3 Results

7.3. i Histology

A detailed description of the methods of histological analysis and the extent of the intended perirhinal lesion are given in chapters 5.3 i and 2.5 respectively.

7.3 ii Post-Operative Learning

No animal attained criterion in acquisition of the discrimination between the two extreme polygons in set 1 or set 2.

Polygon set 1

No animals attained criterion in the task. In order to determine whether the animals showed any evidence of improving their scores over time the percentage of correct responses attained in each session of polygon set 1 were compared. This data was analysed in a 2 (surgical group) x 4 (No. of sessions) Anova with 1 repeated measure. Overall there was no effect of group ($F = <1$), the number of sessions completed ($F = <1$) or interaction between the number of sessions and group ($F = <1$). Therefore, the percent correct scores obtained by the perirhinal and sham animals did not increase with the number of sessions completed. These findings suggest that performance in the task did not improve with experience.

Polygon Set 2

No animals attained criterion in the learning the task with polygon set 2. However, it is possible that animals performances in the task improved as more sessions were completed, indicative of learning the task. The percentage of correct responses attained in the first ten sessions of polygon set 2 were analysed in a 2 (surgical group) x 10 (No. of sessions) Anova with 1 repeated measure. The effect of group ($df = 1, 16$, $F = 3.306$, $p = 0.088$), the interaction between surgical group and number of sessions ($df = 1, 16$, $F = 3.946$, $p = 0.064$) and the effect of number of sessions were not statistically significant ($F = <1$). Therefore, the number of sessions completed had no effect on the performance of either group of animals. If animals were learning the task, it would have been expected

that animals scores would have increased as they completed more sessions. However, these findings suggest that neither group of animals showed any improvement in scores as more session were completed. Figure 7.2 shows the perirhinal and sham animals mean percent correct scores attained at the end of the first 10 sessions of discrimination learning in polygon set 2.

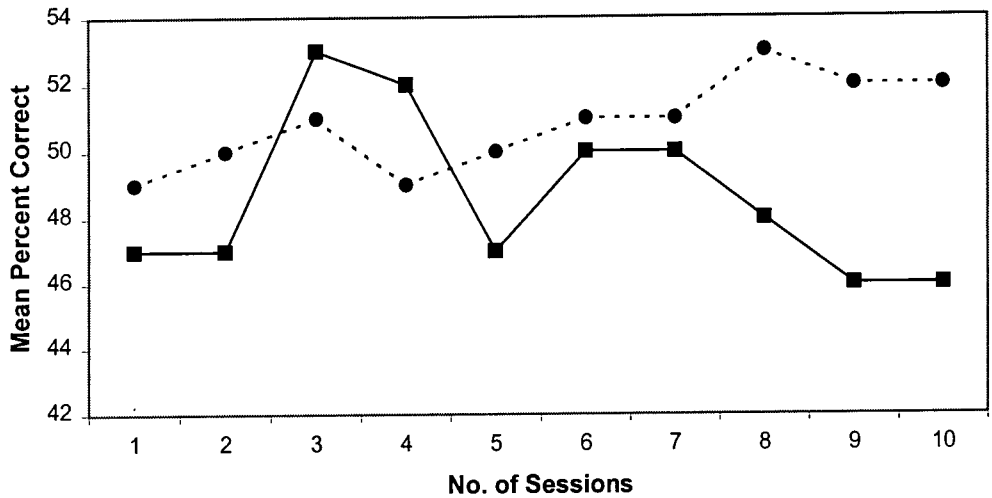


Figure 7.2. Mean percent correct scores achieved by the perirhinal (dots, broken lines) and sham animals (squares) at the end of first 10 sessions of discrimination learning in polygon set 2.

7.4 Discussion

The present study examined the effects of perirhinal ablation on acquisition of a visual generalisation task with complex visual stimuli in the rat. It was found that neither the sham or perirhinal animals could attain a two choice discrimination between complex visual stimuli. Neither group of animals attained criterion in the task, even when correction trials were introduced. These findings suggest that the stimuli

used in the task were too complex for both the sham and perirhinal animals to discriminate between.

There are several possible explanations as to why animals failed to learn the discrimination task. It is possible that discrimination of the stimuli used was beyond the range of rats' visual acuity. Pigmented rats visual acuity is 1.2 cycles/degree (Birch and Jacobs, 1979), therefore the animals in the current study should be able to detect changes of 0.5cm when viewing the stimuli from the position of the first photodetector beams in the maze, a distance of 20cm. The outlines of the shapes used in the current study varied by more than 0.5 cm, suggesting limited visual acuity did not prevent animals from learning the discrimination.

Alternatively, it is possible that the animals in the task did not focus on differences between the shapes of the stimuli in the task, but on the area or luminance. If this were the case, difficulty in discriminating between the stimuli used in the task would be expected, as the stimuli were matched in luminance and shared similar areas. However, this view supposes that rats learn visual discriminations without focusing on the form of the stimuli in the task. It has been shown that rats can discriminate between visual stimuli on the basis of differences in the geometric form of the stimuli. A recent study assessed what properties of visual objects are encoded by rats performing a visual discrimination task in a computer operated Y- maze as used in the current study (Simpson & Gaffan, 1999). In this study animals had to discriminate between visual scenes in a constant negative discrimination task. The spatial arrangement of the

objects within the scenes remained constant, but objects in the same spatial position within each scene could be matched in terms of luminance, area or shape. It was found that when objects in the same spatial position in each scene were matched in terms of shape rats discriminated least well, thus performance was enhanced when the objects varied in shape. However, matching the area or level of luminance of the different stimuli did not have such a detrimental effect on performance. Therefore, animals discriminated between visual objects on the basis of stimuli shape, rather than stimuli area or luminance. These findings suggest animals distinguished between the different classes of shapes used in the experiment, such as ellipses, crosses, polygons, rectangles and circle sectors.

The authors suggest that rats can use cues regarding the luminance or area of stimuli to perform a visual discrimination task, however, when these cues are not fixed rats will rely on cues inherent in the form of the stimuli. In the current study the stimuli were matched in area and luminance, suggesting animals would have to rely on cues within the form of the stimuli to learn the discrimination. Therefore, the form or shape of the stimuli used in the current study may have been too similar to one another or too complex for animals to learn the discrimination.

An alternative explanation of our results is that animals failed to attend to the whole of the stimuli in the discrimination task. It has been shown that rats, performing a visual discrimination task in a duplicate version of the automated Y- maze used in the current study, preferentially

attended to the lower half of the monitor screens (Simpson & Gaffan, 1999). However, animals readily learnt to attend to all sections of the monitor screen, as the previous strategy proved unreliable. Whilst these findings suggest animals learn to attend to the whole of the monitor screen in a visual discrimination task, they tested discrimination of visual scenes, not single objects. Therefore, it is possible that the rats in the present study experienced difficulties in attending to the whole outline of the stimuli, making the discrimination increasingly difficult to perform.

It is uncertain how rats learn to recognise visual stimuli in discrimination learning tasks. It has been suggested that rats recognise visual stimuli in such tasks by self-produced movement cues (Dean, 1990). The stimuli used in the current study may have produced very similar patterns of flicker when scanned, as the stimuli shared the same fill pattern, area, luminance, relative motion and spatial position on the monitor screens. Furthermore, it is possible that the polygons in the current study resembled the square S+ from the generalisation tasks described in chapters 5 and 6. Therefore, the animals in the current task may have transferred learning from the previous study that affected performance in the polygon task.

The results of the current study suggest that rats cannot learn to discriminate between similar, complex 2 dimensional visual stimuli. These findings suggest that the visual stimuli used in the previous generalisation tasks described in chapters 5 and 6 may have been viewed as relatively complex by the animals performing the task. More complex visual stimuli

than that used in chapters 5 and 6 may reveal a more robust impairment in visual recognition following perirhinal ablation. However, the type of stimuli used would have to remain simple enough to be recognisable by unoperated animals.

It has been suggested that visual object recognition within inferotemporal cortex may be organised in terms of a functional hierarchy, in which the perirhinal cortex encodes relatively complex or configured visual stimuli and areas TE and TEO encode simpler elemental stimuli (Murray & Bussey, 1999). However, it is difficult to determine when an object is deemed to be complex enough to tax visual recognition of the perirhinal cortex whilst remaining within rats` recognition abilities. Furthermore, electophysiological evidence suggesting a functional hierarchy within inferotemporal cortex is taken almost exclusively from studies in the primate (Murray & Bussey, 1999). It is possible that the functional organisation of the inferotemporal cortex in rodents differs from that of primates, due to rodents` less developed visual systems. Knowledge regarding rats' visual recognition abilities is not as well documented as knowledge of primates' visual abilities. Whilst it is known that rats can learn to attend to visual objects presented in automated testing apparatus similar to primate testing (Simpson & Gaffan, 1999), the way in which primates and rodents identify visual objects may differ. For example, it has been suggested rodents rely on self-produced movement cues to recognise visual stimuli (Dean, 1990) and may experience

difficulties is producing absolute or referential cues regarding the luminance or size of visual stimuli (Munn, 1950).

Therefore, the results of the current study highlight the need to develop our understanding of how rodents perform visual discrimination tasks in order to produce a range of tasks that place varying demands on visual identification processes. The findings from the current study suggest that the stimuli used in the chapters 5 and 6 may have placed quite high demands on rats' visual recognition abilities. Further research is needed to ascertain whether a different range of complex visual stimuli may reveal a deficit in visual discrimination learning following perirhinal ablation, or whether deficits only occur in discriminating between complex configured visual stimuli.

Chapter 8: The Effects of Perirhinal Ablation on Acquisition of a Visual Configural Learning Task

8.1 Introduction to Experiment 6

The results of experiments 3a, 3b and 4 found visual discrimination learning to be impaired following perirhinal ablation. However, the impairments observed throughout these studies were not very severe. It has been suggested that the perirhinal cortex is necessary for the categorisation or identification of complex visual objects that share common visual features (Eacott & Heywood, 1995). Furthermore, it has been suggested that the perirhinal cortex contributes to visual configural learning, by associating common visual features together to make unique representations of visual objects (Murray & Bussey, 1999). Therefore, perirhinal ablation may result in severe deficits in visual associative learning tasks that assess configural learning or contain complex visual stimuli. The aim of the current study was to compare the effects of perirhinal ablation on acquisition of discrimination learning with complex visual stimuli and the reversal of this discrimination and acquisition of a biconditional configural learning task.

The study of human amnesic patients has led to a conceptual distinction between nondeclarative and declarative memory processes. The medial temporal lobe, in particular the hippocampus, is considered to support declarative or explicit processes of consciously recollecting episodes or events, whereas other cortical and subcortical structures are deemed to support nondeclarative or implicit procedural memory processes (Squire, 1992). It has been suggested that these two memory processes are

characterised by their computational properties. For example, declarative memory relies on the formation of associations with compound stimuli comprised of two or more elements, whereas non-declarative memory relies on the formation of associations with individual features (Metcalfe, et al., 1992). It has been suggested that the associative networks that sustain learning and memory can be divided into configural (CAS) or elemental (EAS) associative systems. The EAS forms representations of individual stimuli, whereas the CAS forms unique representations of a number of individual stimuli (Rudy & Sutherland, 1995). Therefore, it would be expected that amnesic patients would be impaired in performing configural learning tasks that cannot be solved by an elemental associative system. Indeed, there is evidence to suggest that amnesic patients with hippocampal pathology are impaired in a visual transverse patterning task, that requires a non linear solution (Rickard & Grafman, 1998).

Standard tests of configural learning include transverse patterning, biconditional learning and negative patterning (Rudy & Sutherland, 1995). Transverse patterning (Spence, 1952) contains several elemental stimuli that are rewarded or non-rewarded on the basis of the stimulus that they are presented with. The associative strength of each stimulus remains equal, for example A+ B-, B+ C-, C+ A-, where A, B and C represent the stimuli and + and – its rewarded or non-rewarded status. In negative patterning (Rescorla, 1972) the stimuli are rewarded when presented individually, but not rewarded when presented together, for example, A+, B+, AB-. Biconditional learning requires a number of elemental stimuli that combine to form rewarded or non-rewarded compound stimuli, for example AX+,

AY-, BY+, BX-. The elemental stimuli within each compound are equally associated with reward and non-reward, so that recognition of the unique configuration of the elements within the compound stimuli is the only way to discriminate between the compound stimuli.

Rudy & Sutherland, (1989, 1992 and 1995) suggest that configural learning is dependent upon the hippocampal system. There is evidence that hippocampal lesions in rats impair negative patterning tasks (Rudy & Sutherland, 1989) and transverse patterning tasks (Alvarado & Rudy, 1995; Dusek & Eichenbaum, 1998). However, reports that hippocampal lesions spare configural learning processes (Davidson et al., 1993;Gallagher & Holland, 1992; Murphy et al., 1993) have prompted a reappraisal of this theory. It has been suggested that, although the hippocampus may contribute to a configural association system, cortical areas outside of the hippocampus actually sustain configural learning (Rudy & Sutherland, 1995). The authors suggest that the hippocampus enhances the activation of configural representations in cortical areas by decreasing the similarity between configural units and increasing the rate at which configural units acquire associative strength (Rudy & Sutherland, 1995). Therefore, lesions to the rhinal cortices may impair configural associative learning, as they disrupt the flow of polymodal sensory information to the hippocampus. Altenatively, perirhinal cortex itself may contribute to configural learning.

Episodic memory appears to rely on the recollection of whole scenes, distinguishable by the spatial arrangement of the elements within them (Gaffan, 1994a). This process is considered to be reliant upon the extended hippocampal system (Buckley & Gaffan, 1998c; Gaffan, 1992), as

lesions within this system impair object-place associations in the primate (Gaffan & Harrison, 1989a,b; Gaffan & Saunders, 1985). In object-place associative learning, the elements within a scene are configured with their spatial location, a process dependent upon configural learning. It has been suggested that the processes of episodic memory rely upon configural associative processes within the hippocampus (Dusak & Eichenbaum, 1998). However, it has also been suggested that configural learning tasks without spatial demands do not rely upon structures within the hippocampus (Buckley & Gaffan, 1998c). There is evidence that fornix lesions in rats do not impair spontaneous recognition of reconfigured visual objects (Ennaceur & Aggleton, 1994) and actually facilitate performance in a visual transverse patterning task (Bussey et al., 1998). Furthermore, there is evidence that hippocampal lesions in rats do not impair nonspatial negative patterning (Davidson et al., 1993). These findings suggest that the extended hippocampal formation does not contribute to nonspatial configural learning.

One area that may sustain visual configural learning is the perirhinal cortex. There are reports that perirhinal lesions in the primate impair visual-visual associative learning (Higushi & Miyashita, 1996; Murray et al., 1993) and visual biconditional configural learning (Buckley & Gaffan, 1998c). There is also evidence to suggest that the perirhinal cortex in primates contributes to object-in-place associative learning, which requires animals to remember the spatial location of visual objects (Murray, Baxter & Gaffan, 1998). These findings suggest that configural learning regarding visual information may be impaired following perirhinal ablation, although it is

uncertain whether these impairments are due to poor recognition of the visual objects within the scenes, or to deficits in configural learning.

It is uncertain whether the perirhinal cortex contributes to configural learning for stimuli across sensory modalities. Whilst there is evidence that perirhinal ablation in primates disrupts visual configural learning (Buckley & Gaffan, 1998c), it is possible that this deficit is due to the specialised role of the perirhinal cortex in visual object identification. However, there is evidence to suggest that rhinal lesions impair acquisition of an odour guided transverse patterning task in the rat (Dusek & Eichenbaum, 1998). Fornix lesions also produce a deficit in the task, leading the authors to suggest that configural learning across modalities is dependent upon cortical and subcortical inputs from the rhinal cortex and the fornix to the hippocampus (Dusek & Eichenbaum, 1998). Therefore, rhinal lesions may impair configural learning by restricting the flow of sensory information to the hippocampus. If this were the case it would be expected that rhinal lesions would produce deficits in configural learning tasks using multimodal sensory stimuli. Alternatively, the rhinal cortex may play a specialised role in the configuration of visual information.

It has been suggested that the perirhinal cortex sustains visual configural learning by encoding combinations of sensory features that differentiate complex visual objects (Eacott & Heywood, 1995; Murray & Bussey, 1999). Thus, impairments in visual configural learning and complex visual object identification following perirhinal ablation may arise from the inability to represent combinations of elemental features (Murray & Bussey, 1999). The aim of the current study was to compare the effects

of perirhinal ablation on acquisition of two choice visual discrimination learning and its reversal that could be solved by elemental associative learning and a visual biconditional configural learning task that requires configural associative learning. The effects of perirhinal ablation on acquisition of visual discrimination learning and discrimination reversal learning were measured to compare the effects of perihinal ablation on acquisition of both elemental and configural visual discrimination learning with similar visual stimuli.

In the visual discrimination task, animals learnt two sets of discriminations between four pairs of visual stimuli, the reward contingencies of which were then partially reversed. The reward contingencies were partially reversed to increase demands on visual discrimination learning. In addition, the partial reversal task provides a control for partial reversal effects that may be learnt in the configural task. For example, in both the biconditional and the discrimination reversal tasks, animals may learn to approach particular stimuli on the basis of the presence or absence of a particular stimulus or feature. Deficits in configural learning may reflect difficulties in reversing the reward associations of the elemental stimuli in the task. Therefore, the associative processes involved in discrimination reversal learning may also contribute to normal configural learning. The discrimination reversal was included in the study to assess whether perirhinal ablation disrupts the ability to change the reward associations of elemental stimuli. A partial discrimination reversal was introduced, as this may have increased the demands on identifying which stimuli in the task changed their reward associations. Furthermore, the

partial reversal mimics the effects of the partial reversals in the configural learning task. The reward contingencies in the original discrimination were as follows, A+, B-, C+, D-, in the partial reversal, A+, B+, C-, D-. In the biconditional learning task two different visual objects, named A & B and a horizontal and oblique line, named Y & X, were used as stimuli. The rewarded compound stimuli were AY and BX, the non-rewarded compound stimuli were AX and BY.

8.2 Method

8.2. i Subjects

Although seventeen dark agouti rats (5 sham and 12 perirhinal) began training in the current study, only ten animals (4 sham, 6 perirhinal) completed it due to the others developing illnesses partway through testing (Sham: R011; Perirhinal: R04, R020, R021, R017, R07, R016). All animals were aged approximately 17 months at the start of testing and had completed experiments 3a (Chapter 5), 4 (chapter 6) and 5 (chapter 7), the sham animals and perirhinal animals R04, R07, R08 and R010 had also completed experiment 3b (chapter 5). A detailed description of the subjects used is given in chapter 2.1.

8.2. ii Apparatus

The apparatus used was a computer operated Y-maze described in chapter 2.2.

8.2. iii Surgery

All animals underwent either bilateral perirhinal ablation or sham surgery whilst completing experiments 3a or 3b, described in chapter 5. A detailed description of the surgical methods used is given in chapter 2.4.

8.2. iv Post-Operative Behavioural Training

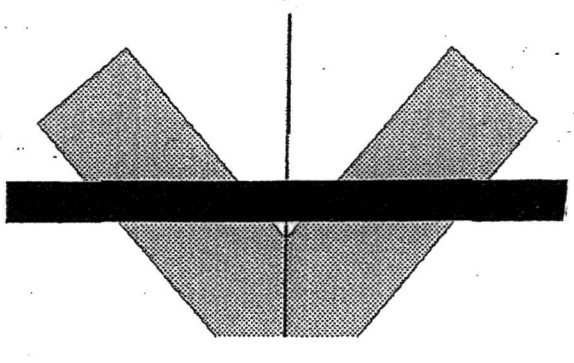
Task 1: Visual Discrimination Learning

All animals learnt four pairs of visual discriminations that were then combined to form two partial discrimination reversals. The stimuli used resembled complex visual shapes with a fill pattern, similar to objects A and B shown in figure 8.1. To begin, animals learnt to discriminate between two visual stimuli, objects 1 and 2. The S+ and S- were presented concurrently in the Y- maze and animals had to learn to approach the S+ for a food reward. A correct response to the S+ resulted in dispension of one reward pellet, when this pellet was collected a new trial began following an intertrial interval of 1 second. If an animal approached the S-, stimuli presentation ended and a new trial began after the 1 second intertrial interval. Training continued until animals attained a preset criterion of 80% correct responses over two consecutive sessions. When criterion was achieved, training began in the same task with a new pair of visual stimuli, objects 3 and 4. When criterion was achieved at this stage, the two pairs of discriminations were combined. The reward contingencies were partially reversed, so that objects 1 and 2, from pair 1, became the S+'s and objects 3 and 4, from pair 2, became the S-'s. In the partial reversal, all four stimuli were presented, so that either S- could be presented with either S+. When animals attained a criterion of 80% correct over two consecutive sessions, or completed over 1000 trials, the procedure was repeated for two more pairs of stimuli. All animals completed up to 100 trials a day, five days a week.

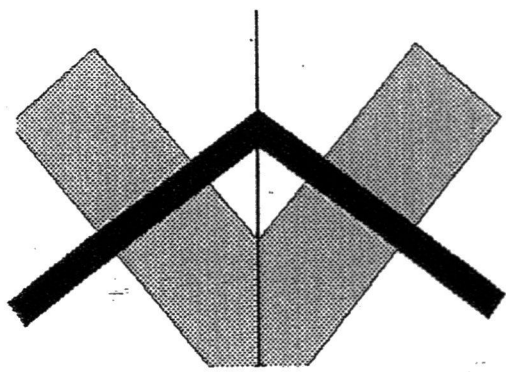
Task 2: Visual Configural Learning

When animals had attained criterion in the partially reversed visual discriminations, they began training on the configural task. The stimuli used in the task were two complex visual shapes, referred to as A and B, presented with a horizontal line or oblique line, named Y and X respectively. A schematic representation of the stimuli used are shown in figure 8.1.

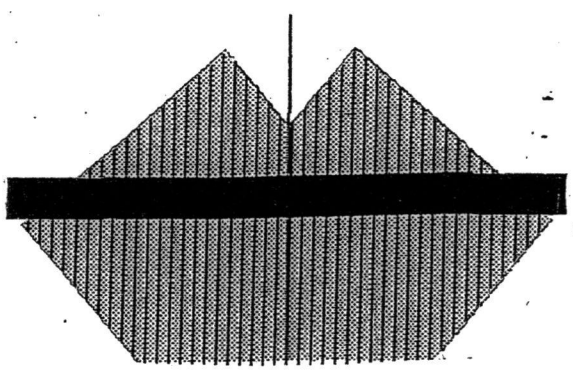
Figure 8.1. The compound stimuli used in the visual configural learning task (not drawn to scale).



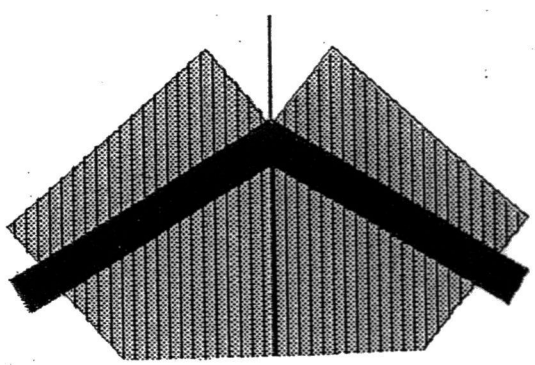
S+, Object A with line Y



S-, Object A with line X



S- Object B with line Y



S+, Object B with line X

The objects were created using a stimuli generating algorithm described in Gaffan and Eacott (1995). The objects were filled with one of five possible fill patterns, including stripes, dots, waves, rows of squares or none. The spatial frequencies of the fill patterns were between 0.6 and 1.5 cycles per degree from the maze centre, so as to remain within rats visual acuity when viewed from the photodetector beams situated 20mm from the monitor screens. The reward contingencies of objects A and B differed when presented with X and Y, so that the rewarded stimuli were compounds AY and BX, the non-rewarded stimuli compounds AX and BY. The stimuli were presented in mirror images across the two monitor screens in each arm of the maze. The stimuli were presented in fixed locations across trials. The brightness of each compound stimulus was varied randomly between trials, so that each compound stimulus could be presented in one of five levels of brightness.

The configural task was learnt in several phases in which animals had to attain a criterion of 80 % correct responses over two consecutive sessions before moving onto the next phase. Training was conducted in different phases to ensure that all animals were performing well in the non configural stages of the discrimination before testing in the configural task. Table 8.1 shows the trial types used in each phase of training. In phase 1 animals learnt to discriminate between the four different pairs of objects. Animals learnt the discriminations in the following order, level 1, AY+, AX-, level 2, AY+, BY-, level 3, BX+, AX- and level 4, BY-, BX+. In level 4 of phase 1 all animals failed to attain criterion after 20 sessions. Therefore, the lengths of the horizontal and oblique lines on all stimuli were

increased to aid animals' performance in the task. The lengths of the lines were increased for all stimuli in phases 2 and 3.

Table 8.1. The trial types used in each phase of training

PHASE ONE	PHASE TWO	PHASE THREE
Level 1 AY+, AX-	Levels 1 & 2 alternated	Levels 5 & 6 alternated
Level 2 AY+, BY-	Level 5 AY+, AX- AY+, BY-	Level 7 AY+, AX- AY+, BY- BX+, AX- BX+, BY-
Level 3 BX+, AX-	Levels 3 & 4 alternated	
Level 4 BX+, BY-	Level 6 BX+, AX- BX+, BY-	

Upon attaining criterion at this stage, animals began training in phase 2. In this phase the stimuli learnt so far were presented alternately before being combined. Therefore animals were tested in levels 1 and 2 of phase 1 on alternate days, when animals attained criterion at this stage the three different stimuli were combined to form level 5. In level 5 the S+ (AY+) was alternately presented with one of two S-'s (BY-, AX-). The trials were presented in blocks of twenty trials, in which there were 10 trials of each trial type, presented randomly. This procedure was repeated for the remaining stimuli in levels 3 and 4 of phase 1, that is BX+, BY-, followed by BX+, AY-. In level 6 all 3 stimuli combined, therefore, levels 5 and 6 formed partial tests of configural learning. As in level 5, the two different trial types in level 6 were presented randomly in blocks of 20 trials.

In phase 3 animals completed alternate days testing in levels 5 and 6 of phase 2 before beginning training in all four pairs of stimuli simultaneously. Therefore in the final stage of testing, level 7, there were

four trial types that were presented in random order, type 1: AY+, AX-, type 2: AY+, BY-; type 3: BX+, BY-; type 4: BX+, AX-. At this level the 4 different trial types were presented randomly in blocks of 20 trials, so that within each block there were 5 presentations of each type of trial. All animals continued testing in the final stage until they had attained criterion or completed more than 800 trials. All animals completed up to 100 trials a day, five days a week.

8.2 v Histology

The histological methods used are described in chapter 2.5.

8.3 Results

8.3. i Histology

The results of the histological analysis are provided in chapter 5.3.i.

8.3 ii Behavioural

Task 1: Visual Discrimination Learning

All animals attained criterion in the simple visual discriminations, however, perirhinal animals R07, R020, R021 all failed to attain criterion in the partial reversal for objects 5 to 8. Figures 8.2 and 8.3 show the trials and errors to criterion accumulated by the perirhinal and sham animals. The number of trials accumulated in attaining criterion in the four pairs of visual discriminations did not differ significantly between the perirhinal and sham animals ($t = <1$). The differences between the number of errors accumulated by the perirhinal and sham animals was approaching significance ($t = 2.021$, $df = 15$, $p = 0.062$). Table 8.2 and figure 8.3 shows that the perirhinal

animals accumulated a higher mean number of errors than the sham animals.

The number of trials and errors accumulated in attaining criterion in the partial reversals were compared between the perirhinal and sham animals. A nonparametric test was used, as three perirhinal animals failed to attain criterion in the partial reversals. There were no statistically significant differences between the numbers of trials ($U = 27$, $p = 0.752$) or errors ($U = 27$, $p = 0.752$) accumulated by the perirhinal and sham animals.

Table 8.2. The number of trials and errors accumulated in attaining criterion in 4 pairs of visual object discriminations and 2 partial discrimination reversals (F = failed to attain criterion).

Rat	Visual Discriminations		Partial Reversals	
	Trials	Errors	Trials	Errors
		Sham Operated Animals		
R03	841	219	1307	560
R05	851	214	981	385
R09	808	243	1118	443
R011	859	174	945	325
R013	1033	292	1418	562
Mean	**878**	**228**	**1153**	**455**
		Perirhinal Operated Animals		
R04	792	244	1095	401
R07	1057	386	(F) 1775	(F) 819
R08	668	249	895	309
R010	793	253	1066	419
R014	813	241	1212	426
R015	1122	405	1862	808
R016	761	255	892	327
R017	901	284	1017	396
R018	807	276	1115	432
R019	885	241	1038	403
R020	797	275	(F) 1443	(F) 618
R021	951	314	(F) 1592	(F) 773
Mean	**862**	**285**	**1250**	**510**

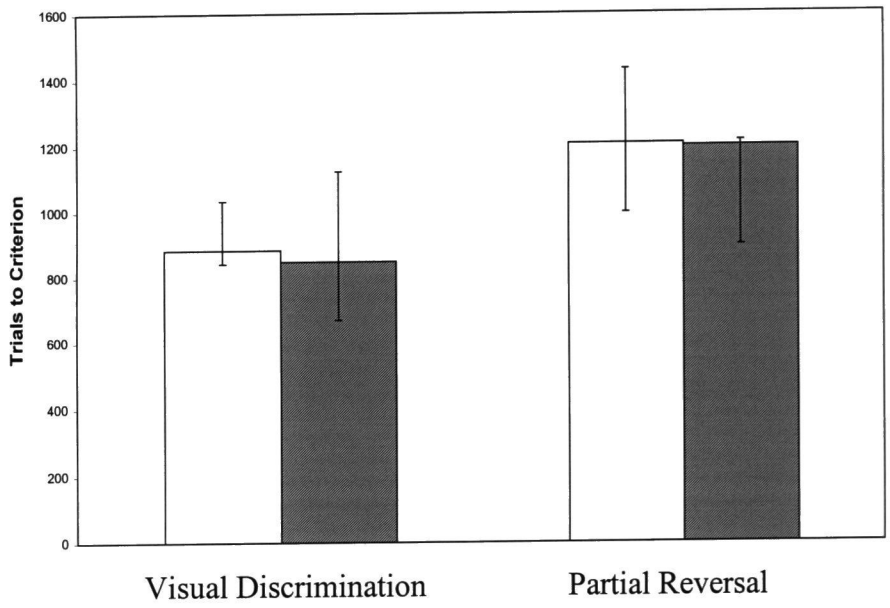


Figure 8.2. The mean number of trials accumulated by the animals that completed the configural task (perirhinal animals, striped bars, sham animals, open bars), in four pairs of visual discriminations and two partial reversals. The error bars show the range of scores.

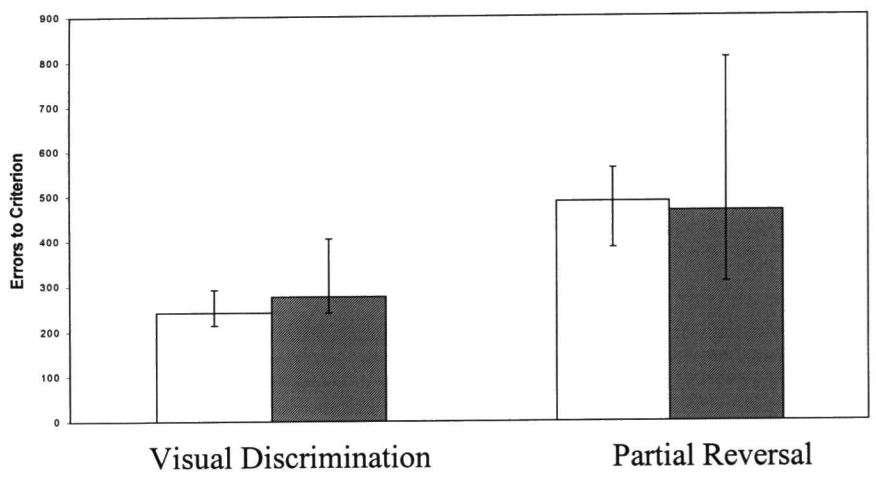


Figure 8.3. The mean number of errors accumulated by the animals that completed the configural learning task (perirhinal animals, striped bars, sham animals, open bars) in four pairs of visual discriminations and two partial reversals. The error bars show the range of scores.

These results suggest that the perirhinal animals were impaired in performing the simple visual discrimination, as they accumulated a higher

number of errors to attain criterion in the task (approaching significance). Similarly, three perirhinal animals failed to attain criterion in the partial reversals for objects 5 to 8, suggesting an impairment. However, although no animals showed any signs of illness during testing in the simple discrimination and reversal, seven animals (perirhinal animals R04, R07, R016, R017, R020, R021 and sham animal, R011) developed illnesses and died before completing the configural learning task. As the simple discrimination and partial reversal tasks were included as control tests for the configural learning tasks, statisistical analysis was performed for those animals that completed both the visual discrimination and the configural discrimination task. The number of trials ($t = <1$) and errors ($t = 1.001$) accumulated in attaining criterion in the four pairs of simple visual discriminations did not differ significantly between the perirhinal and sham animals. Similarly the number of trials ($t = <1$) and errors ($t = <1$) accumulated in attaining criterion in the partial reversals did not differ between the perirhinal and sham animals. Therefore, when those animals that later developed illnesses were removed from the analysis, the perirhinal animals do not demonstrate any impairments in the simple discrimination task or its partial reversal.

Task 2: Visual Configural Discrimination Learning

Figures 8.4 and 8.5 show the mean numbers of trials and errors accumulated by the perirhinal and sham animals in attaining criterion in each phase of the configural task. One perirhinal animal, R015, failed to attain criterion in phase 3 of testing. Phase 1 contained four pairs of visual

discriminations, phase 2 contained two partial configural tasks and phase 3 contained the complete configural task.

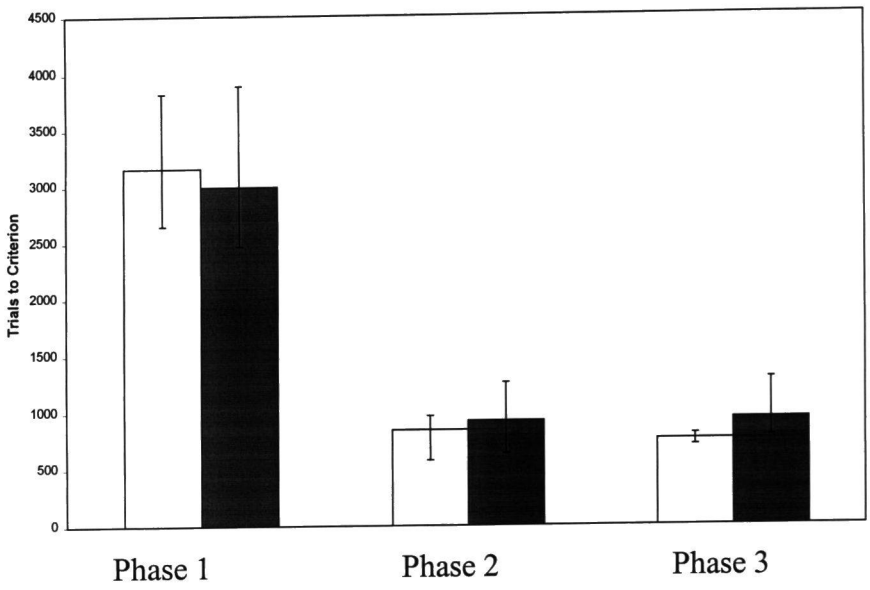


Figure 8.4. The number of trials taken to attain criterion in phases 1, 2 & 3 separately by the sham animals, open bars, and the perirhinal animals, striped bars. The error bars show the range of scores

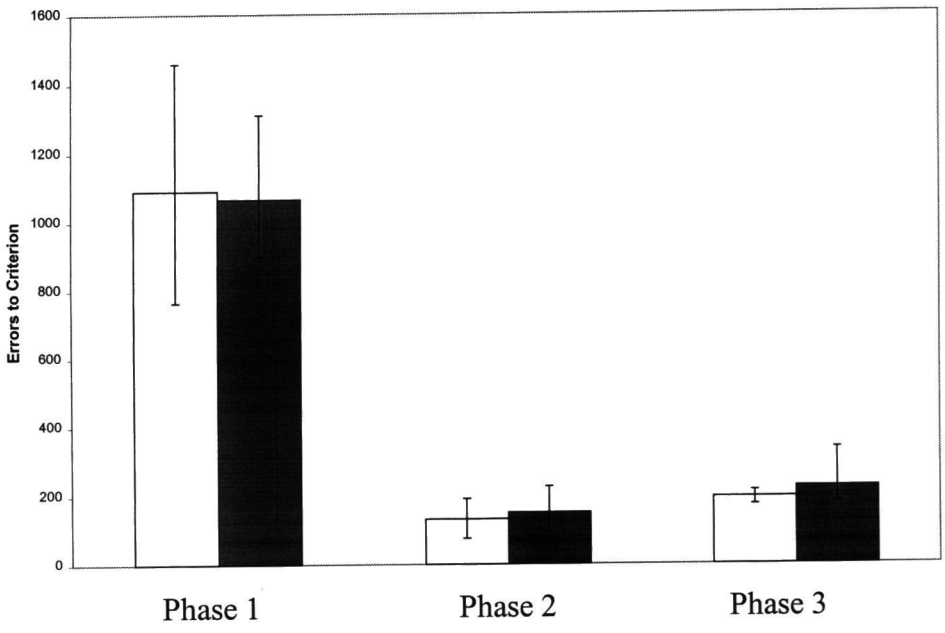


Figure 8.5 The number of errors taken to attain criterion in phases 1, 2 & 3 separately by the sham animals, open bars, and the perirhinal animals, striped bars. The error bars show the range of scores.

Tables 8.3 and 8.4 show the number of errors and trials accumulated by the sham and perirhinal animals in each phase of the configural task. Overall, the perirhinal animals accumulated a higher mean number of trials and errors than the sham animals in attaining criterion in all phases of the task combined. However, this difference was not statistically significant (Trials: $U = 11$, $p = 0.831$; Errors: $U = 9.5$, $p = 0.593$). A non-parametric test was used as one perirhinal animal failed to attain criterion in the task. The number of trials and errors accumulated in attaining criterion in phase 1 of testing were not significantly different between groups (Trials: $t = <1$; Errors: $t = <1$). Therefore, perirhinal ablation did not impair acquisition of the four pairs of visual discriminations. Tables 8. 2 and 8.3 show how the perirhinal animals accumulated a lower mean number of trials and errors to criterion than the sham animals in this stage of learning.

Table 8.3. The number of trials accumulated in attaining criterion in the visual configural learning task (F = failed to attain criterion).

RAT	Total Trials	Trials Phase 1	Trials Phase 2	Trials Phase 3	Trials Phase 2 & 3
		Sham Operated Animals			
R03	5486	3822	964	700	1664
R05	4949	3233	938	778	1716
R09	4025	2649	576	800	1376
R013	4580	2935	900	745	1645
Mean	**4760**	**3159.75**	**844.5**	**755.75**	**1600.25**
		Perirhinal Operated Animals			
R08	4717	3155	734	825	1560
R010	4877	2949	1113	815	1928
R014	5054	2897	1257	900	2157
R015	5815	3894	632	(F) 1289	(F) 1921
R018	4148	2614	753	781	1534
R019	4505	2469	1036	1000	2036
Mean	**4852.6**	**2996.3**	**920.8**	**935**	**1854.5**

Table 8.4. The number of errors accumulated in attaining criterion in the visual configural learning task (F = failed to attain criterion).

RAT	Total Errors	Errors Phase 1	Errors Phase 2	Errors Phase 3	Errors Phase 2 & 3
		Sham Operated Animals			
R03	1851	1459	191	201	392
R05	1485	1135	136	214	350
R09	1034	764	75	195	270
R013	1304	1004	125	172	297
Mean	**1418.5**	**1090.5**	**131.75**	**195.5**	**327.25**
		Perirhinal Operated Animals			
R08	1353	1051	95	207	302
R010	1416	1029	195	192	387
R014	1597	1154	226	217	443
R015	1255	1311	111	(F) 337	(F) 448
R018	1759	952	122	181	303
R019	1272	898	156	218	374
Mean	**1442**	**1065.8**	**150.8**	**225.3**	**376.17**

Tables 8.3 and 8.4 show how the perirhinal animals accumulated a higher number of trials and errors than the sham animals to attain criterion at phase 2, however this difference was not significant (Trials: $t = 1$; Errors: $t = <1$). In phase 3 animals were tested in the full configural learning task. As one perirhinal animal, R015, failed to attain criterion at this stage, nonparametric tests were used to compare the performances of the sham and perirhinal animals. The number of trials taken to attain criterion in phase 3 were significantly different between the perirhinal and the sham animals ($U = 1$, $p = 0.019$), however the two groups did not differ significantly in the number of errors taken to attain criterion ($U = 7$, $p = 0.286$). Tables 8.2 and 8.3 and figures 8.4 and 8.5 show how the perirhinal animals accumulated more trials and errors in phase 3 of the task.

Phase 3 of the task comprised two different stages, the first was alternation of levels 5 and 6 of phase 2, and the second was level 7, in which all four stimuli were presented. Animals' performances in the different

stages of phase 3 were compared separately in one tailed t tests, as it was predicted that the perirhinal animals would accumulate more trials and errors to criterion than the sham animals. The number of trials accumulated in attaining criterion in alternation of levels 5 and 6 were significantly different between the perirhinal and sham animals (One tailed: $t = 2.078$, $df = 8$, $p = 0.036$). However, the number of errors accumulated were not significantly different (One tailed: $t = 1.49$, $df = 8$, $p = 0.087$). Although one perirhinal animal failed to attain criterion in level 7 of phase 3, there were no statistically significant differences between the number of trials and errors taken to attain criterion at this stage (Trials: $U = 9.5$, $p = 0.588$; Errors: $U = 11$, $p = 0.831$). Therefore, these results suggest that the perirhinal animals were more severely impaired when they first had to perform the full configural task. It is possible that the perirhinal animals were impaired in the first stage of phase 3 due to a specific difficulty in alternating discriminations. However, the number of trials and errors accumulated in attaining criterion in alternation of levels 1, 2, 3 & 4 of phase 1 were not significantly different between groups (Trials, $t = <1$; Errors: $t = <1$). Thus, there was no specific difficulty with alternating discriminations when there is an elemental solution.

These results suggest that the perirhinal animals are not impaired in elemental visual discrimination learning (phase1) or in partial configural learning (phase 2), but are impaired in the full visual configural learning task (phase 3). However, it would be expected that the perirhinal animals would experience an intermediate deficit in phase 2, as this was a test of partial configural learning. Further analysis of the deficit scores for each

phase of learning suggests that the perirhinal animals do experience an intermediate deficit in phase 2. A deficit score is defined as the difference between the group means expressed as a percentage of the level of the sham groups' performance, i.e. (sham mean – perirhinal mean)/sham mean x 100. A deficit score of zero would reveal no deficit, a positive score would reveal that the perirhinal animals performed better than the sham animals, whereas a negative score would reveal the converse. Figure 8.6 shows that the perirhinal animals demonstrated a positive deficit score in phase 1, suggesting no impairment. However, as shown in figure 8.6, the perirhinal animals demonstrated a negative deficit score in phases 2 and 3, suggesting an impairment.

The perirhinal animals deficit scores were compared to zero in a one sample t test. It was found that the deficits scores in phase 1 were not significantly different to zero ($t = 1.67$), however the deficit scores in phases 2 ($t = 3.26$, $df = 5$, $p = <0.05$) and 3 ($t = 13.5$, $df = 5$, $p = < 0.001$) were significantly different to zero. Table 8.5 shows that the analysis of both errors and trials produced the same pattern of deficit scores. The deficit score in phase 2 was smaller than the deficit score in phase 3, suggesting a smaller impairment in phase 2 than phase 3. Figures 8.4 and 8.5 show that the perirhinal animals accumulated more trials and errors than the sham animals in phases 2 and 3, but less in phase 1.

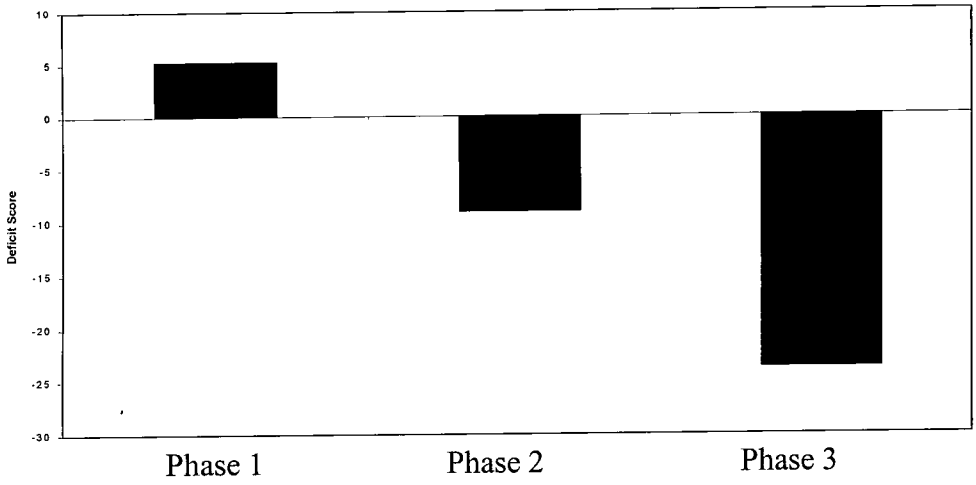


Figure 8.6. The deficit scores taken from the trials to criterion in phases 1 to 3.

Table 8.5 The deficit scores obtained by the perirhinal animals in each phase of testing.

	ERRORS	TRIALS
PHASE ONE	+ 2.3%	+5.2%
PHASE TWO	-14.5%	-9.0%
PHASE THREE	-15.2%	-23.7%

8.4 Discussion

The current study measured the effects of perirhinal ablation on acquisition of 4 pairs of visual discriminations and their partial reversal and acquisition of a visual biconditional configural task. The visual discriminations and partial reversals could be solved by an elemental associative system, as the individual stimuli were associated with reward. However, the configural task contained combinations of four stimuli that were equally presented as part of a rewarding or a non-rewarding compound stimulus and could only be solved by recognising the different stimuli

combinations within the task. Therefore, the current study compared the effects of perirhinal ablation on acquisition of a simple visual discrimination learning task and its reversal with acquisition of a configural learning task.

Although seventeen animals began training in the current study, only 10 animals completed the whole study, due to illness. Seventeen animals completed the simple visual discrimination and partial reversal, whereas only ten animals completed the visual configural task. Therefore, the sham and perirhinal animals performances in the simple visual discrimination and reversal were compared for the full seventeen animals that completed the task and then again for the ten animals that completed the task and went on to complete the configural learning task.

When performances of all animals were compared, the perirhinal animals showed signs of an impairment in the simple visual discrimination task. The number of trials accumulated in learning the discriminations did not differ from the sham animals. However, the difference between the number of errors accumulated by each group was approaching statistical significance, as the perirhinal animals accumulated a higher number of errors. The perirhinal animals performance in the partial reversals was not significantly different to the sham animals. However, the perirhinal animals accumulated more trials and errors than the sham animals and three perirhinal animals failed to attain criterion in the task. Therefore, the perirhinal animals acquisition of the visual discrimination task and partial discrimination reversal appear to be slightly, but nonsignificantly impaired. Although no animals showed any signs of illness whilst performing the discrimination task, it is possible that the early onset of illness affected these

animals performances in the simple visual discrimination and its partial reversal. However, comparison of the performances of those animals that did not become ill and went on to complete the configural learning task found that the number of trials or errors accumulated to attain criterion in the simple visual discrimination or its reversal were not significantly different between the perirhinal and sham animals. The results of those animals that did not become ill suggest that perirhinal ablation did not impair acquisition of the simple visual discrimination and its reversal.

The perirhinal animals` acquisition of the configural learning task was impaired. The perirhinal animals` performance in phase 1 of the task did not differ from that of the sham animals; this was expected as phase 1 measured acquisition of four pairs of two choice discriminations and did not test configural learning. The perirhinal animals experienced an intermediate deficit in acquisition of stage 2 that measured partial configural learning. The perirhinal animals were more severely impaired in phase 3 of the task that actually tested visual configural learning. Therefore, perirhinal ablation impaired performance in the final stages of the visual configural learning task.

The current finding of intact acquisition of the simple visual discrimination task is consistent with reports of intact acquisition of two choice visual discrimination learning following perirhinal ablation in the rat (Astur et al., 1995; Wiig, Cooper & Bear, 1996). The current findings are also consistent with reports of intact acquisition of concurrent visual discrimination learning following perirhinal ablation (Experiment 2, chapter 4, Machin & Eacott, in press). It was suggested in chapter 4 that acquisition

of the concurrent discrimination task remained intact following perirhinal ablation due to possible spatial cues in the stimuli used. However, the findings of the current study suggest that even acquisition of discrimination learning with discrete visual objects may remain intact following perirhinal ablation.

The current findings are inconsistent with reports of impaired acquisition of two choice discrimination learning following perirhinal ablation in the rat (Kornecook, 1995). The findings reported in experiment 3a (chapter 5) and 4 (chapter 6), suggest that acquisition of visual discrimination learning is impaired following perirhinal ablation, providing increased demands are made on identification of the visual stimuli in the task. Therefore, it is possible that the stimuli used in the present simple visual discrimination task did not reveal an impairment in acquisition following perirhinal ablation, as the task did not place enough demands on stimuli identification.

There were no significant differences between the perirhinal and sham animals acquisition of the partial discrimination reversals. However, three perirhinal animals that later became ill failed to attain criterion in the task. It is uncertain whether the poor performance of these perirhinal animals was due to the onset of illness, or to an inability to perform the task. Thus the results of the current study do not provide conclusive evidence as to the effects of perirhinal ablation on acquisition of visual discrimination reversals. However, if perirhinal ablation had a severe detrimental affect on visual discrimination reversal learning, it would be expected that the perirhinal animals that did not develop illnesses would have shown some

signs of impairment in the task. Therefore, the results of the current study suggest that the perirhinal cortex may not play a crucial role in visual discrimination reversal learning. This finding is inconsistent with previous reports of impaired object discrimination reversal learning following perirhinal ablation in the rat (Bussey et al., 1999). There are also reports of impaired acquisition of visual object reversal learning following rhinal ablation in the monkey (Murray, Baxter & Gaffan, 1998). The authors found acquisition of several object discriminations remained intact following perirhinal ablation, yet animals experienced severe deficits in learning a number of discrimination reversals (Murray, Baxter & Gaffan, 1998). It has been suggested that the perirhinal cortex may contribute to reversal learning by virtue of its connections to the orbital frontal cortex (Murray, Baxter & Gaffan, 1998). Therefore, perirhinal ablation may well disrupt the associative processes underlying normal reversal learning, yet, the test of partial reversal learning used in the current study may not have placed enough demands on the processes of discrimination reversal learning to reveal a deficit. The effects of perirhinal ablation on visual discrimination reversal learning need to be investigated more thoroughly, to determine whether the perirhinal cortex in the rat contributes to visual discrimination reversal learning.

It has been suggested that the perirhinal cortex sustains higher order visual processing by constructing complex representations of visual objects and their meaning, whereas representations of simpler object features may be distributed in cells across the perirhinal cortex and inferotemporal area TE (Murray & Bussey, 1999). It is possible that such a process requires

associative flexibility or the need to perform associative reversals, as objects associations and object feature associations may well change over time or in different contexts. The visual stimuli used in the partial discrimination reversal in the current study was not very complex and were not designed to contain overlapping feature elements. Therefore, representations of these stimuli and performance in the partial reversal task may have been sustained by cells in inferotemporal area TE, suggesting that the perirhinal cortex may only contribute to discrimination reversal learning for complex visual stimuli.

The present finding of impaired configural learning is consistent with previous reports of impaired acquisition of visual biconditional learning following perirhinal ablation in the primate (Buckley & Gaffan, 1998c). The current findings are also consistent with reports of impaired visual-visual associative learning following rhinal ablation in the primate (Murray et al., 1993). The results of the current study suggest that acquisition of simple visual discrimination learning and discrimination reversal learning remain intact following perirhinal ablation, whereas visual biconditional configural learning is impaired. Therefore, the impairments in the visual biconditional configural task were not due to a general impairment in visual discrimination learning. Furthermore, these results suggest that the impairments in visual biconditonal configural learning are not due to general impairments in the ability to perform visual discrimination reversals. Together these results suggest that the perirhinal cortex is necessary for nonspatial visual biconditional configural learning. It is not our prediction that perirhinal ablation produces a general deficit in

visual configural learning. It is more likely that perirhinal ablation produces impairments in visual biconditional learning as this task is an example of visual learning regarding stimuli with overlapping visual features.

There are limitations to the argument that the perirhinal cortex is crucial for visual biconditonal configural learning. Firstly, although the perirhinal animals were impaired in performing the biconditonal task, it could be argued that the perirhinal animals deficit in the task was not very severe. The perirhinal animals were significantly impaired in the first stage of phase 3; however, their performance in the final stage of phase 3 was not significantly different to the sham animals. Furthermore, in the current study only one perirhinal animal failed to attain criterion in the configural learning task, whereas three animals failed to attain criterion in the discrimination reversal. If visual configural learning were exclusively dependent upon the perirhinal cortex, then it would be expected that the perirhinal animals might never actually learn the task. Therefore, if the biconditional associative system is rendered ineffective following perirhinal ablation, the maximum accuracy of the perirhinal animals performance would be unlikely to exceed the theoretical maximum level of accuracy obtainable by an elemental associative system (Rickard & Grafman, 1998). If the perirhinal animals relied solely on an elemental system to perform the configural task, then more severe impairments would be expected. Alternatively, the perirhinal animals may have learnt to discriminate between the compound stimuli on the basis of their outline rather than their elemental stimuli, thus improving their performance in the final stages of testing. Therefore, the animals in the current study may have performed the

biconditional discrimination as a series of complex two choice discriminations, solvable by an elemental associative system.

The perirhinal cortex may sustain the identification of complex visual stimuli by integrating individual features within visual objects to provide holistic representations of visual stimuli. Configural learning would be reliant upon this process, as a number of visual stimuli share common visual elements or features. Therefore, the biconditional task is a useful measure, as the compound stimuli are akin to complex visual stimuli that share common features. However, it has been suggested that biconditional learning may not be the most demanding test of visual configural learning (Rudy & Sutherland, 1995), as the elemental stimuli are always presented in pairs of configured stimuli and never alone with their own reinforcement schedule. Therefore, the elements of the compound stimuli do not acquire associative strengths of their own that may conflict with their subsequent conjunctions. Thus, the configural units themselves acquire inhibitory or excitatory associative strengths, suggesting it may be possible to compare the overall shape of each compound as an individual element. This point is salient in the context of the current study, as it is difficult to determine the degree to which animals classify visual objects in terms of their elemental features, or general outline appearance. In the current study, all animals failed to learn to discriminate between the compounds BX and BY, until the lines, X and Y, were slightly lengthened. In the original compounds of BX and BY the overall shapes of the compound stimuli were not markedly different, as the lines X and Y ended just outside of the boundary of the shape, B. These findings suggest that

even the sham animals may have performed the discrimination on the basis of the overall outline of each compound stimuli, rather than the combination of its elements. Even so, the general outline of each compound stimuli would still contain common features, suggesting performance in the task may always rely on the identification of common elements to a certain extent.

One question raised by these results is whether the perirhinal cortex plays a general role in biconditional learning across sensory modalities, or is specialised in visual biconditional learning. It would be of interest to determine whether the perirhinal cortex contributes to visual configural learning for the purposes of identifying visual objects with overlapping feature elements, or whether the perirhinal cortex contributes to biconditional configural learning across sensory modalities. Furthermore, it would be of interest to determine whether forms of configural learning, other than biconditional learning, are disrupted following perirhinal ablation. The effects of perirhinal ablation on cross modal biconditional learning tasks are not known. However, there is evidence that rhinal lesions in rats impair performance in an odour guided transverse patterning task (Dusek & Eichenbaum, 1998). Therefore, the rhinal cortices may play a role in configural learning across sensory modalities. There are several possible explanations why configural learning is disrupted following perirhinal ablation. For example, perirhinal ablation may disrupt the flow of sensory information to other areas that are crucial for configural associative tasks (Dusek & Eichenbaum, 1998). An alternative explanation is the

perirhinal cortex itself sustains complex associative learning processes, including visual configural learning (Murray & Bussey, 1999).

Our findings of impaired visual biconditional learning conflict with the notion that the hippocampus sustains configural learning processes (Sutherland & Rudy, 1989). In a recent review of association theory, it has been suggested that the hippocampus enhances the processes of configural learning in cortical areas (Rudy & Sutherland, 1995). Therefore, combined lesions to the perirhinal cortex and the hippocampus may produce more profound deficits in configural learning. However, it has been shown that lesions to the fornix actually facilitate rats' performances in a visual transverse patterning task (Bussey et al., 1998). The authors suggest that fornix lesions may enable animals to abandon an elemental strategy to perform the task and concentrate on a configural strategy (Bussey et al., 1998). Therefore, it remains to be seen whether combined lesions to the hippocampus and perirhinal cortex produce more or less severe deficits in configural learning than perirhinal lesions alone. It has been suggested that perirhinal lesions disrupt configural learning by depriving the hippocampus of polymodal sensory information (Dusek & Eichenbaum, 1998). It has been found that hippocampal lesion in rats impair recognition of large featureless visual stimuli, whereas recognition of discrete salient objects remains intact (Rawlins et al., 1993). However, cells within the perirhinal cortex in rats respond best to discrete salient visual objects (Zhu, Brown & Aggleton, 1995). Therefore, it would be possible to test the notion that perirhinal lesions impair visual configural learning tasks by depriving the hippocampus of sensory information by testing configural learning tasks

with different classes of sensory stimuli. Such a task would place different demands on the purported need for sensory information from the perirhinal cortices. Therefore it would be expected that perirhinal lesions would not impair configural associative tasks with large featureless visual stimuli.

Reports that perirhinal ablation disrupts configural learning have led to the suggestion that the role of the perirhinal cortex extends beyond visual stimuli recognition and simple associative processes to contribute to configural associative processes (Murray & Bussey, 1999). It has been suggested that the perirhinal cortex may combine visual information with crossmodal sensory information to build rich representations of visual objects and their meaning (Eacott & Heywood, 1995; Murray & Bussey, 1999). The processes of higher order visual processing in the perirhinal cortex may be reliant upon the process of configural associative learning, with more caudal aspects of inferotemporal cortex being capable of sustaining simple visual associative learning (Murray & Bussey, 1999). However, the perirhinal cortex has been shown to contribute to the processes of perceptual learning regarding visual stimuli (Nakamura & Kubota, 1996) and elemental associative learning processes (Buckley & Gaffan, 1997; Eacott, 1998; Eacott & Heywood, 1995). For example, following perirhinal ablation, the animals in experiments 3a (chapter 5) and 4 (chapter 6) were impaired in elemental associative learning regarding relatively simple visual stimuli. However, in the current study acquisition of a simple visual discrimination task remained intact following perirhinal ablation. In experiments 3a and 4, more demands were placed on the identification of the visual stimuli in the tasks. Therefore, perirhinal

ablation may only disrupt the acquisition of elemental visual associative learning if the task assumes relatively high demands on the processes of visual stimuli identification. Therefore, the results of the current study are consistent with previous accounts of the role of the perirhinal cortex in visual configural learning and stimuli identification (Eacott & Heywood, 1995; Murray & Bussey, 1999).

It is uncertain how visual learning processes within the perirhinal cortex may contribute to episodic memory processes or just to semantic memory. It has been suggested that episodic memory is reliant upon the recall of complex visual scenes that represent past events (Gaffan, 1994). The purported role of the perirhinal cortex in this process is to pass information regarding visual objects to the hippocampus to be configured along with spatial information regarding the location of those objects within a scene (Primates: Murray, Baxter & Gaffan, 1998). However, there is evidence to suggest that visual information from the perirhinal cortex is not necessary for rats' performance in a test of allocentric spatial memory in the water maze (Bussey et al., 1999). One possible explanation for the opposing results of the previous studies is differences in complexity of the visual stimuli used in the tasks may have placed different demands on processes normally performed by the perirhinal cortex. Therefore, it remains to be seen whether configural processes within the perirhinal cortex extend to configuring spatial information with visual stimuli in the rat as suggested in the monkey (Murray, Baxter, Gaffan, 1998).

In summary, the current study suggests that perirhinal ablation disrupts visual biconditional associative learning, but not simple elemental

visual discrimination learning and discrimination reversals. These findings are consistent with the proposal that the perirhinal cortex sustains complex or higher order visual processing by encoding combinations of sensory features that differentiate complex visual objects (Eacott & Heywood, 1995; Murray & Bussey, 1999). Further research is needed to ascertain whether perirhinal ablation disrupts other forms of configural learning regarding both visual and nonvisual stimuli, to determine whether it plays a role in establishing multimodal sensory information regarding visual objects. This would help elucidate its role in establishing complex visual scenes, thought to underlie episodic memory (Gaffan, 1996) and knowledge regarding visual objects, thought to underlie semantic memory (Murray & Bussey, 1999).

Chapter 9: General Discussion

9.1 Introduction

The aim of the experiments reported here was to provide new insights into the role of the perirhinal cortex in visual associative learning. This chapter will assess the extent to which this aim has been fulfilled and discuss the findings reported here in light of existing theories of perirhinal function and memory in the medial temporal lobe. Section 9.2 examines the role of the perirhinal cortex in both acquisition and retention of visual discrimination learning. The third part discusses the implications of the findings reported in this thesis for theories of perirhinal function and memory processes within the medial temporal lobe. The fourth section summarises the conclusions that can be drawn from the results of this thesis regarding the role of the perirhinal cortex in visual learning and memory. The final part outlines proposals for future research questions to further our understanding of the wider role of the perirhinal cortex in visual discrimination learning and memory.

9.2 The Role of the Perirhinal Cortex in Acquisition and Retention of Visual Discrimination Learning

The main aim of the studies reported in this thesis was to explore the role of the perirhinal cortex in visual discrimination learning. Therefore, the aim of experiment 1 (chapter 3) was to determine whether perirhinal ablation results in a deficit in the retention of concurrent visual discrimination learning. The aim of experiment 2 (chapter 4) was to determine whether perirhinal ablation impairs acquisition of concurrent visual discrimination learning when increased demands are made on

identification of the visual stimuli in the task. The aim of experiments 3a and 3b (chapter 5) was to determine whether the perirhinal cortex contributes to the sensory process of identifying and generalising to familiar visual stimuli in a discrimination task learnt either prior to (experiment 3b) or following surgery (experiment 3a). The aim of experiment 4 (chapter 6) was to determine whether increasing demands on stimulus identification impaired acquisition of a titrating visual generalisation task. The aim of experiment 5 (chapter 7) was to determine whether perirhinal ablation had a detrimental affect on the acquisition of a visual generalisation task with complex visual stimuli. The aim of experiment 6 (chapter 8) was to determine whether perirhinal ablation impaired acquisition of an elemental visual discrimination tasks and its partial discrimination reversal and acquisition of a configural visual discrimination task.

The results of previous studies in both rodents (Eacott, 1998) and primates (Murray & Gaffan, 1992; Thornton, Rothblat & Murray, 1997) suggest that perirhinal lesions impair the retention of visual discrimination learning, whereas post-operative acquisition remains intact. However, recent findings in the monkey have led to the suggestion that perirhinal ablation impairs acquisition of visual associative learning providing the learning task places sufficient demands on identifying the visual stimuli used in the task (Buckley & Gaffan, 1997). It has been suggested that perirhinal ablation disrupts the retention of visual discrimination learning more readily than acquisition, due to the convergence of object feature representations within the inferotemporal cortex (Murray & Bussey, 1999).

The authors suggest that visual stimuli are encoded as gestalt representations within the perirhinal cortex, following perirhinal ablation this information is lost, resulting in a retention deficit. However, following perirhinal ablation, acquisition of new learning is thought to be sustained by simpler visual feature representations encoded in the more caudal aspects of inferotemporal cortex (Murray & Bussey, 1999).

9.2 i Deficits in Retention of Visual Associative Information

Experiment 1 (chapter 3) measured the effects of perirhinal ablation on retention of visual associative learning. To a lesser extent the findings of experiment 3b (chapter 5) also measured the effects of perirhinal ablation on retention of simple visual discrimination learning, therefore the results of this study will also be considered here. The findings of both studies suggest that lesions to the perirhinal cortex produce deficits in retention of visual discrimination learning for both visual scenes and simple geometric shapes. Experiment 1 compared the effect of perirhinal ablation on retention of two sets of concurrent visual discriminations acquired at different time intervals prior to surgery. It was found that the post-operative retention deficit was limited to immediate post-operative performance, as retention of the second set tested following surgery was comparable to, and in some instances better than, the sham animals. The stimuli used in experiment 1 were junk visual scenes; therefore, areas other than the perirhinal cortex may sustain retention of visual discriminative learning that can be solved by relying on spatial cues. However, perirhinal ablation did result in an initial deficit in retention, suggesting it is implicated in the retention process for visual scenes. The

recovery of function found in experiment 1 maybe due to animals performing the discrimination based on spatial cues, rather than cues inherent in the objects within the scenes.

The first experiment (chapter 3) tested the hypothesis that the perirhinal cortex contributes to a time limited consolidation process for visual associative information. It was found that the time at which the discrimination was acquired prior to surgery had no effect on its subsequent retention. Therefore, the perirhinal cortex does not appear to contribute to a temporally graded consolidation process for visual associative information.

Experiment 3b (chapter 5) measured the effects of perirhinal ablation on post-operative performance in a visual generalisation task learnt prior to surgery. Therefore the task tested retention of the base discrimination and to a lesser extent the transformed stimuli. Post-operative performance in the generalisation task is deemed to be reliant upon identification of the base discrimination and generalisations to the non-rewarded stimuli within it. Thus, the generalisation task required animals to make judgements regarding the sensory classification of the transformed stimuli in the task, i.e. does the transformed stimuli resemble the rewarded or non-rewarded stimuli? However, animals may have performed the task by learning to discriminate between the individual transformations in the task prior to surgery. If this were the case, post-operative deficits in the generalisation task may reflect poor retention of associative information regarding each transformed stimuli. It was found that the perirhinal animals were impaired in generalising to variations in

stimulus form, but not size. Therefore, stimulus type had different effects on post-operative performance in the task. Generalisations to variations in stimulus form may have placed more demands on stimulus identification and classification than generalising to variations in stimulus size. Similarly, the retention of the junk scenes used in experiment 1 may have placed fewer demands on stimulus identification than the generalisation task in experiment 3b, resulting in a transient retention deficit.

The results of experiments 1 (chapter 3) and 3b (chapter 5) both suggest that the perirhinal cortex contributes to the retention of visual associative learning. However, perirhinal ablation led to a transient impairment in the retention of a concurrent visual discrimination task with visual scenes in experiment 1 and impaired generalisations to variations in stimulus form, but not size in experiment 3b (chapter 5). These findings suggest that the nature of the impairments in retention following perirhinal ablation may be influenced by the type of visual stimuli used in the task or the associative demands of the task.

9.2 ii Deficits in Acquisition of Visual Associative Information

It has been suggested that perirhinal lesions only disrupt acquisition of new visual discrimination learning when increased demands are made on identifying the visual stimuli in the task (Buckley & Gaffan, 1997). Experiment 2 (chapter 4) measured the effects of perirhinal ablation on acquisition of a concurrent visual discrimination task that placed increased demands on stimulus identification. It was found that acquisition of the concurrent visual discrimination task with visual scenes remained intact following perirhinal ablation, even when the number of stimuli in

the task was increased to place further demands on stimulus identification. This finding suggests that areas other than the perirhinal cortex sustain new visual learning when the stimuli used are complex visual scenes, containing spatial cues.

Experiment 3a (chapter 5) measured the effects of perirhinal ablation on acquisition of a visual generalisation task in animals with no pre-operative experience in visual discrimination learning. Animals learnt a simple two choice visual discrimination and their generalisations to size or form transformations of the non-rewarded stimulus from the original discrimination were then measured. Acquisition of the base discrimination, containing simple geometric shapes, remained intact following perirhinal ablation. However, the perirhinal animals' performance in the base discrimination was impaired when it was placed in the visual generalisation task. Performing the base discrimination in the generalisation task may have increased demands on stimulus identification, resulting in the deficit seen. If this were the case, this finding supports the view that increasing demands on stimulus identification impairs acquisition of visual discrimination learning following perirhinal ablation (Buckley & Gaffan, 1997). Alternatively, deficits in the base discrimination trials in the generalisation task may reflect disruption to the transfer of knowledge regarding the test stimuli to the novel situation of the generalisation task. This view is consistent with the notion that the perirhinal cortex, along with the other components in the hippocampal formation, sustains the flexible expression of associative information (Eichenbaum et al., 1996).

Experiment 4 (chapter 6) measured acquisition of a titrating visual generalisation task. In this task the demands on object identification were increased, as there were no presentations of the base discrimination or set levels of transformation of the stimuli. It was found that only the perirhinal animals without pre-operative experience in visual discrimination learning, were impaired in acquiring the titration task. The perirhinal animals without pre-operative experience in visual learning were more severely impaired than the perirhinal animals with pre-operative experience. Therefore, the lack of pre-operative experience in visual learning appears to result in more severe acquisition deficits following perirhinal ablation. However, it should be noted that the perirhinal animals without pre-operative experience in the generalisation task had less experience overall than the other animals in the task. This finding suggests that increased experience benefited acquisition of the task. It remains to be seen whether pre-operative and post-operative experience of visual discrimination learning are equally beneficial on post-operative performances in such tasks. In generalisation task, one possible benefit of pre-operative experience in visual discrimination learning may be due to animals gaining experience of the rules of generalisation tasks. Alternatively, perceptual learning regarding the stimuli in the task may have been encoded in areas other than the perirhinal cortex and was of limited used in the acquisition of the titration task described in chapter 4. This finding is consistent with the view that visual stimuli representations may be encoded in multiple traces throughout inferotemporal cortex (Murray & Bussey, 1999).

The deficits in new learning, evident in the generalisation tasks described in experiments 3b (chapter 5) and 4 (chapter 6), suggest that acquisition of discrimination learning with relatively simple visual stimuli is impaired when increased demands are placed on the processes of object identification by introducing a number of similar stimuli. The aim of experiment 5 (chapter 7) was to measure the effects of perirhinal ablation on acquisition of a visual generalisation task with complex visual stimuli, thereby increasing the demands on stimulus identification even further. Both the perirhinal and sham operated animals failed to attain criterion in this task, emphasising the difficulties in judging the complexity of the stimuli used in visual learning tasks.

Experiment 6, (chapter 8) examined the effects of perirhinal ablation on the acquisition of a simple visual discrimination and its partial reversal and a visual configural learning task. In visual discrimination learning configural processes may enable the formation of holistic stimuli representations, that are comprised of a number of individual visual features (Eacott & Heywood, 1995; Murray & Bussey, 1999). It was found that acquisition of the simple visual discrimination and its reversal remained intact following perirhinal ablation. However, acquisition of the configural learning task was impaired. This finding is consistent with the view that the perirhinal cortex contributes to the configural process of object feature convergence (Murray & Bussey, 1999) and classification of large numbers of visual stimuli (Eacott et al., 1994; Eacott & Heywood, 1995).

Therefore, the results of experiments 3a, 4 and 6 suggest that perirhinal ablation impairs acquisition of elemental (experiments 3a & 4, chapters 5 & 6) and configural (experiment 6, chapter 8) visual discrimination learning tasks. However, perirhinal ablation did not impair acquisition of a simple visual discrimination between 4 pairs of stimuli (chapter 8). Furthermore, acquisition of a concurrent visual discrimination with 15 pairs of stimuli remained intact following perirhinal ablation (chapter 4).

These findings support the notion that perirhinal ablation impairs acquisition of visual associative learning tasks in which the demands on object identification are relatively high (Buckley & Gaffan, 1997). Our results suggest that even acquisition of relatively simple two choice visual discrimination learning is impaired following perirhinal ablation, providing sufficient demands are placed on the processes of stimulus identification. Furthermore, the acquisition of the simple discrimination learning task in experiment 6 (chapter 8) may have remained intact, as this task did not place sufficient demands on stimulus identification. However, it could be argued that, if acquisition deficits reflect the demands made on stimulus identification, then more severe deficits would be expected in the configural task described in chapter 8. In this task the perirhinal animals were only impaired in acquisition of phase 3 of learning, not on the earlier phases that were not strictly configural tests, but that placed relatively high demands on the processes of stimulus identification, due to the number of overlapping feature elements. However, judging the demands placed on stimulus identification by the tasks described in this thesis, is not entirely

objective, as we have no independent means of measuring the levels of visual identification required for each task.

The results of experiment 2 (chapter 4) suggest that perirhinal ablation does not impair acquisition of a concurrent visual discrimination learning task, in which the stimuli resembled complex visual scenes. This task placed relatively high demands on object identification processes, as animals had to learn to identify 30 visual scenes that contained a high number of overlapping visual features. It has been suggested that the perirhinal cortex aids the identification of visual scenes by associating individual features with their spatial arrangement (Gaffan, 1994). Therefore, it would be expected that deficits in object memory would prevent learning about objects within visual scenes. One possible interpretation of experiment 2 is that animals performed the discrimination purely on the basis of spatial cues, without relying on recognition of the individual objects within the scenes. The sham animals experienced difficulties in the task at 13 pairs and over, suggesting rats may be predisposed to perform the discrimination by relying on identification of the objects within the scenes, rather than their spatial composition. Therefore, increasing the number of stimuli in the task further may reveal a deficit in acquisition following perirhinal ablation, as scenes with similar spatial arrangements would eventually be introduced. For example, in primates perirhinal ablation leads to an impairment in acquisition of concurrent discrimination learning between 320 naturalistic scenes taken from film stills (Gaffan, 1994).

An alternative explanation is that the concurrent discrimination task used in experiments 1 (chapter 3) and 2 (chapter 4) placed different demands on associative learning processes to the tasks used in experiments 3a, 3b (chapter 5), 4 (chapter 6) and 6 (chapter 8). It has been suggested that concurrent visual discrimination learning is not dependent upon declarative memory processes, but can be solved by a habit learning system (Buffalo et al., 1998; Squire & M.Zola, 1996). Habit learning is thought to be reliant upon interaction between the corpus striatum and neocortex, whereas declarative memory is dependent upon the interaction between the limbic system, including the rhinal cortices, and the neocortex (Gaffan, 1996b; Mishkin & Petri, 1984; Squire & M.Zola, 1996). It has been suggested that inferotemporal area TE, not the perirhinal cortex, sustains concurrent visual discrimination learning (Buffalo et al., 1998). However, this view does not account for either the transient retention deficit reported in experiment 1 or the finding that the severity of damage to area TE had no effect on performance in experiments 1 (chapter 3) or 2 (chapter 4). Furthermore, it has been suggested that all forms of visual associative learning are dependent upon output from the visual association cortex to the corpus striatum so that habit and nonhabit learning may share the same associative mechanisms (Gaffan, 1996b).

In summary, the results reported here suggest that perirhinal ablation impairs both the acquisition and retention of visual associative learning. However, our findings suggest that the perirhinal cortex does not contribute to the acquisition and retention of all forms of visual associative learning, as deficits were not seen across all the tasks described. These

findings suggest that performances in tests of both new learning and retention are determined by the demands placed on associative processes or stimulus identification. The perirhinal cortex appears to be necessary for the acquisition and retention of visual learning that relies upon the discrimination between similar simple objects or more complex visual objects, providing sufficient demands are placed on the processes of stimulus identification. Furthermore, the results of experiment 6 (chapter 8) suggest that the perirhinal cortex may contribute to the acquisition of configural learning regarding visual object features. However, the perirhinal cortex appears to be less crucial for the acquisition and retention of visual associative information regarding visual scenes that may be solved on the basis of spatial cues.

9.3 Theoretical Implications

Although the primary aim of this thesis was to explore the role of the perirhinal cortex in visual discrimination learning, a further aim was to deepen our understanding of how individual structures within the medial temporal lobe sustain different forms of memory. Therefore, the results of this thesis can be interpreted alongside existing theories of memory in the medial temporal lobe and the putative function of the perirhinal cortex in visual memory.

One prominent theory of memory in the medial temporal lobe is that proposed by Squire and Zola Morgan (1991). They suggest that the hippocampus, along with the rhinal and parahippocampal cortices, sustains declarative memory processes by virtue of their extensive connections with neocortex. Therefore, the perirhinal cortex is deemed to contribute to

the consolidation and retention of complex memories by connecting the hippocampus with storage sites in neocortex. This process is temporary, as consolidation and retention is eventually sustained without the need for the hippocampal system for retention. This theory would predict that, following perirhinal ablation, the acquisition of new declarative learning would be impaired, and retrograde deficits would be temporally graded.

The results of experiment 1 (chapter 3) found no evidence to suggest that perirhinal ablation results in temporally graded retention deficits. Furthermore, the results of experiment 2 (chapter 4) suggest acquisition of concurrent visual discrimination learning remains intact following perirhinal ablation. The authors suggest that similar findings in primates are due to the concurrent discrimination task not placing sufficient demands on declarative memory processes (Buffalo et al., 1998; Squire and Morgan Zola, 1996). However, the notion that inferotemporal cortex area TE sustains concurrent discrimination learning (Buffalo et al., 1998) is not supported by the histological analysis of experiments 1 (chapter 3) and 2 (chapter 4).

The impairments in visual discrimination learning reported in this thesis (chapters 5, 6 & 8) support the view that the perirhinal cortex contributes to the retention and consolidation of visual associative information (Squire and Zola Morgan, 1991). However, the finding of intact acquisition in experiment 2 (chapter 4) contradicts the view that the perirhinal cortex contributes to the acquisition of all forms of declarative learning (Squire, Zola Morgan, 1991). More recently Squire and M. Zola (1997) have suggested that the rhinal and parahippocampal cortices may

maintain functionally distinct contributions to different forms of memory. This notion needs to be explored further to explain why perirhinal cortex ablation results in impairments in the acquisition or retention of visual associative learning for complex and simple discrete visual objects, but not acquisition of visual scenes as reported in this thesis.

The theory of memory in the medial temporal lobe proposed by Eichenbaum (1992) suggests that the rhinal and parahippocampal cortices interact with the hippocampus and sites in neocortex to sustain declarative memory. The findings from experiments 3a (chapter 5) and 4 (chapter 6) partly support the view that the perirhinal cortex is necessary for the retention and acquisition of associative information that can then be used in a flexible or relational way. However, it could be argued that performance in the concurrent visual discrimination tasks in experiments 1 (chapter 3) and 2 (chapter 4) also requires the flexible expression of associative information, due to the random pairings of the rewarded and non-rewarded stimuli. The results of these studies question the extent to which the perirhinal cortex is involved in the acquisition and retention of various forms of visual discrimination learning. Eichenbaum et al. (1996) suggests that the perirhinal cortex contributes to configural associative learning by passing sensory information on to the hippocampus. Therefore, the impairments in configural learning outlined in experiment 6 (chapter 8) would be expected, although it remains to be seen whether this is due to depriving the hippocampus of sensory information.

Two alternative views of memory in the medial temporal lobe suggest that declarative memory is maintained by an extended

hippocampal system, composed of the hippocampus, the fornix, the mamillary bodies and the anterior thalamic nuclei (Aggleton & Brown, 1999; Gaffan, 1994, 1998). The perirhinal cortex is thought to contribute to this memory system by providing information regarding visual objects to the hippocampus (Aggleton & Brown, 1999; Gaffan, 1998). The theory of memory proposed by Gaffan (1998) suggests that the perirhinal cortex contributes to episodic memory by providing information regarding visual objects to an extended hippocampal system, where object information is configured with idiothetic place information. The findings reported here support the view that the perirhinal cortex contributes to associative learning regarding visual objects. However, the results reported here have no bearing on how object information from the perirhinal cortex is utilised by the hippocampus.

Aggleton and Brown (1999) suggest that the perirhinal cortex, along with the medial dorsal nucleus of the thalamus, sustains visual familiarity or recognition processes and contributes to memory by passing information regarding visual objects to the extended hippocampal system. A distinction is made between the processes of recognition and recall, so that the separate perirhinal and hippocampal systems encode relations of visual features within objects and scenes respectively. Thus, the authors suggest that the functions of the perirhinal cortex and the hippocampus are dissociable; perirhinal lesions impair performance in visual recognition memory tasks, whereas hippocampal lesions impair performance in spatial memory tasks (Aggleton & Brown, 1999). In support of this view, experiments 1 (chapter 3) and 2 (chapter 4) suggest that the perirhinal

cortex may not be crucial for memory for visual scenes that may be solved on the basis of their spatial composition. However, the results of experiments 3a, 3b (chapter 5), 4 (chapter 6) and 6 (chapter 8) suggest that the perirhinal cortex may contribute to the long term process of object identity. Therefore, the notion that the perirhinal cortex is necessary for visual object recognition memory (Aggleton & Brown, 1999) could be expanded to consider the possible role of the perirhinal cortex in retention and acquisition of visual associative learning and the process of object identify. Therefore, the results of the experiments reported here are consistent with the view that the perirhinal cortex contributes to visual memory processes (Aggleton & Brown, 1999; Gaffan, 1998). However, our results suggest that the perirhinal cortex may also contribute to the identification of visual objects.

It has been suggested that the perirhinal cortex contributes to the categorisation and classification of visual objects (Eacott & Heywood, 1995; Murray & Bussey, 1999). The reports of impaired acquisition and retrieval of visual discrimination learning in chapters 3, 5, 6 and 8 support the view that the perirhinal cortex may contribute to the processes of visual object identification (Eacott & Heywood, 1995). It has been suggested that the perirhinal cortex constructs complete representations of complex visual objects, whereas inferotemporal area TE represents simpler visual features (Murray & Bussey, 1999). The authors predict that perirhinal ablation would lead to deficits in retention due to the loss of complex representations of visual objects, whereas acquisition of new information regarding simple objects can be sustained by area TE (Murray & Bussey,

1999). Therefore, perirhinal lesions would be expected to only disrupt acquisition of visual configural learning or discrimination learning that places high demands on identification of the stimuli in the task. This view is supported by the finding that acquisition of simple visual discrimination learning remains intact, but visual configural learning is impaired following perirhinal ablation (chapter 5, 6 & 8). The impairment in visual configural learning in experiment 6 (chapter 8) supports the notion that the perirhinal cortex sustains object identification by representing visual objects composed of a number of visual features (Eacott & Heywood, 1995; Murray & Bussey, 1999).

Therefore, the results reported here are consistent with previous views on the role of the perirhinal cortex in visual discrimination learning (Eacott & Heywood, 1995; Murray & Bussey, 1999) and provide further support for the notion that the perirhinal cortex maintains holistic representations of objects and their identity.

9.4 Conclusions: The Role of the Perirhinal Cortex in Visual Discrimination Learning

The results reported in this thesis suggest that the perirhinal cortex contributes to both the retention and acquisition of visual stimulus - reward associative learning in the rat. Furthermore, our findings suggest that the perirhinal cortex is implicated in identifying familiar visual stimuli for associative purposes. The functional specialism of the perirhinal cortex may lie in the ability to configure individual feature elements to form representations of complex visual forms. This process would enable identification of familiar visual stimuli presented amongst a high number

of other visual stimuli. This process may contribute to the processes of stimuli classification, as objects that share common features may also share forms of representation.

There is evidence to suggest that perceptual and mnemonic systems may be more closely integrated than previously considered (Eacott & Heywood, 1995;Gaffan, 1996a). For example, associative learning may be enhanced by perceptual learning regarding the stimuli used in an associative task, by enhancing discrimination of the stimuli in the task (Gaffan, 1996a). It has been suggested that an important aspect of perceptual learning is the ability to associate elements within a compound stimulus as complete or holistic representations of visual objects (Gaffan, 1996a; Murray & Bussey, 1999). This configural process would enable perceptual learning about a high number of visual objects that share common features or elements. Therefore, the perirhinal cortex may sustain perceptual learning and stimuli classification by virtue of its configural associative processes (Eacott & Heywood, 1995).

It remains to be seen whether the functions of the perirhinal cortex in discrimination learning are due to specialised mechanisms within perirhinal cells, or whether this area assumes its function by virtue of its connectional characteristics. One means of testing this notion is to consider the role of the perirhinal cortex in other forms of sensory discrimination learning.

9.5 Future Research

The results of the studies reported in this thesis raise further questions that may elucidate the role of the perirhinal cortex in visual

associative memory. The first possibility is to measure the effects of perirhinal ablation on acquisition of configural learning tasks with nonvisual stimuli. This would determine whether the perirhinal cortex contributes to visual configural learning for the purposes of building configural representations of visual stimuli, or contributes to configural learning across sensory modalities. It would also be of interest to consider how mechanisms within the perirhinal cortex may contribute to both visual recognition memory and longer term visual associative learning.

The second possibility is to compare the effects of lesions to the perirhinal cortex and area TE on acquisition of visual discrimination tasks using configured and simple visual stimuli. This would test the hypothesis that the perirhinal cortex and area TE sustain visual associative learning regarding complex and simple visual stimuli respectively.

It would be of interest to determine if information regarding object identity is utilised by the hippocampus to perform object - in - place associations or spatial tasks that require the identification of visual objects.

Finally it would be of interest to test for functional divisions within the perirhinal, postrhinal and entorhinal cortices, to determine how these areas may assume different contributions to visual learning.

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