

**The neural correlates of recognition
memory for complex visual stimuli in
the Medial Temporal Lobe**

by

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A thesis submitted to School of Psychology, Cardiff University,

for the degree of

DOCTOR OF PHILOSOPHY IN PSYCHOLOGY

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Abstract

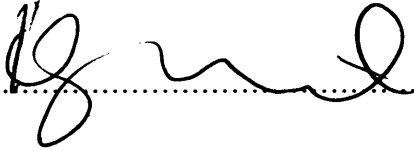
While a general role for the medial temporal lobe (MTL) in long-term memory is undisputed, the specific contributions made by MTL subregions remain contentious. For some accounts, separate but stimulus-independent regions support two different memory processes/types of mnemonic information (recollection and familiarity/items and contexts). According to another account, memory processes are not the primary organising principle of MTL function. Instead, sub-regions process different kinds of stimuli – for example, objects and scenes. The three experiments in this thesis were designed to compare competing models of MTL function by measuring, using functional magnetic resonance imaging, the neural correlates of successful recollection- and familiarity-based memory judgements for different types of complex visual stimuli.

Experiment 1 was designed to explore differences between encoding- and retrieval-related neural activity for faces and scenes. There was some evidence for stimulus-specific memory processing within the perirhinal cortex, anterior hippocampus and parahippocampal gyrus for faces, and the posterior hippocampus for scenes. The data from Experiment 1, however, offered limited insights into the processes that supported memory for these different stimulus types. In Experiment 2 encoding-related activity was assessed in a paradigm where participants had to indicate in which of two contexts/sources objects and scenes had been encountered in a study phase. In the hippocampus and parahippocampal gyrus there was activity predicting successful source encoding only for scenes. Activity in the perirhinal cortex, meanwhile, predicted item memory but not source memory for objects only. These findings are consistent with claims that stimulus-type is important for MTL function and aligns the hippocampus and perirhinal cortex with the processes of recollection and familiarity, respectively.

Experiment 3 was designed to investigate MTL contributions to source memory for objects, incorporating changes to the experiment design that were implemented in light of consideration of reasons for the absence of encoding-related activity predicting source memory for objects in Experiment 2. The critical finding was neural activity in the perirhinal cortex that predicted accurate source memory for objects. Collectively these results are consistent with views that the perirhinal cortex and hippocampus are differentially involved in processing objects and scenes, rather than in supporting distinct kinds of memory process.

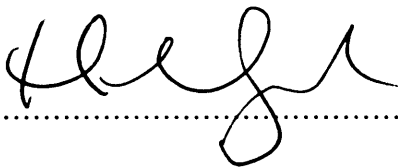
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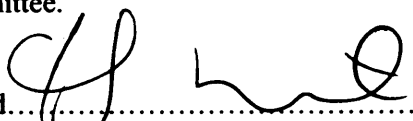
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Chapter 1

Introduction

The term 'memory' has been used by philosophers and psychologists for hundreds of years to encapsulate the mental processes that enable us to acquire, process, and store personal experiences. Due to the vast and diverse range of phenomena that the term memory could cover, it has become necessary to separate aspects of memory into smaller but related units (Tulving, 1983; see below for more details). At the neural level, memory can be broadly defined by changes in the pattern of synaptic connectivity between neurons. While these neural changes occur throughout the brain, the findings from behavioural and cognitive neuroscience suggest that there are distinct neural systems which support different facets of human memory. The experiments described in this thesis have been designed to investigate the neural basis of one of these memory systems, long-term memory, using functional magnetic resonance imaging (fMRI). This is a technique that indirectly measures brain activity. In this Introductory chapter I will provide; (a) further information about current taxonomies of human memory, with a particular focus on long-term memory, (b) a description of key cognitive processes that are thought to support long-term memory judgments, and (c) a discussion of theoretical accounts of how these mnemonic functions map on to regions in the human brain.

1.1. A brief overview of human memory

There is a large experimental literature which suggests that memory comprises a number of functionally distinct, but interactive components (Aggleton & Brown, 1999; Eichenbaum, Yonelinas, & Ranganath, 2007; Jacoby, 1991; Roediger, Zaromb, & Goode, 2008; Schacter & Tulving, 1994; Squire & Zola-Morgan, 1991; Tulving, 1972; 1983; Vargha-Khadem et al., 1997; Yonelinas, 2002). One of the earliest and most widely discussed distinctions in human memory is between short-term and long-term memory (Atkinson & Shiffrin, 1968; Baddeley, 2010; Baddeley & Hitch, 1974; James, 1890; Vallar, 2006). According to Atkinson and Shiffrin's (1968) modal account, short-term memory is a store with limited capacity (5-10 items) that can hold information over short durations (up to a minute). When information is sufficiently

rehearsed, it transfers to a long-term memory store, which has limitless capacity and allows information to be retained indefinitely (Atkinson & Shiffrin, 1968).

It is widely accepted that long-term memory comprises two main components; a conscious form that permits recovery and explicit report about facts and events, and a non-conscious form where memory for events influences behaviour, but is not accompanied by conscious awareness of the event. This classic separation of memory has been characterised as either the declarative/non-declarative (Graf & Schacter, 1985) or explicit/implicit distinction (Squire & Zola-Morgan, 1991). Implicit, or non-declarative, memory has been investigated using indirect tests, which assess memory without giving a reference to the prior learning episode (Squire, 1992; Roediger 2008). In contrast, explicit memory is typically examined by asking participants to respond to a direct request for information about prior experiences (Berntsen & Thomsen, 2005; Conway, Singer, & Tagini, 2004; Fitzgerald, 1988; Gardiner, 1988; Jacoby, 1991; Tulving, 1985; Yonelinas & Jacoby, 1994).

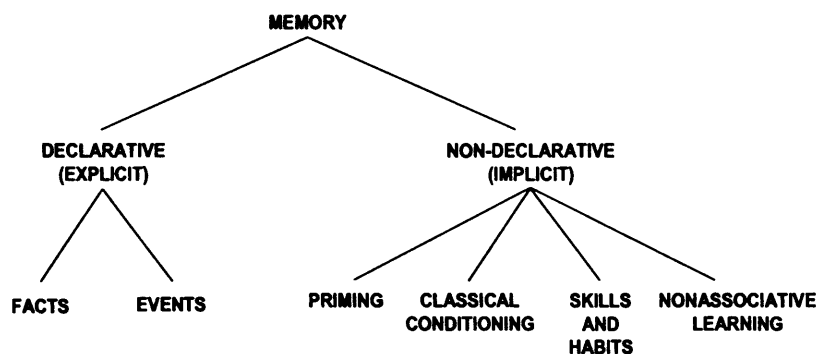


Figure 1.1: *The classification of human long-term memory. Figure adapted from Squire & Zola Morgan (1991).*

According to Squire and Zola-Morgan's (1991) taxonomy of long-term memory (Fig. 1.1), declarative/explicit memory fractionates into two systems, episodic and semantic, which informally accounts for differences between memories for events and facts, respectively (Tulving, 1972; 1983). Episodic memory receives and stores information about episodes and events, as well as the temporal and spatial relationships between them. Semantic memory includes knowledge about words and their meanings, rules, symbols, concepts and algorithms, and the relationships between words and objects. While the semantic/episodic distinction has been

characterised in terms of mutually exclusive stores of information, these stores are, by necessity, highly interactive (Graham, Simons, Pratt, Patterson, & Hodges, 2000; Greenberg, Keane, Ryan, & Verfaellie, 2009; Ryan, Cox, Hayes, & Nadel, 2008; Simons, Graham, Galton, Patterson, & Hodges, 2001; Small & Sandhu, 2008; Tulving, 1983).

The focus in this thesis is on episodic memory, which is typically assessed by performance on direct memory tasks. Recognition memory tasks are one kind of paradigm used to measure episodic retrieval. They have been used extensively to study the processes that support successful episodic memory judgments. In a typical recognition memory task, participants are presented with items, some of which will have been encountered in a prior study phase. The participant is asked to distinguish between items that were presented previously (old items) and items that were not (new items). The test phase of a recognition memory task can occur in the form of yes/no, in which participants respond yes (old) or no (new) to stimuli that are presented sequentially. Alternatively a forced-choice test can be adopted, in which a participant is presented with a pair (or more) of items and must identify which item/s was/were seen previously.

There are different psychological models of how recognition memory judgements are made (Donaldson, 1996; Jacoby, 1984, 1991; Mandler, 1980; Tulving, 1983; Wixted, 2007; Wixted & Stretch, 2004; Yonelinas, 1994, 2001a, 2002; Yonelinas, Kroll, Dobbins, Lazzara, & Knight, 1998), and others that specify the brain regions that support successful recognition (Aggleton & Brown, 1999; Brown & Aggleton, 2001; Davachi, 2006; Diana, Yonelinas, & Ranganath, 2007; Graham, Barense, & Lee, 2010; Mayes, Montaldi, & Migo, 2007; Squire, 2004; Squire, Stark, & Clark, 2004; Squire, Wixted, & Clark, 2007; Squire & Zola-Morgan, 1991). Guided by the findings from early lesion research, neuroanatomical models of long-term memory focus on the role of the medial temporal lobe (MTL). In this thesis, which aims to elucidate the neural basis of recognition memory, four views of MTL function are considered. These will be referred to as (a) unitary/strength-based (Squire & Zola-Morgan, 1991; Squire et al., 2004; Squire, 2004; Squire et al., 2007), (b) dual-process (Aggleton & Brown, 1999; Brown & Aggleton, 2001), (c) informational (Eichenbaum, Otto, & Cohen, 1994; Eichenbaum et al., 2007; Davachi., 2006; Diana

et al., 2007), and (d) representational (Bussey & Saksida, 2005; Cowell, Bussey, & Saksida, 2010; Graham et al., 2010; Murray & Bussey, 1999; Saksida & Bussey, 2010).

According to a unitary account, subregions of the MTL act in concert to form a single declarative memory system (Squire & Zola-Morgan, 1991; Squire et al., 2004; Squire, 2004; Squire et al., 2007). In contrast, dual-process, informational and representational models all agree that MTL regions play different roles in long-term memory. While the dual-process account posits that this functional fractionation is dictated by different operations that underpin episodic memory (Aggleton & Brown, 1999; Brown & Aggleton, 2001), informational accounts emphasise a division of labour that is guided by different types of mnemonic information (Davachi, 2006; Diana et al., 2007). Representational accounts focus on the formation of representations that are processed and stored by different MTL regions, and the circumstances under which these representations are recruited (Bussey & Saksida, 2005; Saksida & Bussey, 2010; Cowell et al., 2010; Graham et al., 2010). Due to the emphasis on representations, the latter form a broader class of MTL account that can make predictions that go beyond long-term episodic memory, and in which the *singular* characterisation of the MTL as a memory system is considered inadequate (Graham et al., 2010).

Different experimental approaches have been developed and used to identify and understand the psychological and neural basis of long-term memory; these include (a) animal lesion studies, (b) neuropsychological investigations of human amnesia, and (c) functional neuroimaging of healthy participants. Below, I discuss investigations that have used these different methodologies with the aim of providing a background to the main theoretical accounts that have subsequently emerged. Due to the emphasis on the MTL, below I provide a brief description of the relevant anatomy and throughout this chapter I concentrate solely on investigations applicable to the MTL.

1.2. The MTL and long-term memory

1.2.1. The anatomy of the MTL

The MTL comprises a number of highly interconnected, but separable, structures. At a broad level, the MTL can be subdivided into the perirhinal, entorhinal and parahippocampal cortices (collectively known as the parahippocampal gyrus), and the hippocampus (see Fig. 1.2). The perirhinal cortex is located in the anterior-medial aspect of the temporal lobe (BA 35 and 36) at the junction between the ventral visual processing stream and the MTL. The parahippocampal cortex (also known as the postrhinal cortex) is found in the posterior aspect of the MTL, immediately rostral to the dorsal visual processing stream. The hippocampal formation, which includes the CA1 and CA3 fields, subiculum and dentate gyrus, lies at the centre of the MTL and is surrounded by the entorhinal, parahippocampal and perirhinal cortices (Fig. 1.2).

In addition to the identification of distinct subregions, corticocortical connectivity in the MTL has been extensively mapped (Fig. 1.3; Burwell, 2000; Burwell & Amaral, 1998; Suzuki & Amaral, 1994; Ungerleider & Haxby, 1994). The majority of connections into the perirhinal cortex come from unimodal areas in the inferior

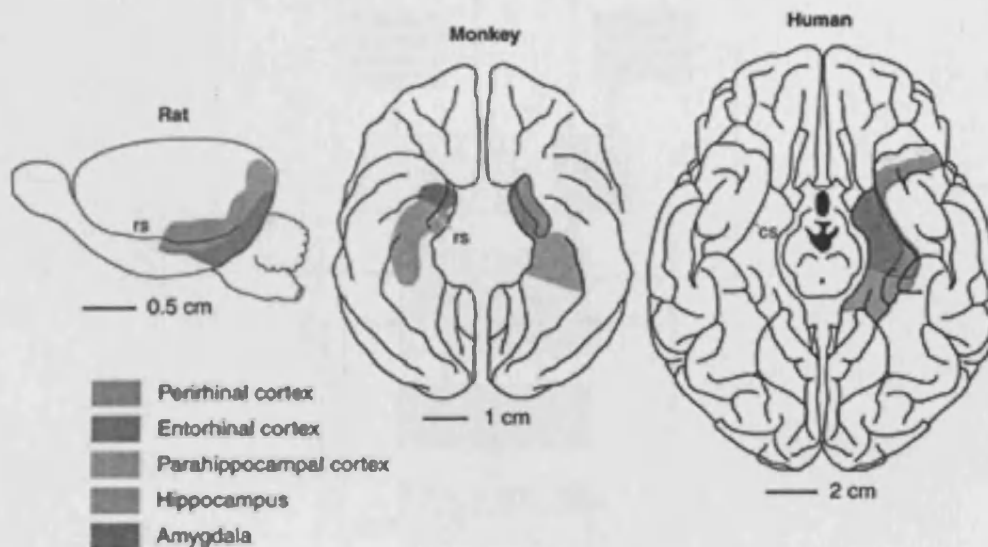


Figure 1.2: Lateral view of the rat brain (left), and ventral views of the rhesus macaque (middle) and human brain (right). Note that the region homologous to the parahippocampal cortex in monkeys is known as the postrhinal cortex in rats. The hippocampus, which is located deep in the temporal lobe, is indicated on the left side of the macaque brain. In rats (Burwell, 2001) and monkeys the boundary between the entorhinal cortex and perirhinal cortex is located near the fundus of the rhinal cortex, whereas in the human brain, much of the perirhinal cortex lies within the collateral sulcus (Insausti et al., 1998). Figure from Murray, Bussey, & Saksida (2007).

temporal cortex, such as TE and TEO in the ventral visual processing stream (which also project directly to the lateral aspect of the entorhinal cortex: Burwell & Amaral, 1998). There are also additional inputs from polymodal areas such as the superior temporal sulcus, somatosensory insular cortex, the auditory superior temporal gyrus, orbitofrontal cortex and cingulate cortex (Suzuki & Amaral, 1994; Ungerleider & Haxby, 1994). In contrast, the parahippocampal cortex receives the majority of its information from inferior parietal sites, such as the cingulate gyrus and retrosplenial cortex (which also project directly to the medial aspect of the entorhinal cortex: Aggleton & Brown, 1999). Notably, different profiles of corticocortical connectivity between unimodal/polymodal sensory areas and the perirhinal and parahippocampal cortices suggest that they receive substantially different types of information.

Although information transfers between the perirhinal and parahippocampal cortices, the majority of afferent perirhinal and parahippocampal connections project to, and relay back from, the lateral and medial aspects of the entorhinal cortex, respectively

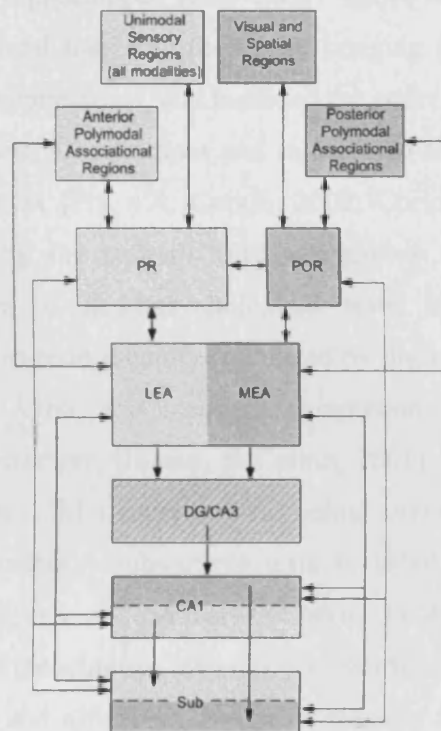


Figure 1.3: Schematic of corticocortical circuitry to show the multiple parallel pathways by which unimodal and polymodal information from the perirhinal and parahippocampal cortices converges (in a segregated fashion) in the hippocampal formation, via the entorhinal cortex. Abbreviations: (PR) perirhinal cortex; (POR) parahippocampal cortex; (LEA) lateral entorhinal cortex; (MEA) medial entorhinal cortex; (DG) dentate gyrus; (Sub) subiculum. Figure from Burwell (2000).

(Suzuki & Amaral, 1994; Burwell & Amaral, 1998). Information then passes from the entorhinal cortex to the dentate gyrus, CA3 and CA1 subfields and the subiculum in the hippocampal formation; the entorhinal cortex, therefore, can be characterised as an intermediate processing site that transfers information between perirhinal and parahippocampal cortices and the hippocampus (Burwell & Amaral, 1998). Consequently, as there are separate connections from the lateral and medial aspects of the entorhinal cortex to the dentate gyrus, CA1/CA3 fields and subiculum, the hippocampus receives combinations of different polysensory information in a segregated manner.

1.2.2. Early MTL lesion research

In 1953 perhaps the most famous patient in neuropsychological history, patient HM, underwent neurosurgery to relieve the symptoms of extremely debilitating epileptic seizures that could not be controlled by medication (Scoville & Milner, 1957). The surgery involved bilateral resection of HM's MTL, and resulted in the almost complete removal of his hippocampus (Fig. 1.4). More recent analysis of HM's brain-damage using structural magnetic resonance imaging (MRI) revealed that his bilateral MTL lesion was symmetrical, and included the entire hippocampal formation (CA subfields, dentate gyrus, hippocampus and subiculum) and amygdala, as well as most of the entorhinal cortex (Fig. 1.4; Corkin, 2002; Corkin, Amaral, Johnson, & Hyman, 1997). Following the surgery, HM's cognitive abilities were formally assessed using a battery of neuropsychological tests, which failed to reveal impairments in his IQ, short-term memory (indicated by digit span, Corkin, 1984; see also Drachman & Arbit, 1966) and language comprehension (Milner, Corkin, & Teuber, 1968; see also Kensinger, Ullman, & Corkin, 2001). On the Wechsler Scale (Wechsler, 1945), however, HM's score was far below average for immediate recall and associative word learning. Subsequent tests revealed that HM's declarative memory impairment was severe and pervasive (Corkin, 1984; Milner et al., 1968); it was apparent regardless of the stimulus material (i.e. words, digits and faces), sensory modality (auditory, visual and olfactory) or type of memory test used (including free recall, cued recall, yes/no recognition and forced-choice recognition).

Surprisingly, however, HM was capable of learning new skills, despite having no recollection of doing so (Corkin, 1968; Gabrieli, Corkin, Mickel, & Growdon, 1993;

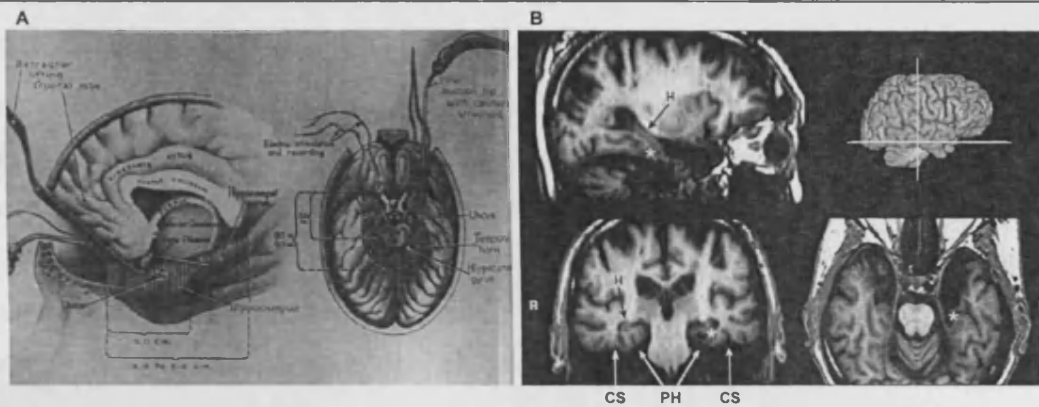


Figure 1.4: (A) A pictorial representation of surgical hippocampal resection, which depicts both 5cm and 8cm removals. The 8cm removal was the procedure performed on H.M. Figure from Scoville & Milner, 1957. (B) Multiplanar views of 18 averaged T1-weighted MRI volumes showing preserved structures in H.M.'s MTL. The asterisk on the transaxial view (top right) marks the intersection of three viewing planes; sagittal (top left), coronal (bottom left), and axial (bottom right). Abbreviations: (CS) collateral sulcus; (EC) entorhinal cortex; (H) hippocampus; (PH) parahippocampal gyrus. Figure from Corkin et al., 2002.

Milner, 1962). The acquisition of new skills, which could be retained for up to a year, was subsequently demonstrated in other patients with MTL atrophy (Gabrieli et al., 1993) and these findings were pivotal for neuroanatomical models of animal and human memory; they suggested that the MTL is critical for long-term declarative memory, whereas short-term and implicit memory (of which skill-learning is one form) are dependent on other neural systems (Milner et al., 1968; Corkin, 1984; Squire & Zola-Morgan, 1991).

These early investigations of MTL amnesia implied that damage to the hippocampus was necessary to cause impairments in declarative memory (Scoville and Milner, 1957). It was also noted, however, that larger MTL lesions, which included the hippocampus and surrounding cortex, resulted in greater memory impairments (Scoville and Milner, 1957). Likewise, in patients with smaller, more focal, hippocampal lesions, memory deficits were less pronounced (e.g. patient PB: Corkin, 1965; Penfield & Milner, 1958). It was concluded, therefore, that regions adjacent to the hippocampus must also contribute to memory (Scoville & Milner, 1957). Due to the variability in the location and extent of lesions in these patients, the specific roles of surrounding MTL regions could not be determined.

Complementary lesion work with animals has proven to be a valuable method of observing how individual brain regions support memory. There are caveats, however, as it is unlikely that humans and animals experience remembering in the same way, and episodic memory may be a uniquely human experience (Suddendorf & Busby, 2003; Tulving, 1983; although see Clayton, Bussey, & Dickinson, 2003; Eacott & Easton, 2010). While the extrapolation of findings to humans must be done with caution, animal lesion research is particularly useful when considered alongside data from amnesic individuals.

In general, animal models of memory are based on how monkeys and rats respond to novel and previously experienced items via their natural tendency to explore novel stimuli. Developed in the late 1970's, the most widely used tasks are known as delayed non-match to sample tasks (DNMS), which are thought to be equivalent to recognition memory paradigms used to assess memory in humans (Mishkin, 1978). In DNMS, animals are rewarded for selecting exemplars over sample items that are re-presented after variable delays. Early research with monkeys indicated that individual lesions to the hippocampus or amygdala did not impair performance on DNMS, even after long delays; however, large combined amygdala-hippocampal lesions did (Mishkin, 1978). As limited damage to the hippocampus was not sufficient to cause impairments, it was suggested that, as with patient HM, damage must encompass the hippocampus *and* amygdala to cause deficits in declarative memory (Mishkin, 1978; Zola-Morgan, Squire, & Mishkin, 1982).

An alternative possibility, overlooked by early investigations, is that the surgical techniques used to remove the amygdala and hippocampus in monkeys, and patients such as HM, were likely to have caused significant damage to the surrounding cortex (Murray & Mishkin, 1986; Squire & Zola-Morgan, 1991; Zola-Morgan, Squire, Amaral, & Suzuki, 1989). As entry via the ventral surface of the temporal lobe (Fig 1.2) is required to surgically aspirate the amygdala and/or the hippocampus, damage can easily co-occur in the perirhinal and parahippocampal cortices. Consequently, it was unclear whether memory impairments following amygdalo-hippocampal lesions, in fact, reflected injury to the parahippocampal, entorhinal and/or perirhinal cortices. In a formal characterisation of this, Zola-Morgan, Squire, & Ramus (1994) systematically demonstrated that, while focal damage to the hippocampus resulted in

modest memory impairments in monkeys, the severity of deficits increased when lesions included the parahippocampal cortex and rhinal cortex (see also Zola-Morgan, Clower, Rempel, & Squire, 1993; Zola-Morgan et al., 1989). These data suggest that, although removal of the hippocampus produces mild amnesia, a substantial part of the severe memory impairments observed in humans with MTL lesions can be attributed to damage to adjacent cortical regions. This study, however, offered little insight into the *independent* mnemonic functions played by the parahippocampal, perirhinal and entorhinal cortices and did not, therefore, rule out the possibility that amnesia could also result from individual damage to these structures.

Conclusive evidence that structures proximal to the hippocampus can make unique contributions to declarative memory was provided by Meunier, Bachevalier, Mishkin, & Murray (1993). Combined ablations to the perirhinal and entorhinal cortices in monkeys resulted in impairments on DNMS which, the authors commented, were as profound as those observed in Mishkin's (1978) initial amygdalo-hippocampal lesion experiment (for similar effects following combined perirhinal and parahippocampal cortex lesions see Zola-Morgan et al., 1989). Furthermore, while focal lesions to perirhinal cortex resulted in a similarly poor performance on DNMS (see also Buckley & Gaffan, 1997; Suzuki, Zola-Morgan, Squire, & Amaral, 1993; and for rats Mumby & Pinel, 1994; Otto & Eichenbaum, 1992a), impairments following damage to the entorhinal cortex were modest (see also Leonard, Amaral, Squire, & Zola-Morgan, 1995). One interpretation, therefore, is that focal damage to the perirhinal and entorhinal cortices, but not the hippocampus or amygdala, is necessary and sufficient to cause amnesia as severe as that observed in patient HM (Meunier et al., 1993). Furthermore, the conclusions made by Meunier and colleagues (1993) are strengthened by observations that, using neurotoxic lesion techniques that selectively damage MTL structures and spare fibres of passage (Buckley, 2005), ablations to the hippocampus and amygdala do not produce impairments on DNMS, even after retention delays of up to 40 minutes (Murray & Mishkin, 1998).

There are also reports, however, that focal lesions to the hippocampus *can* interrupt performance on DNMS in monkeys (Alvarez-Royo, Zola-Morgan, & Squire, 1995; Nemanic, Alvarado, & Bachevalier, 2004; Zola-Morgan, Squire, Rempel, Clower, & Amaral, 1992; Zola et al., 2000) and rats (Clark, West, Zola, & Squire, 2001; Clark,

Zola, & Squire, 2000). These early empirical disagreements, and the continuing emergence of conflicting evidence (Clark et al., 2001; Mishkin, 1978; Mumby, Wood, & Pinel, 1992; Murray & Mishkin, 1998; Zola et al., 2000) have resulted in the formation of opposing accounts of MTL function; (a) those in which the hippocampus and surrounding structures form a single MTL system specialised for long-term memory (Squire & Zola-Morgan, 1991; Squire 2004; Squire et al., 2004; Squire et al., 2007), and (b) others where MTL structures, such as the hippocampus and perirhinal cortex, form separate systems that make functionally distinct contributions (Aggleton & Brown, 1999; Brown & Aggleton, 2001; Davachi, 2006; Diana et al., 2007; Eichenbaum et al., 2007; Graham et al., 2010; Mayes et al., 2007).

1.3. The unitary/strength-based MTL account

One of the most influential accounts of human memory was first proposed by Squire and Zola-Morgan (1991; Fig 1.5), borne from early demonstrations that bilateral damage to the MTL results in severe and pervasive declarative memory impairments, and that lesions limited to the hippocampus are required to cause amnesia (Alvarez-Royo et al., 1995; Clark et al., 2001; Clark et al., 2000; Zola-Morgan et al., 1992; Zola et al., 2000; although see Mishkin, 1978; Mumby et al., 1992; Murray & Mishkin, 1998). According to this single-system approach, the hippocampus and adjacent cortical structures are crucial for the rapid acquisition of new information about facts and events (Zola-Morgan et al., 1989; Zola-Morgan et al., 1994). This model predicts that damage localised to the MTL has three consequences: (a) memory impairments are seen across all sensory modalities and stimuli (Milner, 1972; Squire, Schmolck, & Stark, 2001), (b) short-term or immediate memory remains intact (Drachman & Arbit, 1966; Milner et al., 1968; Milner, Squire, & Kandel, 1998) and (c) perceptual, lexical and intellectual abilities are unaffected (Corkin, 1984; Kensinger et al., 2001; Milner et al., 1968).

As all structures in the MTL contribute to memory, there should be a positive relationship between the extent of MTL damage and degree of memory impairment (Squire, 2004; Zola-Morgan et al., 1994). Consistent with this, patient RB, who suffered atrophy to the CA1 field of the hippocampus (Zola-Morgan, Squire, & Amaral, 1986; see also Press, Amaral, & Squire, 1989; Rempel-Clower, Zola, Squire,

& Amaral, 1996; Victor & Agamanolis, 1990), exhibited a less severe memory impairment than patients with damage to the hippocampus and surrounding cortical structures (e.g. patients HM and EP: Scoville & Milner, 1957; Squire et al., 2004; Squire & Zola-Morgan, 1991; Stefanacci, Buffalo, Schmolck, & Squire, 2000). These findings led to the conclusion that the outcome of MTL damage is not linked to the particular location of a lesion, but rather that all structures in the MTL contribute similarly, and equally, to different aspects of long-term declarative memory. Importantly, while Squire (2004; Squire et al., 2007) has emphasised the combined role of MTL structures, this does not imply that MTL subregions necessarily perform the same function, but when additional structures are damaged memory performance decreases in a quantitative fashion. Squire (2004; Squire et al., 2007) has recently noted that, while it is likely that the subregions of the MTL are functionally heterogeneous, an adequate account of this heterogeneity is yet to be achieved.

1.4. The dual-process MTL account

Over the past thirty years, dual-process models have become a popular account of the processes thought to underlie long-term memory (Mandler, 1980). While there are a number of different dual-process models (Jacoby, 1991; Mandler, 1980; Tulving, 1985; Yonelinas, 1994), one fundamental underlying assumption is that successful memory can be supported by two functionally separate mnemonic processes; familiarity and recollection. The most widely cited current dual-process model is associated with the work of Yonelinas, Jacoby and colleagues (Jacoby, 1984, 1991; Yonelinas, 1994, 2001a, 2002; Yonelinas et al., 1998). According to this model, one process, familiarity, is fast, automatic and acontextual. It is a graded strength signal that can permit judgments of prior occurrence when the strength of the signal is sufficiently high. The second process, recollection, is a slower, largely intentional process that is associated with the recovery of contextual information from the encoding episode (also known as source/associative information). According to the dominant dual-process account, recollection is modelled as an all-or-none (high-threshold) process (Yonelinas, 1994).

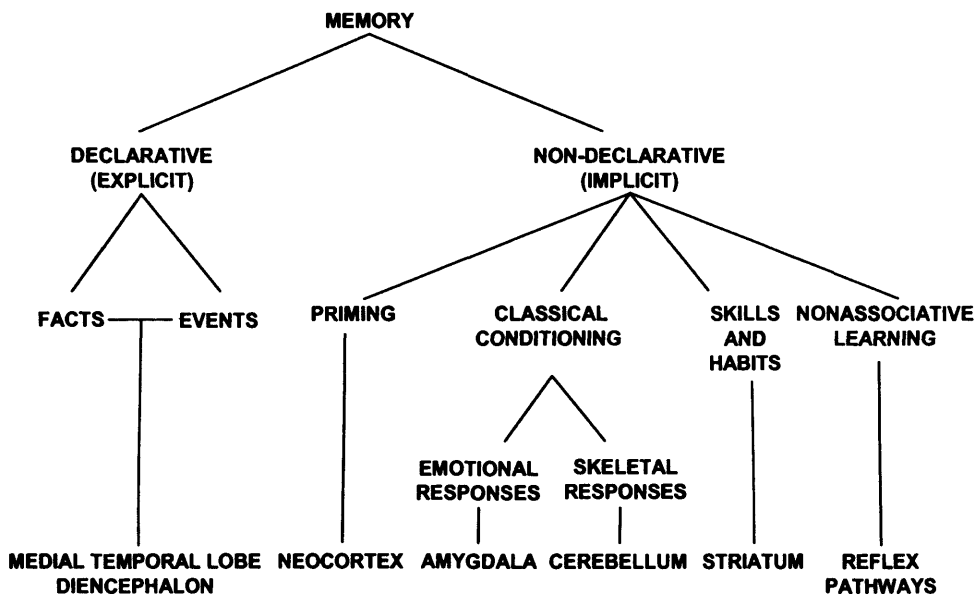


Figure 1.5: The taxonomy of long term mammalian memory, including brain regions, as proposed by Squire and colleagues. Figure adapted from Squire & Knowlton (2000).

In contrast to Squire's unitary account of declarative memory (Squire & Zola-Morgan, 1991; Squire et al., 2004; Squire et al., 2007), it has been proposed that the hippocampus and the perirhinal cortex support recollection and familiarity, respectively (Aggleton & Brown, 1999; Brown & Aggleton, 2001; Eichenbaum et al., 2007; Mayes et al., 2007; Yonelinas et al., 1998; Yonelinas et al., 2002). In the following sections, there is a discussion of data points that are relevant to the question of how different memory processes might be supported by subregions of the MTL.

1.4.1. Process estimation techniques

A number of behavioural approaches have been employed to investigate the processes that support recognition memory. The approach that is most relevant to the work described in this thesis is receiver operating characteristics (ROCs). Prior to an in depth discussion of this technique two other widely employed approaches, the process dissociation procedure (PDP) and the remember/know technique, will be reviewed.

1.4.1.1. Process dissociation procedure

The PDP, developed by Jacoby (1991), was introduced to quantify the contributions of recollection and familiarity to recognition memory judgments. In a PDP study phase, items are commonly presented in one of two different study contexts. At test

participants are presented with old and new items in an 'inclusion' and/or an 'exclusion' phase. During the inclusion phase participants are required to endorse any item as old that they recognise from the study phase. During the exclusion phase participants are required to respond old to test items from one of the two study contexts only (or target items), and new to all other test items (new items as well as items from the alternate study context, or non-targets).

According to a dual-process account, both familiarity and recollection can support correct old judgments to previously seen items in the inclusion phase. Incorrect (old) judgments to non-targets in the exclusion phases, however, are made only on the basis of familiarity. As a result, it is possible to obtain a separate estimate of familiarity from the exclusion phase and when considered alongside the combined recollection and familiarity estimate from inclusion, this permits overall estimates of the contributions of recollection and familiarity to task performance (for one formal development of the equations for this computation see Yonelinas & Jacoby, 1994).

There are three main criticisms of the PDP. First, the PDP rests on the premise that the likelihood of recollecting information is the same in exclusion and inclusion conditions, which may not be correct. As participants are not required to recover contextual information in the inclusion phase, they may engage in effortful recollection to a lesser degree than during the exclusion phase. Second, for some items in the exclusion phase participants may fail to recollect the content that is necessary for the required binary distinction, but may recollect other 'un-probed' contextual details (also known as 'non-criterial recollection', Yonelinas & Jacoby, 1996). In the PDP, however, only information that can support the required discrimination is counted as recollection. As a result, the contribution of non-criterial recollection to memory performance violates the assumption that old judgements to non-targets solely reflect familiarity, leading the procedure to produce distorted estimates of recollection and familiarity. And third, the PDP was designed to incorporate dual-process assumptions, so it is not well-placed to adjudicate between dual-process and other accounts of recognition memory. Estimates of recollection and familiarity from the PDP, however, correspond closely with those obtained via other process estimation procedures (Yonelinas, 2001b).

1.4.1.2. Remember/Know

A phenomenological approach to understanding the processes supporting recognition memory involves asking people about the experiences that accompany judgments. This is known as the remember/know procedure (Tulving, 1985). As with standard recognition memory paradigms, participants study a series of items, which are later re-presented in a test phase. Participants are asked to make one of three responses to test items; new, know (K) or remember (R). A participant makes an R response when they believe an item to be old, and they have recollected contextual information associated with the item. A K response is made for items that feel familiar, in the absence of contextual recollection. The R/K paradigm was explicitly connected with the recollection and familiarity distinction by Gardiner (1988), where R responses were linked to the process of recollection, and K responses to familiarity. As it is now generally considered that R and K responses are not mutually exclusive (see Fig 1.6 and Jacoby, 1991; Yonelinas & Jacoby, 1995), there is now a procedure for estimating recollection and familiarity under the assumption of stochastic independence. This is known as the independence remember/know method (or IRK: Yonelinas & Jacoby, 1995), which suggests that, to avoid underestimating familiarity, the proportion of K responses to old items should be divided by the number of opportunities that the participant has to make a K response ($F = K/(R-1)$).

There are several examples where remember and know responses have been dissociated under different experimental manipulations. Disproportionate *increases* in R responses, relative to K, consistently occur under deeper encoding conditions and when study items comprise low-frequency, or less common, words (Gardiner, 1988;

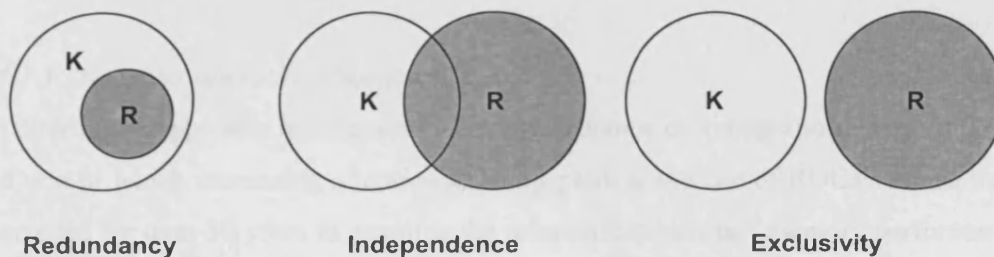


Figure 1.6: Three types of relationship between recollection and familiarity have been proposed; redundancy, exclusivity and independence. For redundancy, all recognised items are accompanied by a feeling of familiarity, a sub-set of which are also recollected. A model of stochastic independence presupposes that a given item can be associated with recollection, familiarity or both. With exclusivity, recollection and familiarity can never co-occur. Figure adapted from Knowlton & Squire (1995).

Gardiner, Java, & Richarson-Klavehn, 1996; Gardiner, Richarson-Klavehn, & Ramponi, 1997; Guttentag & Carroll, 1997; Rajaram, 1993). Larger *decreases* in R responses, however, have been observed when encoding resources are stressed by divided attention (Gardiner & Parkin, 1990; Yonelinas, 2001b). There are number of fluency manipulations, such as briefly flashing a word prior to its presentation (Rajaram, 1993), presenting items in a semantically related context (Rajaram & Geraci, 2000) and revealing words letter by letter (LeCompte, 1995) that have also been shown to increase K responses while leaving R unchanged. In contrast, if the presentation modality between study and test is not matched, the proportion of K responses disproportionately declines (Gregg & Gardiner, 1994).

These selective changes in R and K measures have been interpreted as support for dual-process models of recognition memory. In a series of recent studies, however, the view that R responses are a genuine and exhaustive reflection of a different kind of memory, compared to that which supports K responses, has been challenged (Rotello, Macmillan, Reeder, & Wong, 2005; Rotello & Zeng, 2008; Wais, Mickes, & Wixted, 2008). These challenges include; (a) demonstrations that reaction time distributions for R and K responses are similar, which suggests that R and K are based on the same information (Rotello & Zeng, 2008), (b) the finding that R response rates do not always map onto recollection estimates derived from ROCs (Rotello et al., 2005), (c) demonstrations that the likelihood of R responses changes under different R/K task instructions (Rotello et al., 2005), and (d) circumstances where the accuracy of forced-choice judgements thought to rely on contextual information (source memory) for items that receive a K response is above chance (Wais et al., 2008).

1.4.1.3. Receiver operating characteristics

An alternative approach for characterising performance on recognition memory tasks, and one to which increasing attention is being paid, is the use of ROCs. These have been used for over 30 years to examine the relationship between memory performance and response bias on recognition memory tasks where old/new judgments are required (Mandler & Boeck, 1974; Yonelinas, 1994; for reviews see Wixted, 2007; Wixted & Stretch, 2004; Yonelinas, 2002; Yonelinas & Parks, 2007). In the memory domain, an ROC function relates the proportion of correctly identified old items (hits) with the

proportion of incorrectly identified new items (false alarms), at varying levels of response bias.

To plot an ROC, old/new confidence decisions are typically made on a 6-point-scale (where, arbitrarily, 1 represents highest confidence new and 6 represents highest confidence old). This approach produces probabilities of hit and false alarm rates at different levels of response bias. High confidence is equated with a conservative response bias, where subjects generate far fewer false alarms but also make a smaller proportion of hits, while low confidence is equated with a liberal response bias, where subjects make a high proportion of hits but also generate many false alarms. An ROC curve is produced by plotting hit (y-axis) and false alarm (x-axis) pairs cumulatively as a function of confidence. The left-most point represents hits and false alarms at the highest level of confidence, with each subsequent point becoming more liberal. An ROC curve, therefore, varies from a conservative or high confidence response criterion (lower left corner) to a liberal or low confidence response criterion (upper right corner). As an ROC illustrates memory performance across different levels of response bias, it can be more instructive than data produced by the standard yes/no recognition paradigm. This additional insight is achieved by examining the shape of the ROC curve, which can be done in probability space, or by converting ROC points to z-scores and plotting these.

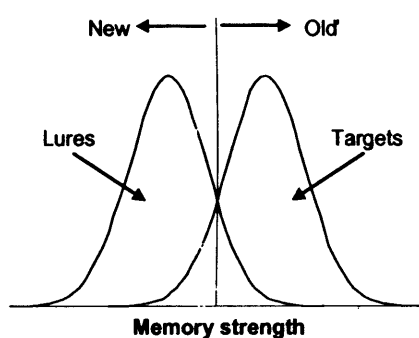


Figure 1.7: *The equal variance signal detection (EVSD) model of recognition memory.*

Different recognition memory models based on signal detection make different predictions about the shapes of ROCs. One incarnation of this is known as the equal variance signal detection (EVSD) model, where the variability in memory strength for old and new items results in two, equally sized, overlapping, Gaussian distributions (Fig. 1.7). The distance between the old and new item distributions can be used to

measure how separable old and new items are. Notably, according to this account, memory can never fail as there is always some level of memory signal produced by the item. People are assumed to set a strength criterion, which can be different across

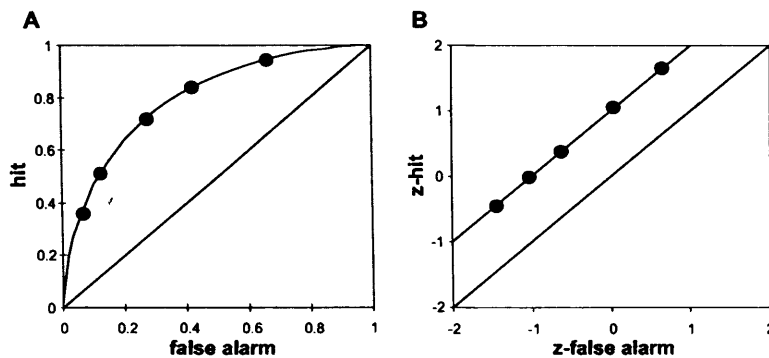


Figure 1.8: (A) and (B) idealised ROC data as predicted by EVSD plotted in probability- and z -pace, respectively.

individuals, with items falling to the right and left attracting old and new judgments, respectively. Criterion placement can be more conservative (moving to the right), or more liberal (moving to the left), which results in disproportionate changes in hits and false alarms. For example, a very strict level of criterion will have greater effects on the proportion of hits, but modest effects on the proportion of false alarms. As a result, these equally sized Gaussian distributions predict ROCs that are curved in standard space and perfectly linear in z space, with a slope of 1 (Fig. 1.8). ROCs obtained in recognition memory tasks typically have slopes of less than 1, and exhibit both curvilinear and asymmetrical components in probability space (Ratcliff, Sheu & Gronlund, 1992; Yonelinas, 1994; Yonelinas, 2002; Yonelinas & Parks, 2007; see Fig. 1.9). This means that a simple EVSD model is not appropriate for recognition memory judgments.

The dual-process signal detection (DPSD) model, proposed by Yonelinas (1994), suggests that the asymmetric and curvilinear components of the average ROC reflect recollection and familiarity. Familiarity is modelled as in EVSD, and recollection is regarded as a threshold process: an item is either recollected with high confidence or not at all. Recollection is assumed to be responsible for the asymmetry of an ROC function, as increased use of recollection pushes up the left-most (highest confidence) points; the more asymmetrical the ROC, the greater the contribution of recollection. As such, according to DPSD, symmetrical ROCs, as predicted by EVSD, occur due to the sole contribution of familiarity. Linear ROCs (in probability space) occur due to the sole contribution of recollection.

According to DPSD, the degree of asymmetry of an ROC curve will vary depending upon how much recollection contributes (Yonelinas, 1994). The relative contributions of recollection and familiarity can be inferred by examining the shape of ROC in probability space and/or in z-space. If a perfectly symmetrical ROC in probability space produces a linear z-ROC with a slope of 1, increased contributions of recollection are represented by curvilinear z-ROCs, with a slope <1 . In addition to this, estimates of recollection and familiarity can be calculated by fitting data points to the model using Yonelinas sums-of-squares search algorithm (Yonelinas et al., 1998). Importantly, DPSD can adequately explain symmetric and asymmetric ROCs and the conditions under which these occur.

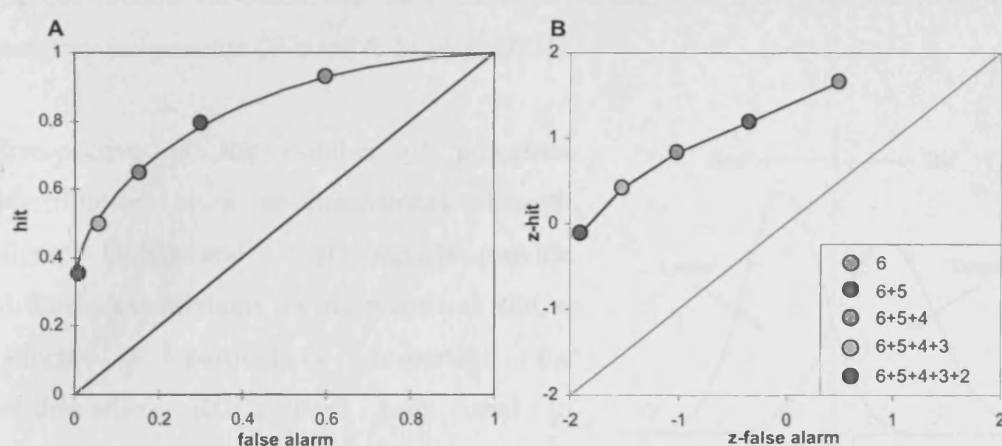


Figure 1.9: Examples of typical recognition memory ROC data summed across a 6-point confidence scale, plotted in (A) probability- and (B) z-space. Figures adapted from Parks & Yonelinas (2008).

There is an alternative model that can also account for z-ROCs with a slope <1 , known as univariate signal detection (UVSD, Wixted, 2007). The key tenet of UVSD is that the variances of old and new item distributions are not equally sized (Fig. 1.10). UVSD suggests that ROCs comprise two components; one for increases in accuracy and the other for ROC asymmetry, that result from fluctuations in old relative to new item variance. When old item variance is greater than new, an ROC will be pushed up on the left side (it will be asymmetric). It has been suggested that old item variance exceeds that of new because not all studied items will increase in strength by the same amount (Wixted, 2007). Generally UVSD presupposes that an ROC will be symmetrical in probability space and linear in z-space (slope = 1).

Because old and new distributions can differ, however, the model also allows for asymmetric ROCs and non-linear z-ROCs (slope <1).

The main theoretical distinction between DPSD and UVSD is that, for the former, recognition memory is modelled by the contributions of two separate and independent processes, whereas for the latter, recognition memory is modelled by a unidimensional strength variable. It has been proposed that two processes can (in combination) contribute to the singular strength output, so UVSD approaches do not necessarily preclude the existence of separate recollection and familiarity processes. For this kind of UVSD, recollection and familiarity are both considered to be continuous variables and their summed strength is the basis for recognition memory judgements (Wixted & Stretch, 2004).

Irrespective of the number of processes contributing to a unidimensional strength signal, DPSD and UVSD models provide different explanations for asymmetrical ROCs, which is particularly important for studies where ROCs have been used to investigate human amnesia (discussed later). For DPSD, the asymmetry arises because of the contributions of two qualitatively distinct processes. For UVSD, the asymmetry arises

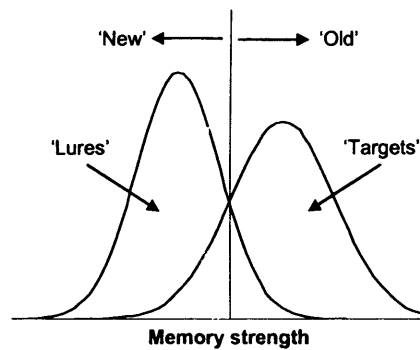


Figure 1.10: The unequal-variance signal detection (UVSD) model of recognition memory.

because of the variability in old item strengths that is introduced at the time of memory encoding. Although UVSD provides a more parsimonious explanation of ROC asymmetry, the model does not specify why old item variance almost always exceeds new and the circumstances that result in increases in old item variance. As a result, the UVSD model does not make predictions about what experimental manipulations would affect the increases in old new item variance and increases/decreases in ROC asymmetry. DPSD deals well with variations in asymmetry found for manipulations such as levels of processing (Glanzer, Kim, Hilford, & Adams, 1999; Yonelinas, 1999b; 2001b; Yonelinas, Dobbins, Szymanski, Dhaliwal, & King, 1996) and divided attention (Yonelinas, 2001b). While UVSD can

allow for these fluctuations in asymmetry, it does not explain how or why these quantitative differences occur.

Perhaps the most compelling evidence for favouring DPSD over UVSD comes from ROCs for source/associative memory. Associative memory tests require the recovery of contextual information in the form of associations learned at study (Eichenbaum et al., 2007; Yonelinas, 1997; 1999a; Yonelinas & Parks, 2007). Associative memory ROCs can be linear or exhibit a slight inverted U-shape in probability space, but they are almost always U-shaped in z-space (Yonelinas, 1997; 1999a; Yonelinas & Parks, 2007; Fig. 1.11). As it is based upon Gaussian strength distributions restricted to ROCs that are curvilinear in probability space and linear in z-space, UVSD cannot account for U-shaped z-ROCs. In contrast, DPSD comprises both high-threshold and Gaussian signal detection components, and therefore can allow for U-shaped z-ROCs.

ROCs are currently the preferred method of estimating recollection and familiarity. DPSD adequately explains and predicts how and why fluctuations in the shape of ROCs occur, and provides a good fit for a large percentage of the existing ROC data (Glanzer et al., 1999; Yonelinas, 2001a; Yonelinas et al., 1996; Yonelinas & Parks, 2007; although see Heathcote, 2003). As recollection is generally endorsed by high confidence memory judgements, and a wider range of confidence judgements are associated with familiarity, items that are recollected can be individually dissociated from those that are not (Yonelinas, 1994; Yonelinas, 2002; Yonelinas & Parks, 2007).

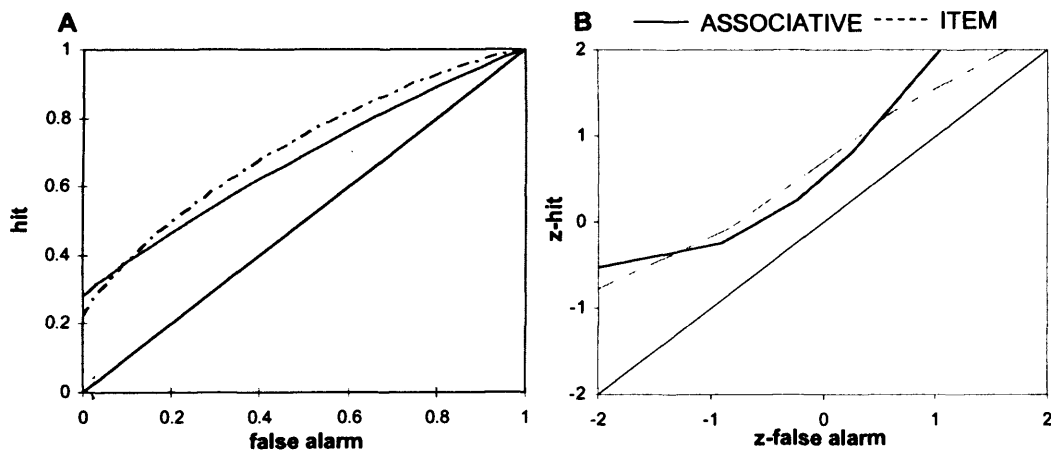


Figure 1.11: Item and associative recognition ROCs (from Experiment 3; Yonelinas, 1997) plotted in (A) probability space and (B) z-space. The item ROC is concave in probability space and linear in z-space, whereas the associative ROC is linear in probability space and U-shaped in z-space. Figure adapted from Parks and Yonelinas (2008).

Although the PDP can produce overall process estimates, it is not possible to isolate single items that have been recognised based upon recollection or familiarity. Using a remember/know paradigm recollected items can be individually dissociated from familiar items. It remains unclear, however, whether process estimates obtained using the remember/know paradigm reliably reflect the distinction between recollection and familiarity (Rotello et al., 2005; Rotello & Zeng, 2008; Wais et al., 2008).

The ROC procedure has been employed in neuropsychological and neuroimaging studies to infer the neural correlates of recollection and familiarity (Aggleton et al., 2005; Bowles et al., 2007; Cohn, Moscovitch, Lahatb, & McAndrews, 2009; Daselaar, Fleck, & Cabeza, 2006; Ranganath et al., 2004; Yonelinas et al., 1998; Yonelinas et al., 2002). In line with this approach, confidence ratings for old/new judgements were collected during the test phase of all of the functional magnetic resonance imaging (fMRI) recognition memory experiments described in this thesis. By collecting confidence data it was possible to plot ROCs to make inferences about the contributions of recollection and familiarity to recognition memory, and to investigate the associations between different levels of recognition memory confidence and activity within MTL subregions.

1.4.2. Neuropsychological evidence for a dual-process account

The identification of patients with different profiles of pathology in the MTL, especially in light of recent advances in structural MRI scanning, has enabled further investigation of possible divisions of labour within the human MTL. Furthermore, by testing patients with limited or focal MTL lesions on a variety of different recognition memory tasks, such as the process estimation procedures described above, it has been possible to ascertain whether damage to certain MTL regions is more commonly associated with impairments in recollection and/or familiarity.

In contrast to recognition memory, as recall tasks require participants to retrieve information with minimal environmental support, they are thought to be more dependent on recollection. A number of studies have shown that patients with MTL lesions perform poorly on tests of recall (or recollection: Brown & Aggleton, 2001), but that recognition memory performance is within the normal range (Aggleton & Shaw, 1996; Aggleton et al., 2005; Baddeley, Vargha-Khadem, & Mishkin, 2001;

Barbeau et al., 2005; Holdstock, Mayes, Gong, Roberts, & Kapur, 2005; Mayes, Holdstock, Isaac, Hunkin, & Roberts, 2002; Mayes et al., 2001; Turriziani, Fadda, Caltagirone, Giovanni, & Carlesimo, 2004; Vargha-Khadem et al., 1997). In a meta-analysis of the literature relating to recognition memory in amnesic individuals, Aggleton & Shaw (1996) observed that damage to the hippocampal formation, mamillo-thalamic tract or anterior thalamic nuclei was associated with gross impairment on a range of visual recall tasks, but only mild impairments on recognition memory tasks. When MTL damage included structures surrounding the hippocampus, both recall and recognition were at chance levels (Aggleton & Brown, 1999; Aggleton & Shaw, 1996; Yonelinas, Sauve, & Knight, 2004). More recently, impaired recall but spared recognition was observed in two MTL amnesics, both of whom had bilateral pathology to the hippocampus (patient YR: Mayes et al., 2001; Mayes et al., 2002; patient BE: Holdstock et al., 2005). Notably, patient YR's memory was assessed with the 'Doors and People test' (Baddley, Emslie, & Nimmo-Smith, 1994), which controls for the differences in difficulty that are classically observed between recall and recognition tasks; therefore, her recall deficit did not merely reflect the outcome of a 'milder amnesia' (Mayes et al., 2002; Tsivilis et al., 2008; Vann et al., 2009). Disproportionate deficits in recall memory following hippocampal atrophy have been interpreted as key evidence for selective impairments in recollection.

Recognition memory deficits in hippocampal amnesia are commonly observed using associative memory tests. Associative memory generally occurs in two main forms; item-item and item-context (discussed later). In the former, participants are required to remember pairs of items that are presented together at study. At test, participants must correctly identify intact (target) pairs that are presented amongst pairs formed by recombining studied items (foils). As all items are old, participants may be unable to identify target pairs based on familiarity alone, hence item-item associative memory is generally considered to require recollection (although see Section 1.5; Diana, Yonelinas, & Ranganath, 2008; Haskins, Yonelinas, Quamme, & Ranganath, 2008; Mayes et al., 2007; Quamme, Yonelinas, & Norman, 2007; Yonelinas, Kroll, Dobbins, & Soltani, 1999). Notably, as participants remember intact pairs based upon the *relationships* formed between items at study, the formation of associations is also known as relational memory (Cohen, Poldrack, & Eichenbaum, 1997; Eichenbaum et al., 1994; Eichenbaum et al., 2007). Disproportionate impairments for item-item

associations/relations, relative to memory for single items, have been reported in single-case (Holdstock et al., 2005; Mayes et al., 2002; Mayes et al., 2004) and group studies in patients with damage to the hippocampus (Giovanello, Verfaellie, & Keane, 2003; Turriziani et al., 2004; Vargha-Khadem et al., 1997).

Observations that associative recognition and recall is impaired in patients with focal hippocampal atrophy suggest that the hippocampus is important for recollection. By contrast, as item recognition memory impairments are exacerbated by more extensive MTL damage, extra-hippocampal regions could be important for familiarity. In a formal characterisation of these observations, Aggleton & Brown (1999) suggested that there is a functional fractionation within the MTL according to recollection and familiarity. While recollection is supported by the hippocampus and its diencephalic projections (including the fornix) to the thalamus, familiarity operates via perirhinal cortex (Fig. 1.12; see also Brown & Aggleton, 2001).

The investigation of MTL amnesia using ROCs (Fig. 1.13) has consistently demonstrated that focal damage to the hippocampus is associated with a disproportionate loss of the asymmetric component of a standard recognition memory ROC (Aggleton et al., 2005; Wais, Wixted, Hopkins, & Squire, 2006; Yonelinas et al., 1998; Yonelinas et al., 2002). Likewise, when brain-damage includes the hippocampus and surrounding MTL structures, ROCs are curvilinear and lower in

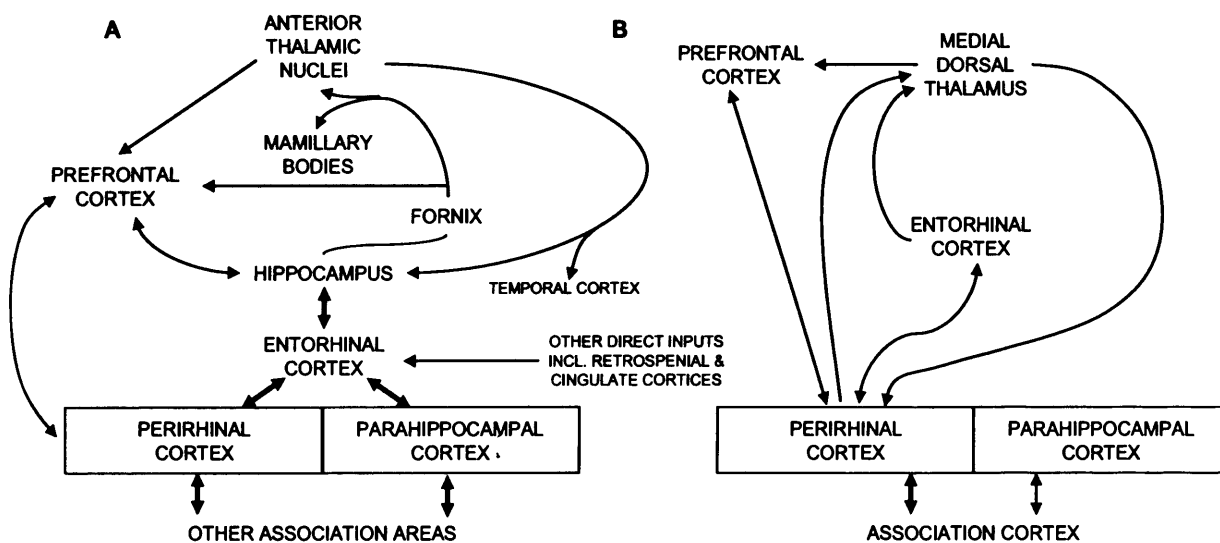


Figure 1.12: Schematic diagrams of the principal pathways that support (A) recollection and (B) familiarity-based recognition. The relative thickness of the lines indicates the presumed importance of the connection. Figure adapted from Aggleton & Brown (1999)

probability space (Yonelinas et al., 2002). Finally, while levels of processing manipulations increase the asymmetry of control ROCs, deeper encoding conditions do not affect the curvilinearity of patient ROCs (Aggleton et al., 2005; Yonelinas et al., 1998; although see Wais et al., 2006). One collective interpretation is that reduced ROC asymmetry following hippocampal injury reflects a decreased contribution from recollection¹ and when damage encompasses additional MTL regions familiarity is also disrupted (Yonelinas et al., 2002; Yonelinas et al., 2004).

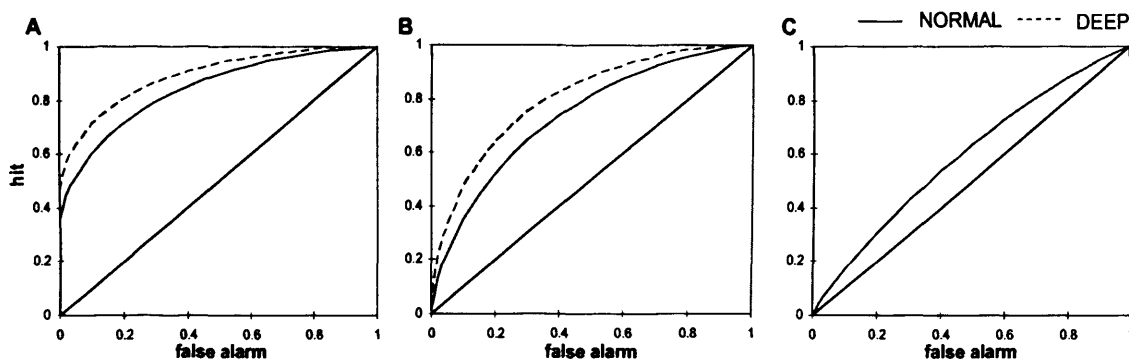


Figure 1.13: *Representative ROC data across patient studies for: (A) healthy controls; (B) individuals with focal hippocampal atrophy and (C) individuals with large MTL lesions, which include the perirhinal cortex and hippocampus (Aggleton et al., 2005; Yonelinas et al., 1998; Yonelinas et al., 2002). Under normal encoding conditions the shape of the ROC becomes more curvilinear and lower in probability space as MTL atrophy includes the hippocampus and surrounding structures. Notably, under deep encoding conditions, the hippocampal ROC moves up in probability space, but remains curvilinear.*

The fornix provides a major connection between the hippocampus and the anterior nuclei of the thalamus (Fig. 1.12; Aggleton & Brown, 1999). Colloid cyst removal within the third ventricle generally results in damage to the fornix and adjacent mamillary bodies. Moreover, patients who have undergone colloid cyst removal from the third ventricle often exhibit deficits in recall but not recognition (Aggleton et al., 2000; Tsvillis et al., 2008). Vann et al. (2009) formally assessed the mnemonic performance of a large cohort of colloid cyst patients. These patients were split into two main sub-groups based on the size of mamillary body damage; this resulted in the

¹ See also Bastin et al., 2004 who observed impaired recollection, but intact familiarity in single anoxic hippocampal patient using the PDP.

formation of a small mamillary body group (SMB) and a large mamillary body group (LMB). Using ROCs and remember/know it was observed that the SMB group produced lower recollection estimates, but equivalent familiarity estimates to the LMB group.

Working within Aggleton and Brown's (1999) dual-process framework, if damage to the hippocampus selectively impairs recollection, then damage to the perirhinal cortex should affect familiarity. Using remember/know and ROCs, Bowles et al. (2007) assessed the integrity of recollection and familiarity in patient NB, who suffered rare focal damage to the left entorhinal and perirhinal cortices, following resection of the left anterior temporal lobe. NB's overall recognition memory performance was within the normal range. Estimates of familiarity, however, were significantly reduced, relative to healthy controls, and NB produced an abnormally asymmetric ROC and a numerically higher estimate of recollection. The authors concluded that the qualitative adjustments in NB's ROC function resulted from reduced contributions of familiarity. When considered alongside the findings from individuals with damage to the hippocampus or the extended hippocampal system, these data demonstrate a double dissociation between the roles of the hippocampus and perirhinal cortex in recollection and familiarity (see also Yonelinas et al., 2007; Wolk et al., 2011; Bowles et al., 2010).

Other researchers still propose that regions within the MTL support declarative memory in a 'cooperative' fashion (see Section 1.3; Squire & Zola-Morgan, 1991; Squire, 2004; Squire et al., 2004; Squire et al., 2007), citing studies that have observed similar impairments in recall and recognition (Kopelman et al., 2007; Manns, Hopkins, Reed, Kitchener, & Squire, 2003; Manns & Squire, 1999; Wixted & Squire, 2004) and item and associative memory (Gold et al., 2006; Stark, Bayley, & Squire, 2002; Stark & Squire, 2003) following focal damage to the hippocampus. Notably, neuroradiological examinations can fail to reveal brain atrophy that is apparent in histological examinations (i.e. covert pathology), and often in cases of severe hypoxia both perirhinal and parahippocampal regions are damaged together in the MTL (Rempel-Clower et al., 1996; Yonelinas et al., 2004). As contaminant damage to surrounding MTL structures could also interrupt familiarity (Yonelinas et al., 2004), this, in part, could explain why amnesics that *appear* to share the same

pathology perform differently on tests of recognition, recall and associative memory (e.g. Gold et al., 2006; Holdstock et al., 2005; Manns et al., 2003; Mayes et al., 2002; Mayes et al., 2001; Vargha-Khadem et al., 1997).

As previously discussed, according to Squire's unitary account, lesions to MTL structures result in a global memory deficit, which is exacerbated when more structures are damaged; therefore, the difference between memory impairments for hippocampal amnesics, compared to individuals with extensive MTL lesions, is quantitative not qualitative (Squire et al., 2004). If interpreted according to UVSD (see Section 1.4.1.3; Wixted, 2004; Wixted, 2007), curvilinear ROCs produced by hippocampal amnesics do not reflect selectively impoverished recollection, but quantitative decrements in memory strength (Squire et al., 2007; Wais et al., 2006). Using ROCs, Wais et al. (2006) assessed the memory performance of 6 hypoxic patients with limited hippocampal damage. In keeping with findings from investigations of a similar nature, the amnesic participants produced a curvilinear ROC. Control ROCs became similarly curvilinear when memory was weakened by a substantial delay between study and test (> 7 days). Moreover, when the patients had to retain fewer study items (10 instead of 50), their ROC was asymmetric (Fig. 1.14). The authors interpreted these changes in ROC shape across patients and controls to reflect fluctuations in memory strength.

The data from Wais et al. (2006) are inconsistent with previous investigations which have shown that levels of processing manipulations do not affect the shape of amnesic recognition memory ROC (Aggleton et al., 2005; Yonelinas et al., 1998). Notably, however, Wais et al. (2006) had limited neuro-radiological information for some of their patients. Recent findings indicate, however, that the location and extent of hippocampal damage can have markedly profound consequences for mnemonic function (Holdstock et al., 2008). It is possible that, while all of the patients from the Wais et al. (2006) study suffered from damage to the hippocampus, some may have had sufficient sparing of the hippocampal formation to retain a degree of recollective ability, which would be more apparent after deeper encoding (like that demonstrated by Wais et al., 2006). Detailed individual subject neuro-radiological information is crucial for evaluating the conclusions from this study.

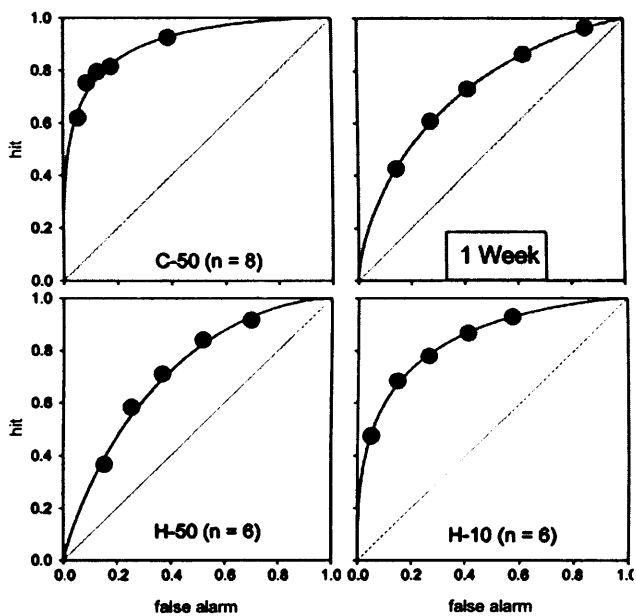


Figure 1.14: Recognition ROCs from Wais et al. (2006). (A) Controls tested with 50 items. (B) Controls tested with 50 items after 1 week. (C) Hippocampal patients tested with 50 items. (D) Hippocampal patients tested with 10 items.

Wais et al., 2006). Extensive MTL lesions that include the hippocampus and perirhinal cortex, however, generally result in impairments on recall and recognition memory (Aggleton & Shaw, 1996), in addition to reduced overall recognition memory accuracy, relative to individuals with focal damage to the hippocampus (as indicated by lower ROCs in probability space; Yonelinas et al., 2002; Yonelinas et al., 2004). The majority of these data points support a dual-process account, which suggests that the hippocampus and perirhinal cortex support recollection and familiarity, respectively (Aggleton & Brown, 1999; Brown & Aggleton, 2001). This conclusion is strengthened by the observation that focal damage to the perirhinal cortex selectively disrupts familiarity (Bowles et al., 2007).

1.4.3. Animal lesion evidence for a dual-process account

One explanation for the discrepancies produced by early DNMS animal studies (see Section 1.2.2) is that the hippocampus provides a unique contribution to recollection, and the perirhinal cortex to familiarity. Like item recognition memory in humans (Aggleton & Shaw, 1996; Aggleton et al., 2005; Baddeley, Vargha-Khadem, & Mishkin, 2001; Barbeau et al., 2005; Holdstock et al., 2005; Mayes et al., 2002;

In general, the evidence from amnesia indicates that lesions to the hippocampus and the extended hippocampal system are associated with deficits in recall and associative memory, and reductions in the asymmetric component of standard recognition memory ROCs (Aggleton & Shaw, 1996; Aggleton et al., 2005; Vann et al., 2009; Yonelinas et al., 1998; Yonelinas et al., 2002; although see Gold et al., 2006; Kopelman et al., 2007; Manns et al., 2003; Manns & Squire, 1999; Stark et al., 2002; Stark & Squire, 2003;

Mayes et al., 2001; Vargha-Khadem et al., 1997), it is possible that, where necessary, performance on DNMS can be supported by familiarity (Mishkin, 1978; Murray & Mishkin., 1998; Mumby et al., 1992), thus impairments are likely following damage to the perirhinal cortex (Zola-Morgan et al., 1989; 1994; Meunier et al., 1993 Suzuki et al., 1993; Buckley & Gaffan, 1997; Otto & Eichenbaum, 1992a; Mumby & Pinel, 1994). It follows, therefore, that the site of MTL lesions, the extent of hippocampal damage, and differences in task demands, will all result in variations in DNMS performance (Aggleton & Brown, 1999; Eichenbaum et al., 2007).

By adopting a specialised DNMS experimental technique using olfactory memory, Fortin, Wright and Eichenbaum (2004) assessed the effect of selective lesions to the hippocampus on recognition memory judgements that were made across a range of response criteria. Memory judgements were used to plot ROCs. Memory ROCs for the control rats were similar to those produced in humans using a confidence ROC procedure (Yonelinas, 1994; Yonelinas & Parks, 2007; see Section 1.4.1.3). The ROCs for rats with lesions to the hippocampus, however, were curvilinear and did not exhibit an asymmetric component. After imposing a 75-minute delay between study and test, control rats suffered an overall decrease in memory performance, but produced a linear ROC. According to DPSD (Yonelinas, 1994, 1999a, 2002), a linear recognition memory ROC reflects an exclusive contribution of recollection (see Section 1.4.1.3). Using the same ROC technique, Sauvage, Fortin, Owens, Yonelinas and Eichenbaum (2008) recently reassessed the effects of localised damage to the hippocampus on item-item associative memory in rats. Again, as predicted by DPSD, the control rats produced a linear ROC. While the hippocampal rats' ROC curves were reduced in asymmetry, they also exhibited a curvilinear component. Sauvage et al. (2008) concluded that, under circumstances of diminished recollection, by means of compensation, familiarity could support associative memory.

In summary, the recognition memory ROC data from rats indicates that subregions of the MTL support recognition memory in a qualitatively distinct fashion. This claim is supported by the observation that damage to the hippocampus results in decrements in recollection, not overall memory strength (Fortin et al., 2004). Furthermore, these data suggest that, in the absence of hippocampal function, the perirhinal cortex may form configural representations of pairs of items so that familiarity can support

associative memory (Sauvage et al., 2008; see also Diana et al., 2008; Haskins et al., 2008; Mayes et al., 2007; Quamme et al., 2007; Yonelinas et al., 1999).

1.4.4. Functional imaging evidence for a dual-process account

Prior to recent developments in functional neuroimaging, investigation into the neural basis of recognition memory was almost exclusively studied via lesion research. Neuropsychological double dissociations between memory processes and MTL structures, however, are few. This is because focal and complete lesions to structures such as the perirhinal cortex in humans are extremely rare, and neuro-radiological assessment of lesion site does not always reflect the findings from histological examination (Rempel-Clower et al., 1996). As a result, functional imaging techniques that measure changes in blood flow within the brain as an indirect measure of neural activity provide a valuable additional research tool.

fMRI investigations of long-term declarative memory can be divided into two main classes; those that identify effects at memory encoding and those that measure memory-related activity at the time of retrieval. Generally speaking, memory encoding effects (also known as ‘DM effects’, Paller & Wagner, 2002) are identified by contrasting brain activity associated with items from the study phase that are later remembered (*DMhit*) versus those that are subsequently forgotten (*DMmiss*). Retrieval studies classically make comparisons between remembered old test items (hit) and correctly identified new test items (correct rejection), or, less commonly, forgotten old test items (miss). Using simple contrasts between remembered and forgotten/new items, early fMRI investigations confirmed the importance of the MTL during long-term memory encoding (Brewer, Zhao, Desmond, Glover, & Gabrieli, 1998; Otten, Henson, & Rugg, 2001, 2002; Wagner et al., 1998) and retrieval (Daselaar et al., 2001; Donaldson, Peterson, & Buckner, 2001). As fMRI experimental designs and data analysis techniques have become more sophisticated researchers have been able to investigate the relationship between subregions of the MTL and different measures of successful recognition memory.

As outlined in a previous section (1.4.2), individuals with damage to the hippocampus often exhibit selective deficits in their memory for associations, relative to their memory for single items (Giovanello et al., 2003; Holdstock et al., 2005; Mayes et al.,

2002; Mayes et al., 2004; Turriziani et al., 2004; Vargha-Khadem et al., 1997). Associative memory generally requires the recovery of contextual information; therefore it is reasonable to assume that activity in the hippocampus may relate more to memory for item-context associations than to memory for single items in healthy individuals. In an fMRI study by Davachi, Mitchell and Wagner (2003), participants were scanned whilst they encoded words that were assigned to one of two study contexts. Outside the scanner participants completed a recognition memory test that required them to indicate whether an item was old or new and, if old, to identify the study context (source) in which they initially saw the item. Test performance was used to categorise encoding trials into items that were later remembered with their source (*DMhit-hit*), items later remembered without their source (*DMhit-miss*) and items later forgotten (*DMmiss*). A subsequent source memory effect, as characterised by a significant increase in activity for *DMhit-hit* relative to *DMhit-miss*, was identified in the hippocampus and posterior parahippocampal gyrus bilaterally. By contrast, activity in perirhinal cortex was greater for hits overall, but was not modulated by source memory accuracy ($DMhit-hit = DMhit-miss > DMmiss$).

In another study, Ranganath et al. (2004) also revealed a dissociation between source memory ($DMhit-hit > DMhit-miss$) and item memory effects in the hippocampus and perirhinal cortex, respectively. Notably, item memory effects within perirhinal cortex were indexed by a graded increase in activity that related to subsequent item memory strength (using confidence judgements collected at test), but did not vary according to source memory accuracy (Fig. 1.15). This linear increase in activity based on confidence is in keeping with the predictions of DPSD (Yonelinas et al., 1994; see Section 1.4.1.3), which characterises familiarity as a graded signal based on memory strength.

Source and item memory effects at retrieval are identified by making contrasts between test items that are remembered with their source (hit-hit), test items remembered without their source (hit-miss) and correct rejections. Using these contrasts, significant source memory effects (hit-hit > hit-miss) during retrieval have been identified in the hippocampus and posterior parahippocampal gyrus (Cansino, Maquet, Dolan, & Rugg, 2002; Dobbins, Rice, Wagner, & Schacter, 2003; Kahn, Davachi, & Wagner, 2004; although see Kirwan & Stark., 2004). Interestingly, while

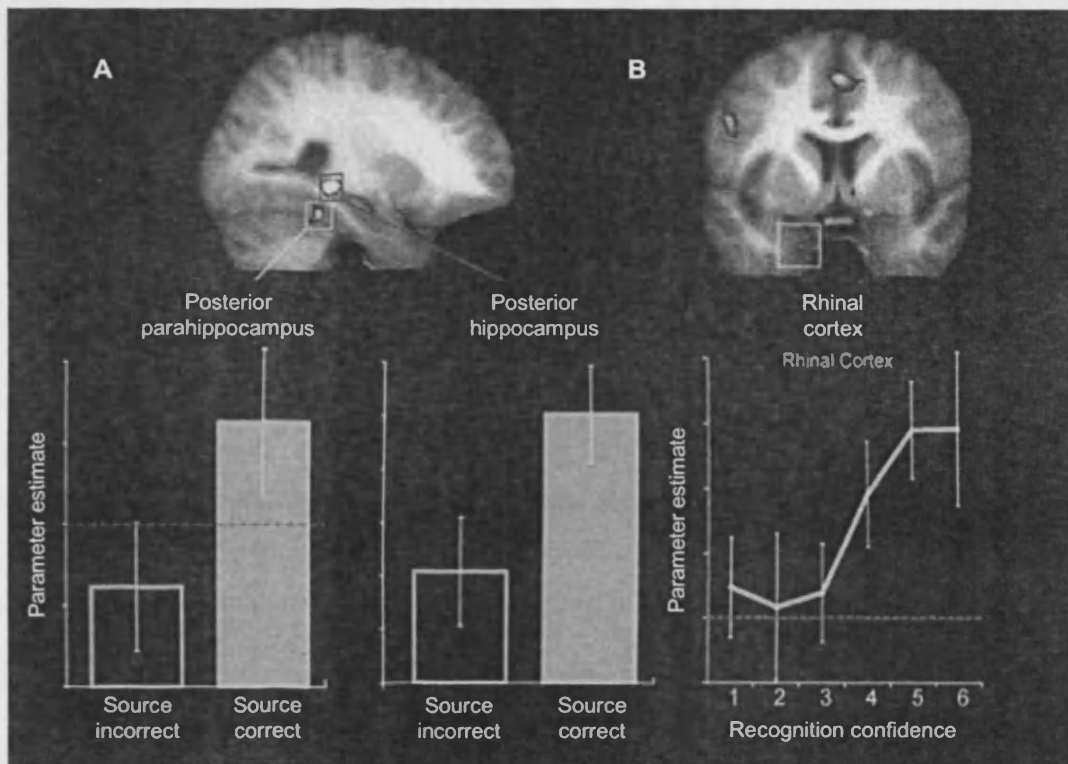


Figure 1.15: (A) Subsequent recollection effects, as indexed by greater activity for DMhit-hit (source correct) vs. DMhit-miss (source incorrect), in the posterior parahippocampal gyrus and hippocampus. (B) A subsequent familiarity effect, as indexed by a linear increase in activity with increasing recognition memory confidence. Figure adapted from Ranganath et al. (2004).

source memory effects remain positive, as indexed by greater activity for hit-hit than hit-miss, item memory effects at retrieval are commonly negative. For example, in a systematic review of fMRI memory-retrieval experiments, Henson, Cansino, Herron, Robb, and Rugg (2003) noted that the anterior MTL, which includes the perirhinal cortex, consistently exhibits greater activity for correct rejection relative to hit. Moreover, the negative relationship between hit and correct rejection in anterior MTL is not modulated by the retrieval of contextual information (correct rejection > hit-hit = hit-miss: Cansino et al., 2002). There are two accounts of this negative item memory effect. First, the perirhinal cortex shows reductions in neural activity to representations of items indicating relative changes in familiarity strength, which is known as repetition suppression. Second, the perirhinal cortex engages in preferential encoding of novel items. As these functions are not mutually exclusive, it is plausible that perirhinal cortex supports item familiarity memory via repetition suppression, as well as novelty encoding (Henson et al., 2003; Henson, 2005).

To summarise these findings, the studies discussed above reveal that there is a dissociation between activity within the hippocampus and anterior MTL that is associated with the recollection of contextual information, compared to memory for single items. In addition to these findings, it has also been demonstrated that encoding-related activity in left posterior parahippocampal gyrus is greater for subsequently remembered items, than for those that elicit a know response (Johnson & Rugg, 2007), whereas the right anterior parahippocampal gyrus is more active for items that subsequently feel familiar (know items) than those that are subsequently recollected (Henson, Rugg, Shallice, Josephs, & Dolan, 1999). Remember responses have been associated with activity in the hippocampus and posterior parahippocampal gyrus during memory retrieval (Dolcos, LaBar, & Cabeza, 2005; Eldridge, Knowlton, Furmanski, Bookheimer, & Engel, 2000; Wheeler & Buckner, 2004). Moreover, Uncapher & Rugg (2005) reported a double dissociation between activity in left anterior hippocampus and right anterior parahippocampal gyrus that related to subsequent remember (remember > miss) and subsequent know (know > miss) responses, respectively.

According to DPSD (see Section 1.4.1.3, Yonelinas, 1994), recollection is a threshold process, whereas familiarity operates via a continuous strength based signal. In turn, while recollection-based memory is generally indexed by high-confidence judgements, familiarity-based memory can be associated with a wide range of confidence responses (Yonelinas, 2001b). In light of the assumptions made by DPSD, and as revealed by Ranganath et al. (2004), scanning participants whilst they make subjective confidence memory judgements to old/new items can provide insights into how regions in the MTL support recollection and familiarity.

Montaldi, Spencer, Roberts and Mayes (2006) conducted an fMRI investigation to identify the neural correlates of familiarity memory for everyday scenes. During the scanned retrieval phase, participants were instructed to deliberately base their memory judgements on familiarity using a 3-point confidence scale (high, medium and low familiarity) and to report items for which they experienced recollection (Fig. 1.16). A significant effect of recollection, as indexed by greater activity for recollected items relative to all 3 levels of familiarity (e.g. recollection, R > high familiarity, F3 =

medium familiarity, F2 = low familiarity, F1), was observed in the hippocampus. A linear decrease in brain activity according to increases in familiarity strength only (F1 > F2 > F3 = R), was identified in the perirhinal cortex.

Yonelinas, Otten, Shaw, & Rugg (2005) also observed greater activity in the hippocampus for remember responses compared to two levels of familiarity strength and forgotten items (remember > high confidence old = low confidence old = low confidence new = high confidence new), but did not observe a graded familiarity signal within the perirhinal cortex. In fact, the latter effect also occurred in the hippocampus. This disparity is likely to be an empirical one, as Montaldi et al. (2006) employed a specialised familiarity only procedure that measured familiarity across 3 levels of strength. As Yonelinas et al. (2005) included 2 levels of familiarity strength only, their high confidence recollection category may have comprised recollection and a large proportion of high strength familiarity responses. Using a similar design to Yonelinas et al. (2005), however, Daselaar et al. (2006) identified a step-wise increase in activity for the highest level of confidence, compared to all others in the hippocampus, and a linear decrease in brain activity based on confidence responses in the perirhinal cortex.

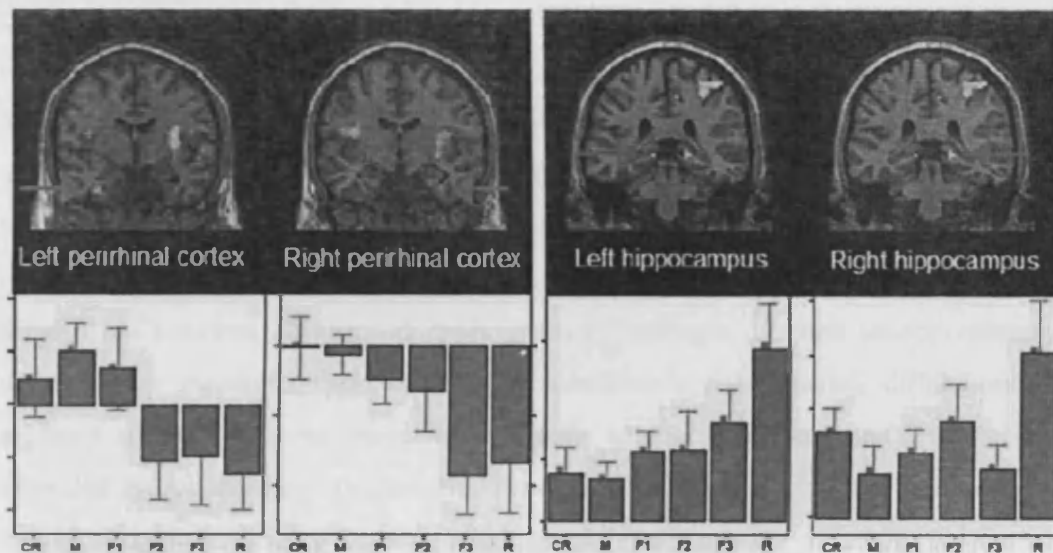


Figure 1.16: Contrasting memory effects in the perirhinal cortex (left) and hippocampus (right). In the perirhinal cortex there was a linear decrease in activity according to increases in familiarity strength, whereas activity in the hippocampus was greater for recollected item, relative to all levels of familiarity strength. Figure from Montaldi et al. (2006).

It would appear that activity within the hippocampus is generally associated with remember responses and high recognition memory confidence, and that the perirhinal cortex is uniquely sensitive to linear modulations in brain activity according to increases in item familiarity strength. Notably, parametric increases in brain activity based on increases in item memory strength at encoding (Ranganath et al., 2004) often reverse at retrieval (Daselaar et al., 2006; Gonsalves, Kahn, Curran, Norman, & Wagner, 2005; Montaldi et al., 2006). This pattern of response, however, makes sense, if the perirhinal cortex supports item familiarity memory via novelty detection (mentioned earlier); enhanced novelty encoding of items during the study phase will lead to greater levels of de-activation when items are re-presented at test.

The above findings need to be considered alongside fMRI evidence that the hippocampus and perirhinal cortex are not differentially sensitive to associative memory (Gold et al., 2006; Kirwan & Stark, 2004; Kirwan, Wixted, & Squire, 2008; Wais, Squire, & Wixted, 2010) or graded increases in item memory strength (Kirwan et al., 2008). Furthermore, according to Squire and colleagues (2007; Kirwan et al., 2008), fMRI contrasts made between recollection and familiarity estimates are not process pure and are, in fact, confounded by differences in memory strength. For example, it has been noted that memory accuracy for correct source, R and high confidence memory judgements almost always exceeds that for item only, K and medium confidence responses (Wixted, Mickes & Squire, 2010; although see Montaldi et al., 2006). Furthermore, Kirwan et al. (2008) argue that item memory strength (as indexed by confidence ratings) is generally higher for items associated with correct source judgments, than for incorrect source judgements. Consequently, a contrast between correct (hit-hit) and incorrect source (hit-miss) actually reflects differences between strong and weak memory strength. When source memory contrasts are restricted to items that are confidently remembered, differences in memory strength between hit-hit and hit-miss categories are equated. Using this amended source memory contrast, Kirwan et al. (2008) failed to detect brain activity that later predicted source memory within the MTL (Kirwan et al., 2008, for similar effects at retrieval see Wais et al., 2010).

In response to these criticisms, Cohn et al. (2009) conducted an experiment that compared fMRI activity within the hippocampus for behavioural measures of

recollection and familiarity judgements to studied word pairs, while minimising differences in strength for these response categories. Specifically, in the retrieval phase participants were presented with uncued trials that included studied and unstudied words, followed by the presentation of cued trials that included old (intact) and new-old word pairs which directly corresponded to the word presented in the uncued trial (e.g. STUDY: pumpkin thread; UNCUE TEST TRIAL: pumpkin; CUED TEST TRIAL: pumpkin thread). For both uncued and cued test trials participants either made a recollection (R) response or, for non-recollected items, a confidence judgement on a four-point scale (1= sure new to 4 = sure old; see Yonelinas et al., 2005). This paradigm therefore, allowed the direct comparison of neural activity for items judged as familiar in the first decision (rated 3 or 4) that remained familiar on the second decision (rated 3 or 4), with those that 'converted' to recollection (rated R on the second decision).

In the Cohn et al. (2009) study there was hippocampal activity for trials that converted to recollection but not for those that remained familiar, despite subjective memory strength for these items being equivalent in the initial uncued test trial. Replicating previous studies (Daselaar et al., 2006; Montaldi et al., 2006; Yonelinas et al., 2005), there was also a significant increase in activity for recollected cued targets compared to cued targets that were highly familiar ($R > 4$), that was not accompanied by a linear increase in familiarity strength ($1 > 2 > 3 > 4$). The hippocampus, therefore, was sensitive to qualitative changes in memory retrieval from uncued to cued test trials (familiar to recollected vs. familiar to familiar), as opposed to quantitative differences in memory strength. It is notable that, despite Cohn et al. (2009) providing some evidence against unitary/strength-based account (Squire et al., 2007; Kirwan et al., 2008; Wais et al., 2010; Wixted et al., 2010), differences in accuracy (hit / hit + false alarm) for remember and high confidence familiarity responses were not equated. As such, Wixted argues (Wixted et al., 2010) that differences in activity for high confidence familiarity and remember responses could still reflect variations in recognition strength and that the validity of the strength account remains. Importantly as there is an example of increased hippocampal activity for R, compared to high confidence familiarity responses for which accuracy is matched (Montaldi et al., 2006), Wixted's (Wixted et al., 2010) explanation seems unlikely (Montaldi & Mayes, 2010).

Some of the seemingly inconsistent results in fMRI studies may well have come about because the MTL is a relatively small area of the brain that contains several closely interconnected structures; it is difficult to ascertain the precise location of significant effects (Olman, Davachi, & Souheil, 2009). Furthermore, the MTL, and in particular the perirhinal cortex, is susceptible to signal loss and distortion artefacts and there are substantial differences between fMRI acquisition parameters and fMRI analysis techniques across experiments. As such, it is unsurprising that findings within the MTL remain variable (Eichenbaum et al., 2007; Henson, 2005; Montaldi et al., 2006). Despite this variability, however, activity in the posterior parahippocampal gyrus and hippocampus is most commonly associated with encoding and retrieval of source/associative information, remember judgements and high confidence old responses, whereas the perirhinal cortex is sensitive to memory for single items, know responses and exhibits linear modulations in activity (which increase at encoding and decrease at retrieval) according to recognition confidence (Cansino et al., 2002; Daselaar et al., 2007; Davachi et al., 2003; Henson et al., 1999; Montaldi et al., 2006; Ranganath et al., 2004, Yonelinas et al., 2005; although see Gold et al., 2006; Kirwan & Stark, 2004; Kirwan et al., 2008; Wais et al., 2010). These data are broadly in keeping with a dual-process account of MTL function (Aggleton & Brown., 1999), with the addition that the posterior parahippocampal gyrus (i.e. parahippocampal cortex) also appears to contribute to recollection (Diana et al., 2007).

1.5. Informational accounts of MTL function

Another interpretation of the findings from the fMRI literature, when considered alongside the anatomical characteristics of the MTL (see Section 1.2.1; summarised in Fig. 1.17), is that the parahippocampal cortex, hippocampus and perirhinal cortex process and support different kinds of mnemonic information (such as items, contexts and item-context associations), which map on to the phenomenological processes of recollection and familiarity. The majority of neocortical inputs into the MTL that carry item-based, or 'what', information project to the perirhinal cortex via the ventral visual processing stream. In contrast, the parahippocampal cortex receives a greater input of contextually based, or 'where', information from the neocortex via the dorsal visual stream (Ungerleider & Haxby, 1994; Suzuki & Amaral, 1994). 'What' and

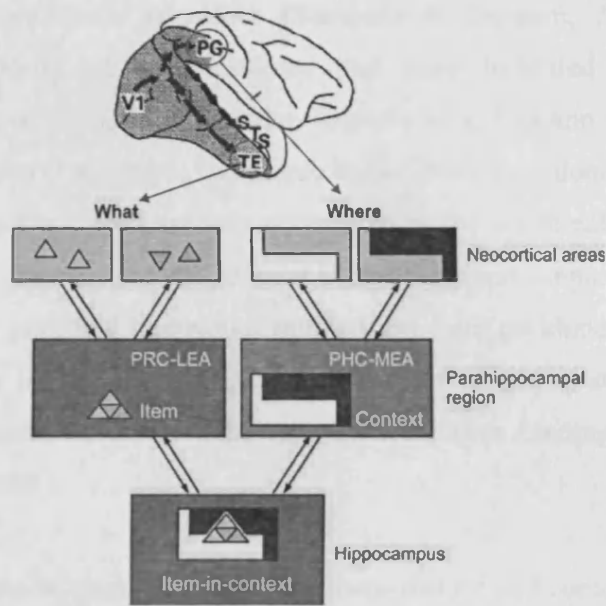


Figure 1.17: A proposed functional organisation of the MTL based on connectivity between MTL subregions and the dorsal and ventral visual processing streams. Abbreviations: (PG) inferior parietal cortex; (TE) inferior temporal cortex; (PRC) perirhinal cortex; (PHC) parahippocampal cortex; (LEA) lateral entorhinal cortex; (MEA) medial entorhinal cortex. Figure adapted from Ungerleider & Haxby (1994), and Eichenbaum et al. (2007)

'where' streams then converge in the hippocampus, via afferent connections from the parahippocampal and perirhinal cortices. As a result, it is possible that perirhinal cortex engages in selective encoding and reinstatement of 'what' or item-based information, the parahippocampal cortex processes the global context ('where' and 'when' information) in which an item was initially encountered and, as a site of convergence, the hippocampus forms representations of item-context associations (Eichenbaum et al., 2007).

According to one such informational account of MTL function, the perirhinal cortex and parahippocampal cortex differentially contribute to domain-specific item and spatial-contextual encoding, whereas the hippocampus supports domain-general associative memory processing (item-context account: Davachi, 2006). The item-context account is not explicitly tied to predictions regarding recollection and familiarity, as domain-specific item representations in the perirhinal cortex are not necessarily supported by familiarity-based processing. For example, Davachi (2006) proposes that the perirhinal cortex can support associative encoding if source details

comprise an item feature, such as colour (Staresina & Davachi, 2006; 2008). Consequently, the majority of fMRI studies that have indicated the unique contribution of the hippocampus to associative memory (e.g. Cansino et al., 2002; Davachi et al., 2003; Kahn et al., 2005; Ranganath et al., 2004) have done so by using source information that is not processed or represented in the perirhinal cortex. An additional prediction of the item-context account is that the hippocampus, as a site of convergence that binds item and contextual information from perirhinal cortex and parahippocampal cortex to form domain-general associative representations, should be sensitive to the amount, rather than the type of associative binding that occurs (Staresina & Davachi, 2008).

Using an associative memory task that comprised item-feature and contextual source details, Staresina and Davachi (2008; Fig. 1.18) showed that activity in the perirhinal cortex correlated with the subsequent recollection of associated item feature details, but not subsequent memory for the associated contextual information (see also Awipi & Davachi, 2008, which is discussed later). In the hippocampus, however, there was a graded increase in activity that related to the amount of associative information recovered at retrieval and therefore, by implication, bound at encoding (2 source correct > 1 source correct > item only; see also Uncapher, Otten, & Rugg, 2006).

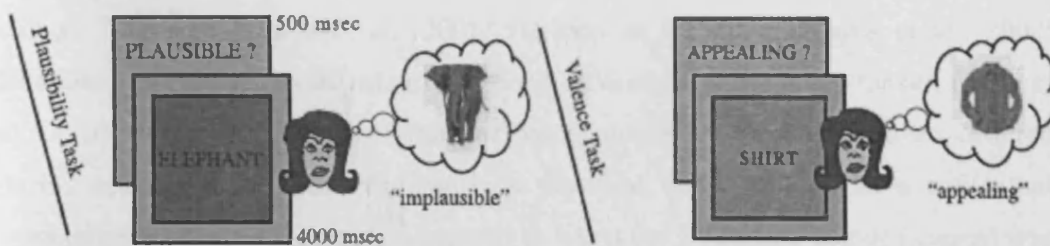


Figure 1.18: The encoding task from Staresina & Davachi (2006). Participants were presented with words and instructed to vividly imagine the referent of the noun in the colour presented (item feature source detail) and to indicate if the imagined representation was plausible/implausible or appealing/unappealing (contextual source detail). Figure from Staresina & Davachi (2008).

There is an alternative informational account of MTL function, known as the binding of item and context model (BIC model: Diana et al., 2007). As with Davachi's (2006) item-context account, BIC predicts that perirhinal and parahippocampal cortices differentially encode item and context information, which is subsequently bound by

the hippocampus to form domain-general associative representations. BIC also proposes, however, that both spatial and non-spatial contextual information is processed by the parahippocampal cortex. For example, it has been shown that activity in the posterior parahippocampal cortex relates to processing non-spatial contextual information such as faces, objects, words and emotional pictures (Aminoff, Grounau, & Bar, 2007; Bar, Aminoff, & Ishai, 2008; see also Bar & Aminoff, 2003; Bar, Aminoff, & Schacter, 2008; Kensinger & Schacter, 2006). According to BIC, therefore, context and bound item-context representations in the parahippocampal cortex and the hippocampus (respectively) support recollection. In a similar vein, another key tenet of the BIC model is that perirhinal cortex item representations predominantly support familiarity, which does not require the recovery of contextual information. Moreover, enhanced encoding within perirhinal cortex results in greater item memory strength; thus BIC can also accommodate graded modulations in perirhinal cortex activity based on increasing familiarity strength (Daselaar et al., 2006; Montaldi et al., 2006; Ranganath et al., 2004).

An additional prediction of the BIC model is that the perirhinal cortex can support associative/source memory under two circumstances: (a) when source information is encoded as an item feature (Staresina & Davachi, 2006; 2008; Diana, Yonelinas, & Ranganath, 2010) and (b) when items and their associations are processed as a single unit or 'unitised' (Diana et al., 2008; Haskins et al., 2008; Mayes et al., 2007; Quamme et al., 2007; Yonelinas et al., 1999). Considering evidence for (a), Diana et al. (2010) asked how activity within the hippocampus and perirhinal cortex differed during retrieval of colour-word pairings that had been encoded as a contextual association (context condition), compared to when the associated colour (source) was a feature of the item to be encoded (item condition). Importantly, the information to-be-remembered in these conditions was equivalent; therefore, only the way in which participants processed the colour-based source information differed. In keeping with the findings from previous fMRI investigations (Cansino et al., 2002; Dobbins et al., 2003; Kahn et al., 2004), activity within the hippocampus (and posterior parahippocampal gyrus) correlated with recollection of item-based and contextual source details for items from both conditions. A novel finding, however, was that successful source recognition in the item detail condition also correlated with activity

in the perirhinal cortex. The authors concluded that source memory retrieval can be supported by the perirhinal cortex if it comprises item feature information.

In keeping with (b) above, it has been demonstrated that patients with MTL damage are less impaired on their memory for associative pairs when they are studied under a task manipulation that encourages unitisation (e.g. making a new compound word from presented word pairs: Quamme et al., 2007; see also Giovanello, Keane, & Verfaellie, 2006). Using fMRI, Haskins et al. (2008) showed that, with similar task manipulations, encoding of 'unitised' word pairs activated the perirhinal cortex during memory encoding to a greater degree than 'non-unitised' word pairs. Moreover, the authors identified a linear modulation in activity in the perirhinal cortex that related to recognition memory confidence ratings collected during the retrieval phase. This linear increase in activity for associative memory strength significantly overlapped with the activity for unitised pairings (Fig. 1.19).

Clearly, the demonstration that some forms of associative memory can be preserved by familiarity is at odds with the proposition that all associative memory requires recollection (Aggleton & Brown, 1999; Brown & Aggleton, 2001). It has been

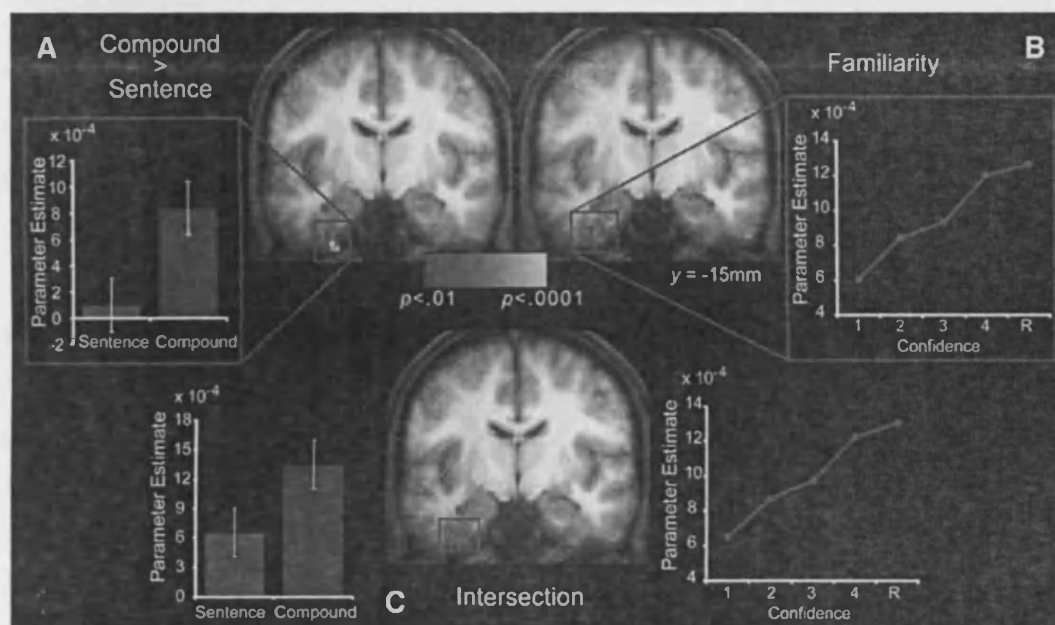


Figure 1.19: (A) MTL voxels in which activation was significantly greater for words from the unitised (compound) vs. non-unitised (sentence) encoding conditions. (B) MTL voxels in which there was a linear increase in subsequent familiarity strength. (C) Significant overlap of the two contrasts in perirhinal cortex. Figure from Haskins et al. (2008).

observed, however, that common to all instances under which individuals with focal damage to the hippocampus demonstrate intact associative memory is that pairs of items were from the same processing domain (e.g. face-face or word-word: Giovanello et al., 2006; Mayes et al., 2004; Quamme et al., 2007; Vargha-Khadem et al., 1997, although see Turriziani et al., 2004). When items are from different domains (i.e. face-word), however, associative memory remains impaired (Holdstock et al., 2002; Holdstock et al., 2005; Mayes et al., 2004; Turriziani et al., 2004; Vargha-Khadem et al., 1997). In light of these observations, another model of MTL function, referred to as Domain Dichotomy (DD: Mayes et al., 2007), has been proposed, which also focuses on the instances under which the perirhinal cortex could support memory for novel associations. Similar to a dual-process account (Aggleton & Brown, 1999; Brown & Aggleton, 2001), this view predicts that recollection and familiarity are supported by the hippocampus and perirhinal cortex, respectively. A divergent property of DD, however, is that the perirhinal cortex can support familiarity for *non*-unitised (as well as unitised) associations between items from the same processing domain (e.g. face-face or word-word pairs).

In more detail, the DD account proposes that the formation of novel associations is contingent upon the amount of information that can converge within a given MTL structure, based upon the proximity of mnemonic representations. As items from the same (or within) domain are represented within close proximity to one another in the perirhinal cortex, these separate items can be bound together (see Fig. 1.20). In contrast, as items from different (or between) domains are processed distally within the perirhinal cortex they cannot sufficiently converge, thus the hippocampus is required to link these items together. A common feature of the unitisation account and DD, therefore, is that under certain circumstances memory for novel associations can be supported by familiarity. While the unitisation account requires that associative representations must be configurally bound into a single unit, according to DD within-domain associations in the perirhinal cortex still comprise two separate, but related mnemonic representations.

There are at least two important outstanding issues for the DD account. First, to date, there is no single published fMRI study that has directly compared levels of activity within the perirhinal cortex for within- and between-domain item-item associations.

Second, although the patient data interpreted in support for DD are compelling (Mayes et al., 2002; Mayes et al., 2004; Vargha-Khadem et al., 1997), the concept of unitisation also provides a good explanation for most of these findings (Quamme et al., 2007). As such, the current literature cannot reliably adjudicate between a unitisation or DD account of perirhinal contributions to associative memory.

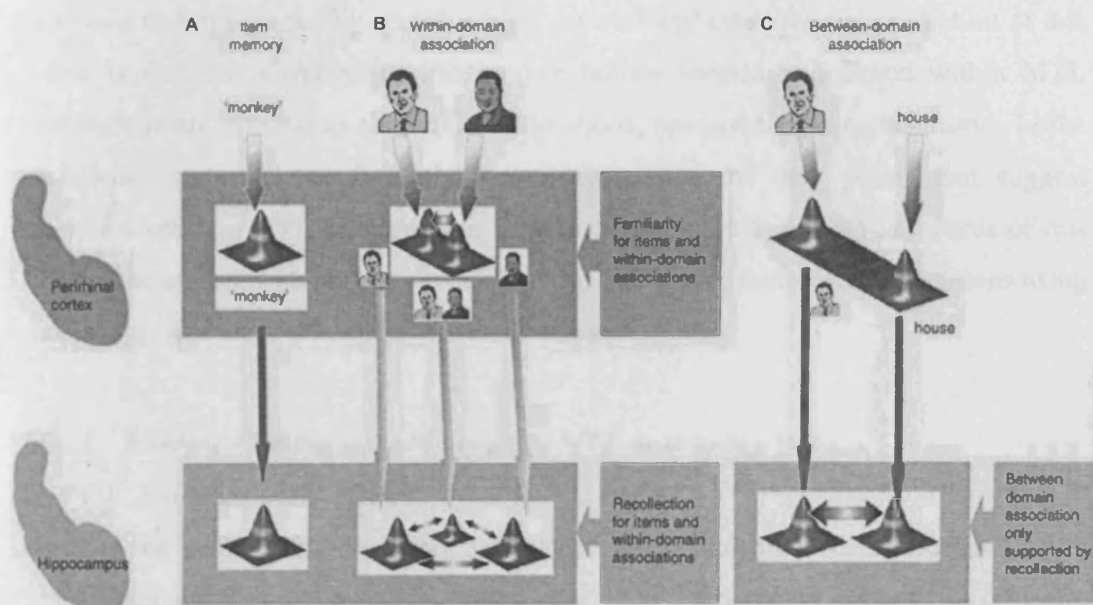


Figure 1.20: The Domain Dichotomy account. (A) Inputs of already unitised item representations ('monkey') are processed by the perirhinal cortex, which then project in a unitised form to the hippocampus. (B) As within-domain inputs (face-face pairs) are represented in close proximity to each other in the perirhinal cortex these can be bound into a non-unitised association that can be supported by familiarity. The hippocampus receives this information as an association and as separate components to form flexible recollection-supported associations between these items and any additional contextual information. (C) Due to their relatively distal representations, between-domain associations (face-word pairs) do not sufficiently converge within the perirhinal cortex. In the hippocampus, however, these representations can be bound to each other and other contextual representations, supporting recollection. Figure from Mayes et al. (2007).

1.6. The representational MTL

The data reviewed above suggests that the division of labour within the MTL is dictated by the type of information, rather than the specific processes, associated with recognition memory (Davachi, 2006; Diana et al., 2007). A recently articulated version of this type of view proposes that information-based divisions of labour are, in fact, guided by the nature of the to-be-remembered material and that MTL subregions

differ in their contribution to different types of visual stimuli, with the hippocampus necessary for spatial processing and the perirhinal cortex for object processing (Lee, Barense, & Graham, 2005; Graham et al., 2010; see also Bird & Burgess, 2008; Bussey & Saksida, 2005; Saksida & Bussey, 2010). In an attempt to account for a developing literature that has demonstrated mnemonic and perceptual deficits in MTL amnesia that are guided by stimulus type, a novel and controversial prediction of this view is that the stimulus-specific representations formed and stored within MTL subregions are integral to all cognitive functions, not just long-term memory. In the following sections, therefore, there is a review of the data points that suggest stimulus-specific MTL contributions to memory and, while not the key focus of this thesis, the experiments that have identified similar stimulus-specific distinctions using tasks with limited or no explicit memory demands.

1.6.1. Evidence for the stimulus-specific MTL in memory

1.6.1.1. Evidence from animals

Due to the variety of information that projects to the perirhinal cortex from unimodal cortical areas within the ventral visual, or ‘what’, processing stream, it is ideally suited for forming complex multi-sensory representations of objects (see Section 1.2.1 and Fig. 1.3). Evidence from electrophysiology has highlighted the stimulus-specific nature of perirhinal cortex cells, which selectively respond to the presentation of single objects (Zhu, Brown & Aggleton, 1995). Moreover, perirhinal cortex firing rates also provide information about the familiarity of objects (Brown & Xiang, 1998; Ringo, 1996). Unlike the perirhinal cortex, cells within the hippocampus are not sensitive to presentations of single items (Zhu et al., 1995), or repetitions of items (Otto & Eichenbaum, 1992b). It is possible that, as focal damage to the entorhinal cortex only causes mild impairments on DNMS (see earlier, Meunier et al., 1993), object based information from the perirhinal and entorhinal cortices is not passed on to the hippocampus, despite the numerous interconnections between these structures (Aggleton & Brown, 1999).

As previously discussed, focal lesions to the hippocampus are rarely associated with impairments on delayed-non-matching to sample (DNMS) tasks for objects (Mishkin, 1978; Mumby et al., 1992; Murray & Mishkin, 1998), whereas damage to the

perirhinal cortex is sufficient to cause impairments on object-based DNMS. There is evidence, however, that lesions to the hippocampal system in monkeys (Buckley, Charles, Browning, & Gaffan, 2004; Hampton, Hampstead, & Murray, 2004) and rats (Aggleton, Hunt, & Rawlins, 1986; Morris, Garrud, Rawlins, & O'Keefe, 1982) do result in selective impairments on tasks that are spatially demanding.

There is also a wealth of electrophysiological data from animals that neural activity within the hippocampus is sensitive to changes in spatial environment, alterations to the spatial arrays of items, and associations between items and their locations (Eichenbaum, 2004; O'Keefe, 1976; O'Keefe, Burgess, Donnett, Jeffrey, & Maguire, 1998; O'Keefe & Dostrovsky, 1971; O'Keefe & Nadel, 1978). These cells have been labelled 'place cells', which selectively fire when an animal is placed in a particular location in an environment, or 'place field' (O'Keefe & Nadel, 1978). In turn these 'place cells' form a context-dependent map (O'Keefe & Nadel, 1978), which can remain stable for several weeks and can support long-term memory of 'place fields' (Lever, Wills, Cacucci, Burgess, & O'Keefe, 2002). These maps are also flexible, as place cells can rapidly remap to form representations of novel environments (Muller & Kubie, 1987). 'Place cells' are yet to be identified in the perirhinal cortex and lesions to the perirhinal cortex do not impact significantly upon spatial memory (for a review see Aggleton, Kyda, & Bilkey, 2004).

The evidence described above suggests a fractionation between the perirhinal cortex and hippocampus for visuo-object and visuo-spatial processing. Recently, Winters, Forwood, Cowell, Saksida and Bussey (2004) assessed the performance of rats with perirhinal cortex or hippocampal lesions on tasks of object and spatial memory. The object recognition memory task was designed to minimise spatial and contextual confounds (Fig 1.21). While rats with perirhinal cortex lesions were severely impaired on the object task, rats with hippocampal lesions did not differ from controls, even after retention delays of up to 48 hours (Forwood, Winters, & Bussey, 2005). By contrast, only the hippocampal rats were impaired on the spatial memory task (see also Buckley et al., 2004; Gaffan, 1994, for similar effects following damage to the fornix). These data, therefore, provide compelling double dissociations between the perirhinal cortex and hippocampal contributions to object and spatial memory.

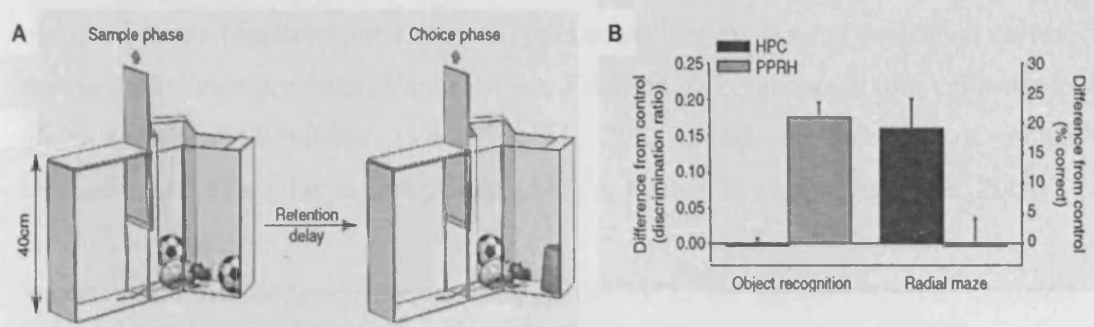


Figure 1.21: (A) An illustration of the spontaneous object recognition task from Winters et al. (2004), which was carried out in a modified apparatus to minimise the potentially confounding influence of spatial or locomotive factors. (B) The double dissociation between impairments in object based and spatial memory following perirhinal cortex and hippocampal damage, respectively. Figures from Winters et al. (2004).

Despite the empirical success of lesion research, one limitation is that it can overlook the functional significance of brain regions that are associated with, but not critical for, a particular cognitive function. For example, damage to the perirhinal cortex may fail to have an effect on spatial memory due to the compensatory action of parallel processing routes to the hippocampus (Aggleton & Brown, 2005). As a result, the functional properties of brain regions such as the perirhinal cortex and hippocampus have also been assessed using immediate early gene (IEG) *c-fos* imaging (for reviews see Brown & Aggleton, 2001; Aggleton & Brown, 2005). This method involves measuring the expression of IEG *c-fos*, which occurs when neurons are active. In turn, *fos* proteins can be visualised and used to quantify neural responses within different brain regions to certain experimental manipulations. An additional benefit of *c-fos* imaging over lesion research is that it permits the functional comparison of different regions in the same animals.

Paralleling findings from electrophysiology and lesion research, significant increases in *fos* levels have been identified in the perirhinal cortex and area TE, but not in the hippocampus or entorhinal cortex, for the presentation of novel compared to familiar objects (Zhu, McCabe, Aggleton, & Brown, 1997). Moreover, when novel and familiar objects are presented in different visual fields, there are hemispheric differences in *c-fos* activity in the perirhinal cortex and area TE, whereas no differences occur in the hippocampus or entorhinal cortex (Wan, Aggleton, & Brown,

1999; Zhu, McCabe, Aggleton, & Brown, 1996). Increased *c-fos* activity has been observed in the hippocampus and parahippocampal cortex, but not perirhinal cortex, during spatial memory tasks (Vann, Brown, Erichsen, & Aggleton, 2000), exposure to novel-spatial environments (Vann et al., 2000) and presentation of novel arrangements of familiar objects (Jenkins, Amin, Pearce, Brown, & Aggleton, 2004).

When considered alongside the anatomy of the MTL, the animal research discussed above also indicates that the perirhinal cortex and hippocampus do not contribute equivalently to object versus spatial processing. The perirhinal cortex is highly specialised for processing object based information, selectively responds to the presentation of objects and, when damaged, causes significant impairments on object based DNMS (Meunier et al., 1993; Winters et al., 2004; Zhu et al., 1995; Zhu et al., 1996, 1997). Cells within the hippocampus appear to be sensitive to spatial information, and lesions to this area cause impairments on spatially demanding tasks (Aggleton et al., 1986; Bird & Burgess, 2008; Eichenbaum, 2004; Forwood et al., 2005; Morris et al., 1982; O'Keefe, 1976; O'Keefe et al., 1998; O'Keefe & Dostrovsky, 1971; O'Keefe & Nadel, 1978; Vann et al., 2000; Winters et al., 2004).

1.6.1.2. Evidence from amnesia

To date, few experiments have directly assessed the memory performance of amnesic populations for different stimuli. In a recent study, the performance of two patient groups, individuals with focal hippocampal atrophy and individuals with wider MTL damage, was compared to matched controls on a forced-choice recognition memory task where the stimuli comprised faces and scenes (Taylor, Henson, & Graham, 2007). Patients with focal hippocampal lesions showed intact recognition memory for faces, but not scenes, whereas patients with damage to the hippocampus and perirhinal cortex were impaired on both face and scene recognition memory. Likewise, it has been demonstrated that semantic dementia, which is generally associated with disproportionate cell loss in the perirhinal cortex (Barense, Rogers, Bussey, Saksida, & Graham, 2010; Davies, Graham, Xuereb, Williams, & Hodges, 2004; Lee, Levi, Rhys Davies, Hodges, & Graham, 2007), can cause profound impairments in memory for unfamiliar faces while memory for scenes or landscapes remains intact (Cipolotti & Maguire, 2003).

As faces can be processed holistically (Tanaka & Farah, 1991), it is been proposed that recognition memory for faces may rely more on familiarity-based memory processing (Yonelinas et al., 1999). Differential impairments in face and scene memory, such as those detailed above, could therefore reflect differences in the availability of recollection and familiarity due to the integrity of the hippocampus and perirhinal cortex, respectively. Similar disproportionate impairments in

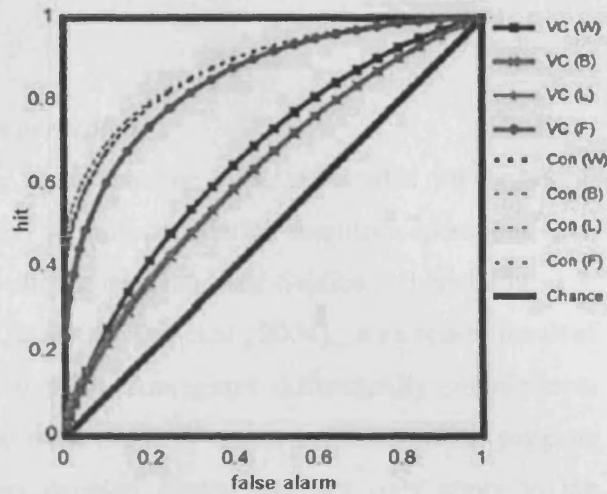


Figure 1.22: Hippocampal amnesic VC and control (Con) recognition memory ROCs for words (W), buildings (B), landscapes (L) and faces (F). VC's ROC for faces was similarly asymmetrical to the controls, suggesting intact recollection for this stimulus type. Figure from Cipolotti et al. (2006).

scene and face recognition memory have been observed in 3 hippocampal amnesics using the ROC procedure (patient VC: Cipolotti et al., 2006; patient RH: Bird, Shallice, & Cipolotti, 2007; developmental amnesic Jon: Bird, Vargha-Khadem, & Burgess, 2008; although see data for patient JC, Bird et al., 2007). The ROC data, however, indicate that, if interpreted under the assumptions of DPSD, recollection for faces was intact in these patients (Fig. 1.22). In a similar vein, equivalent performance on item and associative memory for faces, but impairments on both measures for buildings and landscapes, has been identified in a patient with hippocampal pathology (Carlesimo, Fadda, Turriziani, Tomaiuolo, & Caltagirone, 2001).

The key implication of these findings is that MTL contributions to visual recognition memory may not be uniform and cannot be easily explained by a classic distinction between item versus associative memory (Carlesimo et al., 2001), or recollection versus familiarity (Bird et al., 2007; Bird et al., 2008; Cipolotti et al., 2006). These data points are, however, consistent the findings in the animal literature that indicates

that the perirhinal cortex and the hippocampus selectively support memory for objects (including faces) and scenes.

1.6.2. The stimulus-specific MTL in perception

Modular accounts of human memory claim that the MTL is essential for long-term declarative memory, but is not required for non-declarative cognitive operations such as perceptual learning, priming and motor learning (see Section 1.3 and Fig. 1.5; Squire & Zola-Morgan, 1991; Squire, 2004; Squire et al., 2004). As a result, much of the focus has been on identifying how MTL subregions differentially contribute to declarative memory, whereas less has been made of recent evidence which suggests that the stimulus-specific distinctions detailed above may not only apply to the explicit memory domain (Barese et al., 2005; Barese, Gaffan, & Graham, 2007; Barese, Rogers et al., 2010; Bartko, Winters, Cowell, Saksida, & Bussey, 2007a, 2007b; Buckley, Booth, Rolls, & Gaffan, 2001; Buckley & Gaffan, 1997, 1998; Bussey, Saksida, & Murray, 2002, 2003; Eacott, Gaffan, & Murray, 1994; Eacott, Machin, & Gaffan, 2001; Lee, Buckley et al., 2006; Lee, Buckley et al., 2005; Lee, Bussey et al., 2005).

Early animal lesion research largely suggested that the perirhinal cortex exclusively formed part of a mnemonic system, as deficits following damage were delay dependent (e.g. Meunier et al., 1993; Suzuki et al., 1993). In a study using non-human primates, however, Eacott et al. (1994) demonstrated that lesions to the perirhinal cortex could result in equivalent impairments on zero-delay object match-to-sample (MTS) tasks, when the objects were particularly difficult to discriminate. Likewise, monkeys also exhibit impairments on concurrent object discrimination following perirhinal cortex damage when object identification is made highly taxing, either by means of increasing the number of distracting stimuli or presenting the stimuli from multiple views (Buckley et al., 1997; Buckley et al., 1998, Eacott et al., 2001; although see Buffalo et al., 1999; Buffalo, Ramus, Squire, & Zola, 2000; Buffalo, Stefanacci, Squire, & Zola, 1998).

These findings suggest that perirhinal cortex contributes to zero-delay object discrimination, but only when the task is sufficiently perceptually demanding. To formally examine this, Buckley et al. (2001) designed a series of 'odddity' tasks that

varied in perceptual complexity. On each trial, monkeys were rewarded for correctly identifying an odd-one-out target item amongst 5 visually similar foils. Real-world object oddity was presented in two conditions to directly manipulate perceptual complexity; same-view and different view. In the same-view condition 5 identical views of one object were presented along with one view of a different object. In the different-view condition 5 different views of one object were presented along with one view of a different object. In addition to the object oddity, Buckley et al. (2001) also presented subjects with easy and difficult colour, shape and size oddity trials. Perirhinal cortex lesions did not affect performance on the easy and difficult colour, size and shape or the same-view object oddity trials. Interestingly, however, perirhinal cortex lesions did cause impairments on the different-view object oddity trials. The authors concluded that deficits occurred on the different-view condition as this involved complex-feature discrimination, which is perirhinally dependent (Buckley et al., 2001; Buckley et al., 2005).

In a series of further experiments it was also demonstrated that perirhinal cortex lesions result in impairments during concurrent discrimination of, or when solving single pair discriminations for, objects that share many features (Bussey et al., 2002; 2003; Bartko et al., 2007a; 2007b). For example, Bussey et al. (2002) demonstrated that monkeys with perirhinal cortex lesions could discriminate between pairs of items that contained few overlapping features. In this study, however, perirhinal cortex atrophy was associated with impairments in visual discrimination at the maximum level of feature overlap between items (Fig 1.23). Similarly, monkeys with perirhinal cortex lesions were unable to distinguish between highly overlapping pairs of morphed items (Bussey et al., 2003). To account for these findings, Bussey and Saksida (2002; see also Murray & Bussey, 1999) developed the perceptual-mnemonic/feature-conjunction (PMFC) model of object identification. According to the PMFC, there is a representational hierarchy along the ventral processing stream, with the perirhinal cortex forming the apex of this pathway. Object information is passed downstream with the emergence of increasingly complex conjunctions of features. The perirhinal cortex houses the most complex conjunctive object representations and the PMFC predicts that memory and perception (discrimination) of objects with simple, non-overlapping features does not require the perirhinal cortex (Cowell et al., 2010). When there are high levels of feature overlap, or 'feature

ambiguity' (Bussey & Saksida, 2005; Saksida & Bussey, 2010; Cowell et al., 2010) between objects, damage to the perirhinal cortex impairs performance because of the requirement to integrate multiple object features to successfully distinguish between items (although see Suzuki, 2009; Suzuki & Baxter, 2009).

The PMFC provided an intuitive explanation for the circumstances under which deficits in concurrent discrimination of objects occur, and why other animal lesion experiments have failed to reveal these findings. In an attempt to extrapolate the predictions of the PMFC to humans, the performance of hippocampal and MTL patient groups (described earlier in Section 1.6.1.2 for Taylor et al., 2007) was compared on a paired object discrimination task (adapted from Bussey et al., 2002), where pairs of items varied in feature ambiguity to small, intermediate or large degrees (Barens et al., 2005; see also Barens et al., 2007). At low levels of feature ambiguity both patient groups performed within the normal range. Under conditions of high feature ambiguity patients with perirhinal cortex damage were significantly impaired (Fig. 1.23). Similar impairments on high ambiguity object discriminations have also been demonstrated in individuals with semantic dementia (Barens, Rogers et al., 2010), which is characterised by cell loss in the perirhinal cortex (Davies et al., 2004; Lee et al., 2007).

In another study, Lee, Bussey et al. (2005) assessed single pair discrimination of faces, objects and scenes with increasing levels of feature overlap in amnesic individuals with selective hippocampal damage or more extensive MTL lesions (Taylor et al., 2007; Barens et al., 2005; Barens et al., 2007). Both patient groups were impaired in their discrimination of scene pairs, while the patients with damage that included the perirhinal cortex demonstrated an additional impairment for object and face pairs. Furthermore, all deficits were exacerbated by increasing levels of feature ambiguity. This study provides compelling evidence that a representational hierarchy based on increasing complexity of stimuli, as predicted by the PMFC, could also be applicable to the dorsal processing stream for spatial stimuli (Graham et al., 2010).

Extending these findings, Lee, Buckley et al. (2005; Fig. 1.24) conducted a study using modifications to the oddity tasks used to assess visual discrimination in

monkeys with perirhinal cortex lesions (Buckley et al., 2001). MTL and hippocampal patients (Lee, Bussey et al. 2005) conducted trial-unique oddity tasks that comprised same/different view faces and virtual reality rooms. Both patient groups were impaired on the different-view virtual reality room oddity. Patients with extensive lesions to the MTL, however, exhibited additional impairments for the different-view face oddity. In parallel with the findings from Buckley et al. (2001), MTL damage did not result in impairments on the face or scene same-view oddity tasks. Moreover, as a trial unique design was adopted, the deficits in the patients could not have resulted from an inability to learn and remember the stimuli across trials, bolstering the conclusion that these deficits were necessarily due to impaired long-term memory (Lee, Buckley et al., 2005; see also Barense et al., 2007; Lee et al., 2010).

The evidence reviewed here indicates that MTL subregions can contribute to perceptual discrimination in animals (Bartko et al., 2007a; 2007b; Buckley et al.,

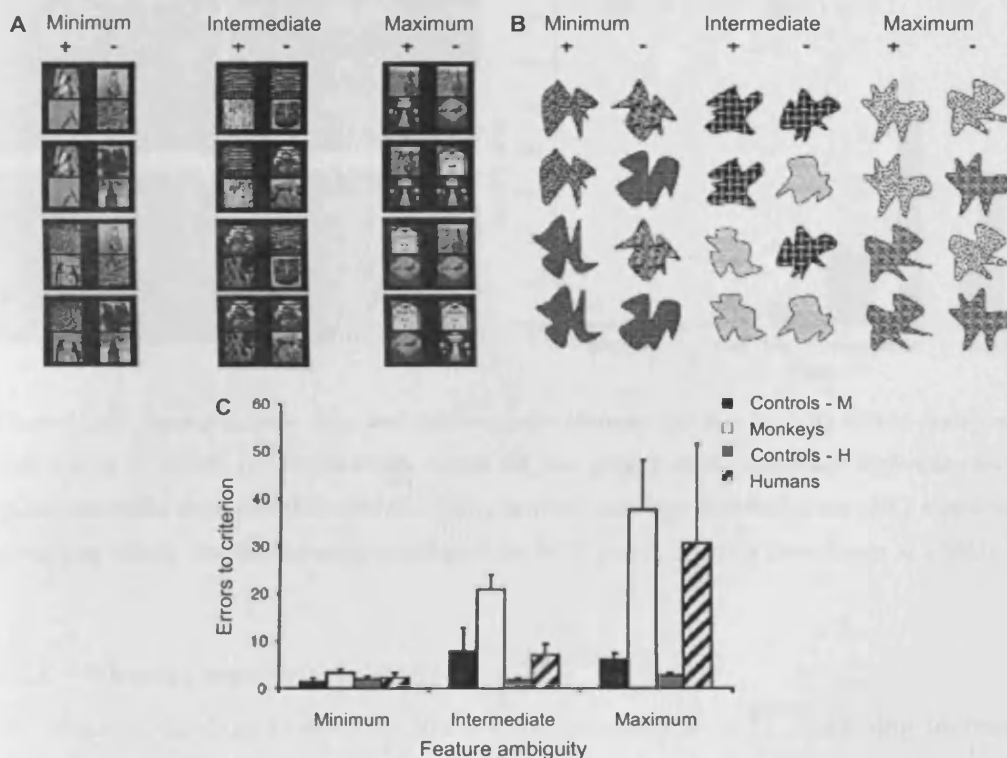


Figure 1.23: Stimuli used by (A) Bussey et al. (2002) and (B) Barense et al. (2005) to test concurrent discrimination in monkeys and MTL amnesics, respectively. (C) Performance of animals with perirhinal lesions and humans with broad MTL lesions, which included the perirhinal cortex, across minimum, intermediate and maximum feature ambiguity. Abbreviations: (M) control monkeys; (H) healthy human participants. Figure from Graham et al. (2010).

1997; Buckley et al., 1998; Buckley et al., 2001; Bussey et al., 2002; 2003; Eacott et al., 2001; although see Buffalo et al., 1999; Buffalo et al., 2000; Buffalo, Stefanacci et al., 1998) and humans (Barens et al., 2005; Barens et al., 2007; Lee, Buckley et al., 2005; Lee, Bussey et al., 2005; although see Buffalo, Reber, & Squire, 1998; Levy, Shrager, & Squire, 2005; Shrager, Gold, Hopkins, & Squire, 2006; Stark & Squire, 2000). As with the memory deficits detailed earlier, the profile of perceptual impairment appears to be contingent upon the stimuli employed in the task and the site of MTL damage. These data indicate that the perirhinal cortex contains representations of complex objects, and possibly the same relationship exists between the hippocampus and scenes (Lee, Barens et al., 2005; Lee, Buckley et al., 2005; Lee, Bussey et al., 2005; Graham et al., 2010). These findings are consistent with the view that these representations are able support both memory and perception (Bussey & Saksida, 2005; Cowell et al., 2010; Graham et al., 2010; Saksida & Bussey, 2010).

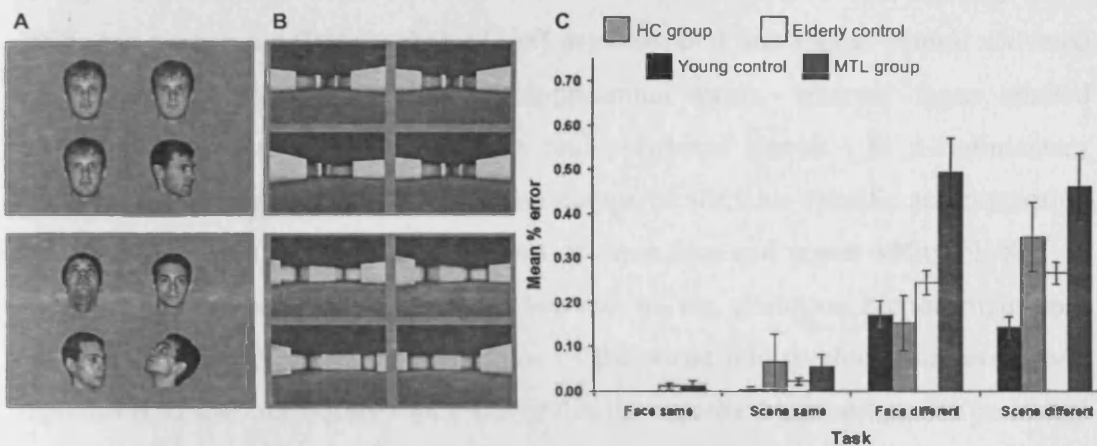


Figure 1.24: Example same- (top) and different-view (bottom) (A) face and (B) virtual-reality oddity from Lee et al. (2005). (C) Performance across the four groups on the same- and different-view face and scene oddity from Lee et al. (2005). Young controls were age matched to the (HC) hippocampal group and elderly controls were age matched to the MTL group. Figures from Lee et al. (2005).

1.6.3. Stimulus-specificity in fMRI

The neuropsychological evidence for a stimulus-specific MTL is gaining increasing support from functional imaging. Data from a number of recent fMRI investigations have shown that perirhinal cortex is (a) active during face and object odd-one-out decisions compared to size judgements (Barens, Henson, Lee, & Graham, 2010; Lee, Scahill, & Graham, 2008), (b) exhibits modulations in activity across manipulations

that may differentially stress processing of object feature conjunctions (e.g. feature-overlap: Devlin & Price, 2007), and viewpoint (e.g. different-view > same-view: Barense, Henson et al., 2010) during face and object oddity, and (c) is sensitive to presentations of novel objects in familiar arrays (Lee, Bandelow, Schwartzbauer, Henson, & Graham, 2006). Similarly, scene odd-one-out judgements result in significant activity in posterior hippocampus (Lee et al., 2008), although there can also be some activity (above baseline) for other categories within this region (different-view > same-view faces, Barense, Henson et al., 2010). Notably, there is convergent evidence from a number of different fMRI studies that the posterior hippocampus is predominantly sensitive to spatial stimuli and spatially demanding tasks (Barense, Henson et al., 2010; Kohler, Danckert, Gati, & Menon, 2005; Lee, Bandelow et al., 2006; Pihlajamaki et al., 2004; Rudebeck & Lee, 2010).

Using a trial unique oddity task (similar to Buckley et al., 2001; Lee, Buckley et al., 2005; see Section 1.6.2), Lee et al. (2008) demonstrated that spatial stimuli activated the posterior hippocampus and parahippocampal gyrus, whereas faces elicited activation in the anterior hippocampus and perirhinal cortex. In a rudimentary analysis of memory, Lee et al. (2008) also compared stimulus-specific activity within the MTL across three identical repetitions of these face and scene oddity blocks. A significant decrease in activity was observed in the posterior hippocampus and parahippocampal gyrus across repetitions of the scene oddity block; however, over repetitions of the face oddity block activity in the anterior hippocampus or perirhinal cortex did not change. Decreases in activity within the posterior hippocampus and parahippocampal cortex across repetitions of the scene-oddity block, therefore, provided some evidence that subregions within the MTL may make stimulus-specific contributions to mnemonic processing.

Stimulus-specific distinctions between MTL regions have also been demonstrated using working memory tasks (Litman, Awipi, & Davachi, 2009; Pihlajamaki et al., 2004; Rudebeck & Lee, 2010). Litman et al. (2009) revealed a dissociation between object and scene processing in perirhinal cortex and posterior parahippocampal gyrus during a 1-back working memory task. Anatomical region of interest analyses indicated that this pattern of activity was graded across the MTL; the relative difference between activity for scenes relative to objects (scenes > objects) decreased

in a linear fashion from posterior parahippocampal gyrus through to the perirhinal cortex. It has also been shown that, over short-retention delays, the perirhinal cortex is sensitive to presentations of novel objects, while presentations of novel arrangements of familiar objects activated the posterior hippocampus (Pihlajamaki et al., 2004; although see Buffalo, Bellgowan, & Martin, 2009). Likewise, the perirhinal cortex responds more to novel compared to familiar objects, whereas activity in the hippocampus is greater for novel relative to familiar spatial arrays of familiar objects, as well as rearranged arrays, compared to intact familiar object pairs (Kohler et al., 2005). More recently, Rudebeck and Lee (2010) identified increases in activity in the posterior hippocampus and parahippocampal gyrus for complex, compared to simple, spatial arrays, that was also modulated by working memory load.

To date, there have been two important fMRI studies that have directly compared long-term memory effects for different types of complex visual stimuli in subregions of the MTL, one of which also asked how long-term memory for different stimuli was modulated by recollection and familiarity (Preston et al., 2010; Awipi & Davachi, 2008). Preston et al., (2010) studied the encoding of novel faces and scenes in the hippocampus, perirhinal cortex and parahippocampal cortex to identify how activation within these regions related to subsequent recognition memory performance. Critically, while subsequent memory effects in the posterior parahippocampal cortex were scene selective, the hippocampus (see also Prince, Dennis, & Cabeza, 2009) and perirhinal cortex exhibited significant subsequent memory effects for faces and scenes. As stimulus-specific memory encoding activity was evident in the parahippocampal cortex only, the authors concluded that the hippocampus and perirhinal cortex perform domain-general roles in recognition memory.

In another experiment, Awipi & Davachi (2008) measured brain activity for item-item associative memory encoding of novel scenes that were paired with 1 of 6 repeating objects. During a subsequent memory test, participants had to identify the scenes that were previously presented, and indicate which of 6 objects the individual scenes were originally presented with. According to a dual-process account, recollection is indexed by the recovery of contextual or source information (Mandler, 1980; Jacoby, 1991; see Section 1.4), and in this task the contextual information comprised the paired object. It was assumed, therefore, that memory for the scenes (or scene item

memory) could be supported by recollection and familiarity, but to remember the object/scene pairs, participants must recollect the object. While activity in the posterior hippocampus and posterior parahippocampal gyrus was greater for novel scenes that were later remembered versus those that were forgotten, there was not an additional increase in activity according to subsequent memory for the paired object (remembered scene + object = remembered scene > forgotten scene). In contrast, activity in the perirhinal cortex uniquely correlated with subsequent recollection of the object/scene pairs; activity within this region was not sensitive to item memory for the scenes (remembered scene + object > remembered scene = forgotten scene). The data from this study supports the notion that subregions within the MTL engage in stimulus-specific recollection and familiarity processing.

Although not a direct comparison of memory for different stimuli, in an investigation conducted by O'Neil, Cate and Kohler (2009) participants were scanned during a task that concurrently assessed long-term memory retrieval and perceptual discrimination of faces. In this experiment participants were presented with trials that comprised three morphed faces. Prior to presentation, participants were either cued to choose the odd-one-out (perception), or to indicate the face that had been previously studied (memory retrieval). When individually contrasted with a baseline task, overlapping activity associated with memory and perception trials was identified in the perirhinal cortex. Moreover, activity within this region was greater for correct than incorrect

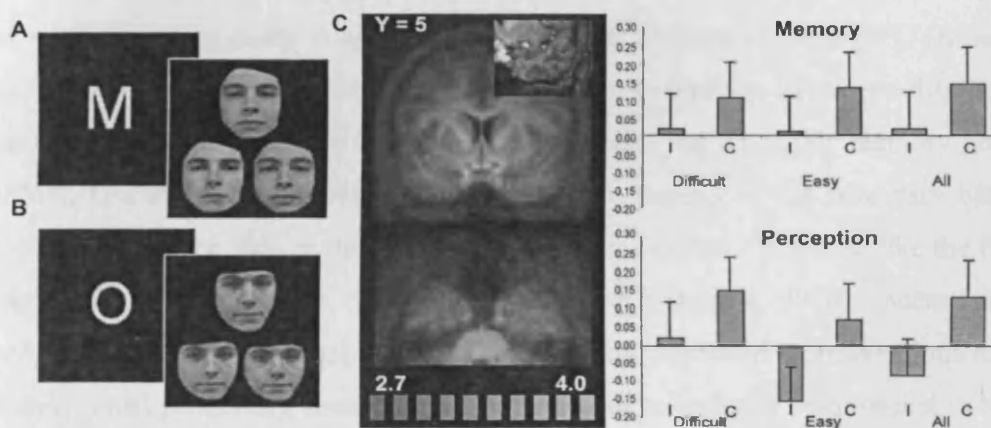


Figure 1.25: (A) and (B) examples of face memory retrieval and face perception trials from O'Neil et al. (2009). (C) Overlapping activity in perirhinal cortex that predicted performance accuracy on face memory and face perception trials. Figure from O'Neil et al. (2009).

responses for both tasks (Fig. 1.25). In sum, activity that related to long-term memory retrieval and perception of faces activated the same area in the perirhinal cortex, to the same degree. The findings from this study suggest that stimulus type, not declarative memory demands, is the overriding factor in the recruitment of the perirhinal cortex.

The converging evidence from fMRI studies indicates that activity in the perirhinal cortex consistently correlates with tasks that employ objects/faces, while the posterior hippocampus and posterior parahippocampal gyrus is generally associated with the presentation of scenes (Awipi & Davachi, 2008; Barense, Henson et al., 2010; Devlin & Price, 2007; Epstein, Higgins, Parker, Aguirre, & Coopermana, 2006; Lee, Bandelow et al., 2006; Lee et al., 2008; Litman et al., 2009; Preston et al., 2010; Rudebeck & Lee, 2010). Notably, these stimulus-specific effects have been demonstrated in a variety of cognitive tasks, including visual discrimination, short-term and working memory, as well as long-term memory.

1.7. Key features of representational accounts

The data reviewed above suggests that MTL subregions engage in stimulus-specific processing that can support both memory and perception depending upon the nature and complexity of the stimuli, and the specific demands of the task. The general pattern is that while the perirhinal cortex is associated with supporting object (and face) processing, spatial processing is dependent on the hippocampus. Notably, this relationship is particularly apparent when the stimuli are complex and/or when groups of stimuli contain many conjunctive features. In addition to the PMFC (Bussey & Saksida, 2002; 2005; Saksida & Bussey, 2010), these findings have been discussed in the context of another recent representational view, the emergent memory account (EMA, Graham et al., 2010) in which there is a blurring of the boundary between memory and perception in the MTL and surrounding cortex. In EMA, like the PMFC model (Bussey & Saksida, 2002; 2005; Saksida & Bussey, 2010), mnemonic and perceptual processes are supported by hierarchically organised representations formed within visual processing streams, which increase in complexity from caudal to rostral sites. EMA also proposes that the perirhinal cortex houses complex representations of objects, and based on neural dissociations between object and scene processing,

makes an additional claim that complex conjunctive spatial representations are formed and stored within the hippocampus.

There are multiple integral components of these representational accounts: (a) processing within the MTL is not restricted to long-term memory, but can support short-term memory, implicit memory and perception, (b) contributions from MTL regions are dictated by stimulus type, (c) memory processing can occur in visual processing regions that are located in the dorsal and ventral processing streams, such as the extrastriate cortex, and finally (d) MTL regions will be recruited when complex/highly configural representations are required by the task; when stimuli are less configural, or there is minimal feature overlap between items, memory and perception are supported by regions of extrastriate cortex. Notably, while the PMFC and EMA share the prediction outlined in (d), EMA is more explicit about the differing roles of regions within the extrastriate cortex compared to the MTL.

A central component of EMA is that the division of labour within the MTL is determined by representations of complex and conjunctive visual stimuli. This does not discount the phenomenological processes of recollection and familiarity, but instead, suggests that recollection- and familiarity-based memory can be driven by the same representation. As such, Graham et al. (2010) propose that object recollection and familiarity for scenes can occur within the perirhinal cortex (see also Awipi & Davachi, 2008) and hippocampus, respectively. Currently there is no evidence that familiarity for scenes can be supported by the hippocampus, but linear modulations in brain activity based on increases in item memory strength for scenes have been identified in the perirhinal cortex during memory encoding (Preston et al., 2010) and retrieval (Montaldi et al., 2006). Importantly, however, while EMA claims that the perirhinal cortex and hippocampus are predominantly associated with processing objects and scenes (respectively), a degree of functional overlap can be expected if a scene contains a lot of objects or if a particular task encourages participants to process visuo-object information, rather than, or in addition to visuo-spatial information within a scene (Graham et al., 2010; Preston et al., 2010). This idea is expanded upon in the following chapter (Section 2.1).

1.8. Comparison of MTL accounts

The literature reviewed in this chapter covers three accounts of functional fractionation within the MTL. First, the dual-process model proposes that subregions within the MTL differentially support recollection- versus familiarity-based memory processing (Aggleton & Brown, 1999). Second, informational theories imply that MTL regions encode and retrieve different types of mnemonic information (Davachi, 2006; BIC, Diana et al., 2007). Third, according to representational accounts (Graham et al., 2010; see also Bussey & Saksida, 2002; 2005; Saksida & Bussey, 2010) MTL regions process and store representations of different complex visual stimuli, which can support both memory and perception. There are some points of agreement between these accounts (Fig. 1.26). In the first instance, all of these models argue against the idea that MTL subregions act in concert to form a single declarative memory system (Squire & Zola-Morgan; Squire, 2004; Squire et al., 2004; Squire et al., 2007). Moreover, the BIC, item-context and EMA models focus on the contents of memory, proposing that there is not a simple mapping of recollection and familiarity to the hippocampus and perirhinal cortex, respectively. Note, however, that the BIC model asserts that patterns of memory-related activity seen in the perirhinal cortex and hippocampus will generally adhere to a dual-process account. Both the BIC and item-context model agree that the parahippocampal cortex (or posterior parahippocampal gyrus) processes contexts, the perirhinal cortex items, and the hippocampus forms domain-general relational representations. And finally, although Davachi's (2006) model has been described as an informational account, the item-context model and EMA both characterise anatomical distinctions between information/representations within the MTL based on stimulus types.

While the item-context model proposes that spatial contextual information is processed by the *parahippocampal cortex*, in EMA the *hippocampus* encodes and stores complex representations of scenes. When required, these stimulus-specific representations are engaged to disambiguate complex conjunctive stimuli, regardless of specific task demands (memory vs. perception). As a result, EMA predicts that recollection for objects and familiarity for scenes can be supported by the perirhinal cortex and hippocampus, respectively. According to BIC, the perirhinal cortex can support recollection if an object and its associations become unitised, or if the

	Dual-process	BIC	Item context	EMA
PRC	Familiarity	Item information	Object (item) information	Object representations
HC	Recollection	Item-context representations	Item-context representations	Spatial representations
PHC	No prediction	Context information	Spatial (context) information	No prediction

Figure 1.26: Four main accounts of MTL function. Some of the neural predictions made by these accounts are highly overlapping. Abbreviations: (PRC) perirhinal cortex, (HC) hippocampus and (PHC) parahippocampal cortex.

associated source information comprises an item-feature detail (Diana et al., 2010; see also Staresina & Davachi, 2006; 2008). As it has been described as a domain-general binding site, however, a stimulus-specific memory effect or a pattern of neural activity that reflects familiarity in the hippocampus would be problematic for BIC and item-context accounts. The three fMRI experiments described in this thesis have been designed to focus on the instances in which these predominant accounts diverge, via the direct comparison of the MTL correlates of recollection and familiarity for different kinds of complex visual stimuli.

Chapter 2

Recognition memory for faces and scenes: An event-related fMRI investigation

2.1. Introduction

As discussed in the Introductory chapter, there are competing accounts for how subregions in the MTL contribute to memory. According to a dual-process account (see Section 1.4), MTL subregions differentially contribute to recognition memory based upon recollection and familiarity (Aggleton & Brown, 1999; Brown & Aggleton, 2001), and there is now considerable evidence from the neuropsychological and neuroimaging literatures that links the perirhinal cortex and hippocampus to familiarity and recollection, respectively (Aggleton & Brown, 2005; Bowles et al., 2007; Cansino et al., 2002; Cohn et al., 2009; Daselaar et al., 2006; Davachi et al., 2003; Henson et al., 1999; Montaldi et al., 2006; Ranganath et al., 2004; Yonelinas et al., 1998; Yonelinas et al., 2002; Yonelinas et al., 2005). The vast majority of experiments have, however, used verbal stimuli (although see Montaldi et al., 2006) it is unclear, therefore, whether this division of applies to complex visual stimuli such as faces and scenes.

There are also recent representational accounts (see Section 1.6 and 1.7) which suggest that the kinds of stimuli employed in mnemonic and perceptual tasks separate the roles played by MTL subregions (Graham et al., 2010; see also Bussey & Saksida, 2005; Cowell et al., 2010; Saksida & Bussey, 2010). For example, according to the emergent memory account (EMA: Graham et al., 2010; see Section 1.7), subregions of the MTL differentially process representations of complex visual information, such as objects and scenes. Recent empirical findings have indicated that the perirhinal cortex is consistently associated with processing objects and faces, while the hippocampus processes scenes and is engaged by spatially demanding tasks (Awipi & Davachi, 2008; Barense et al., 2005; Barense et al., 2007; Barense, Henson et al., 2010; Kohler et al., 2005; Lee, Bandelow et al., 2006; Lee, Buckley et al., 2005; Lee, Bussey et al., 2005; Lee et al., 2008; Litman et al., 2009; Pihlajamaki et al., 2004;

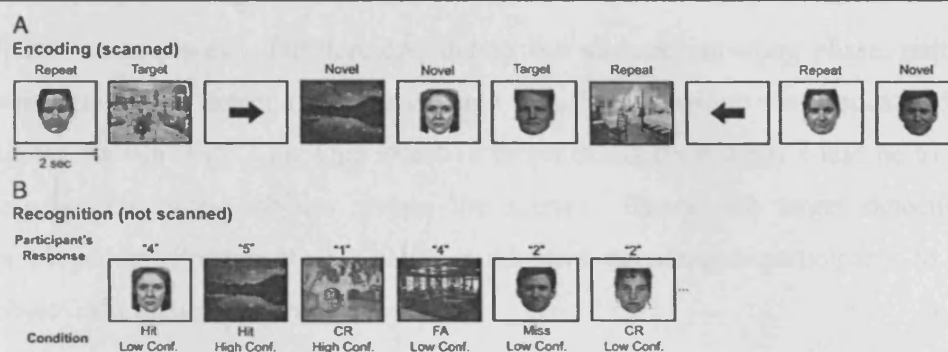


Figure 2.1: Example of the materials and task design from Preston et al. (2010). (A) In the scanned encoding phase participants performed a target detection task on novel and repeated face and scene stimuli. (B) During the unscanned test phase participants were presented with novel stimuli from the encoding phase along with unstudied faces and scenes. They responded to items using a 5 point confidence scale (1 = sure new; 2 = somewhat sure new; 3 = unsure new; 4 = somewhat sure old; 5 = sure old).

Taylor et al., 2007; Rudebeck & Lee, 2010). It is currently unclear, however, whether a given MTL region will be recruited solely based upon the requirements posed by different stimulus types, or according to the processes that support memory judgements. It is also possible that recruitment of MTL subregions will be based upon some interaction between stimulus and process (Graham et al., 2010).

How consistent are the predictions of EMA with the findings from previous fMRI studies that have directly contrasted long-term memory for different types of complex visual stimuli within the same experiment? In a comparison of recognition memory for faces and scenes, Preston et al. (2010) identified subsequent memory effects in the posterior parahippocampal cortex that were scene selective, but within the hippocampus and perirhinal cortex memory-related activity was domain-general (for similar domain-general effects at encoding and retrieval within the hippocampus see Prince et al., 2009). These data were interpreted as evidence against a strict stimulus-specific division of labour between MTL subregions. Importantly, however, while EMA claims that the perirhinal cortex is associated with processing object features and the hippocampus spatial features, these functional differences are not absolute. For example, it is possible that the perirhinal cortex will be recruited to process individual objects within a scene (Graham et al., 2010). The scenes used by Preston et al. (2010) comprised indoor and outdoor scenes, most of which contained multiple distinctive objects (such as a dining room full of tables and chairs, table settings and

floral centre pieces). Furthermore, during the scanned encoding phase, participants were required to detect a target scene and face, both of which were repeated 50 times across the run (Fig. 2.1). One effective target detection strategy could be to identify unique and salient objects within the scenes. Hence, the target detection task employed by Preston et al. (2010) could have encouraged participants to process object information in scenes.

Awipi and Davachi (2008) identified stimulus-specific brain activity at encoding that predicted recollection for objects in the perirhinal cortex and item memory for scenes in the posterior hippocampus and parahippocampal gyrus. Participants were presented with scenes that were paired with 1 of 6 repeating objects at encoding, their memory for which was assessed in a subsequent test phase (see Section 1.6.3). To identify content sensitive 'recollection' of the objects the authors compared encoding trials for which the scene was later remembered with and without the paired object. Importantly, the encoding task required participants to imagine using the object within the presented scene, which may have encouraged them to process the scene/object pair as a single unit. If they encoded a scene and object pair as a single unit (Diana et al., 2008; Haskins et al., 2008; Quamme et al., 2007; Yonelinas et al., 1999), old/new judgements, as well as accurate source judgments for these unitised pairings might be made using familiarity (see also Mayes et al., 2007).

This object source memory effect was identified by making comparisons across conditions in which there was subsequent memory for different stimulus types (e.g. remembered object + scene > remembered scene). As a result, the activity for object/scene pairs in perirhinal cortex could merely reflect visual processing of the object or object viewing (Awipi & Davachi, 2008), which may relate indirectly to subsequent memory. As such, these effects could reflect stimulus-specific *perceptual* processing within the MTL (such as that seen in Barense, Henson et al., 2010; Devlin & Price, 2007; Lee, Bandelow et al., 2006), as opposed to subsequent recollection of the object (Awipi & Davachi, 2008). Stronger evidence of content sensitive recollection, therefore, could be derived by making comparisons between memory conditions for the same stimulus type (e.g. recollection of objects > familiarity for objects). These caveats, when coupled with the fact that these data also diverge from

those reported by Preston et al. (2010), emphasise the need for further investigation into the roles played by MTL subregions in memory for different stimulus types.

The current study was designed to re-examine long-term memory processing for faces and scenes within the MTL at encoding and also at retrieval, using a different encoding task and stimulus materials to those utilised by Preston et al. (2010). During a scanned encoding phase, participants were presented with novel faces and scenes and completed a pleasant/unpleasant task. The majority of the study materials comprised the face and scene stimuli from Taylor et al. (2007), who successfully demonstrated stimulus-specific memory deficits in MTL amnesia. Scenes that contained distinctive and/or numerous objects were not used, and the additional real-world scenes photographed for this experiment also contained few objects.

To identify stimulus-specific memory effects during retrieval, participants were also scanned during the test phase. At test, participants made memory judgments about the previously studied, and novel, faces and scenes. As confidence data have been used extensively to plot ROCs and compute behavioural estimates of recollection and familiarity (see Section 1.4.1.3; Yonelinas, 1994; Yonelinas, 2002), participants made memory judgements to test items on a 6-point scale that ranged from sure new through to sure old. If memory accuracy is greater for faces or scenes, or there are differences between recollection and/or familiarity estimates, stimulus-specific memory effects could reflect differences in how memorable one stimulus is over the other, and/or disproportionate dependence on the type of mnemonic processing supported by respective regions. This would, therefore, undermine the conclusion that any stimulus-specific activity reflects differences in processing and storing complex visual information used during memory encoding and retrieval. Likewise, if recollection and familiarity estimates for faces and scenes are equivalent, patterns of stimulus-specific memory activity within subregions of the MTL have important implications for dual-process accounts. Using the confidence data, it was also possible to observe how patterns of memory-related activity within the MTL were modulated by increases in memory strength, and to infer how these patterns may map onto recollection and/or familiarity (Cohn et al., 2009; Daselaar et al., 2006; Ranganath et al., 2004; Yonelinas et al., 2005; also see Section 1.4.4).

Memory encoding and retrieval of faces and scenes were investigated within face and scene-sensitive functionally defined areas of the hippocampus, parahippocampal gyrus and perirhinal cortex. In keeping with the findings from the neuropsychological studies described previously (Lee, Buckley et al., 2005; Lee, Bussey et al., 2005; Taylor et al., 2007), and in keeping with a representational account, it is predicted that areas of the MTL that are more active when processing faces rather than scenes (e.g. perirhinal cortex) will also show a pattern of activity that relates to memory accuracy for faces, but not for scenes. The corresponding prediction for scenes, patterns of activity that track memory for scenes, applies to regions (e.g. posterior hippocampus) that are more active during the processing of scenes than faces. According to a dual-process account (Aggleton & Brown, 1999; Brown & Aggleton, 2001), however, significant effects should be domain-general and patterns of memory-related activity in the hippocampus (as well as the posterior parahippocampal gyrus; Diana et al., 2007) and perirhinal cortex should differentially reflect recollection and familiarity, respectively. It is possible, however, that domain-general effects could appear stimulus-specific if memory for faces or scenes disproportionately relies on recollection or familiarity (e.g. a higher familiarity estimate for faces coupled with a face-specific memory effect in perirhinal cortex). As such, interpretations of stimulus-specific memory effects are contingent upon important aspects of the behavioural data (e.g. overall memory accuracy and ROC estimates for faces and scenes).

2.2. *Materials and methods*

2.2.1. *Participants*

Nineteen volunteers (13 females) took part. According to self-report, all were right-handed native-English speakers with normal or corrected to normal vision and no neurological and/or psychiatric disorders. One participant (female) was removed from the analyses due to a level of performance ($p(\text{hit}) - p(\text{false alarm}) = 0.19$ for faces) that was significantly poorer than the overall group ($z = -2.09$). The mean age of the remaining 18 participants was 22.9 years (range = 19-30). All participants gave written informed consent prior to the experiment and were paid £10/hour for their participation. The experiment received ethical approval from the Cardiff University School of Psychology Ethics Committee.

2.2.2. Materials

Stimuli comprised a set of 222 black and white images of Caucasian male and female faces with neutral expressions and a set of 222 black and white images of landscapes, streets and buildings devoid of people (Fig. 2.2). These items overlapped with the stimuli used by Taylor et al. (2007) to investigate recognition memory for faces and scenes in patients with MTL lesions. Any scenes that contained distinctive and/or numerous objects were removed, replacing them with additional photographs of landscapes that were taken specifically for this experiment. Additional face stimuli were obtained from a database held at Cardiff University. Twelve items from each set were used in a practice session, with the remaining items separated into 120 faces and 120 scenes presented at study and test ('old' stimuli) and 90 faces and 90 scenes presented at test only ('new' stimuli).

2.2.3. Tasks and procedure

The experiment was run using E-Prime version 2.0. Images were projected from a stimulus presentation machine to the screen within the scanner, which was manually adjusted for each participant to ensure the image was centred correctly. The MR projector system comprised a Canon SX60 LCOS projector, coupled to a Navitar SST300 zoom converter lens. Two MR compatible button boxes, one for each hand, were employed. The fMRI data were collected on a General Electric 3-T HDx MRI system using an 8 channel receiver-only head coil.

Participants were scanned during study and test phases (Fig 2.2). The experiment consisted of 3 separate study and test runs, with an equal number of faces and scenes shown in each run. Forty faces and scenes were presented in each study phase; these were seen again in the test phase, which followed immediately, along with 60 unstudied stimuli (30 faces and 30 scenes). No stimuli were encountered in more than one study-test run, and the order of face/scene presentation at study, as well as test, was randomised for each participant.

Study items were presented in the centre of the screen against a black background for 2000ms, separated by a jittered inter-stimulus interval (ISI: 800ms-1500ms, mean = 1000ms) during which the screen remained black. Participants made a

pleasant/unpleasant judgement for each stimulus, using left and right index fingers. The hand used to signal pleasant/unpleasant judgements was counterbalanced across participants and prompts for the pleasant/unpleasant judgement appeared beneath each study item, which remained onscreen for the duration of each trial.

Test items were presented in the centre of the screen for 4000ms, separated by a jittered inter-stimulus interval (800ms-1500ms, mean = 1000ms) during which the screen was black. Participants were told that they were to distinguish between old (studied) and new stimuli and to indicate their confidence in the old/new judgment on a 6-point scale (1: high confidence new, 2: medium confidence new, 3: low confidence new, 4: low confidence old, 5: medium confidence old, 6: high confidence old; see Fig. 2.2). As with previous experiments that have used a 6-point confidence scale, participants were encouraged to make use of the entire scale (Yonelinas et al., 2005). Responses were made using the right/left ring (high confidence), middle (medium confidence) and index (low confidence) fingers. The hand used for old judgments was counterbalanced across participants. Throughout each trial, prompts for the high, medium and low old/new confidence ratings appeared beneath the test item. The presentation order of the 3 study/test runs was counterbalanced across participants.

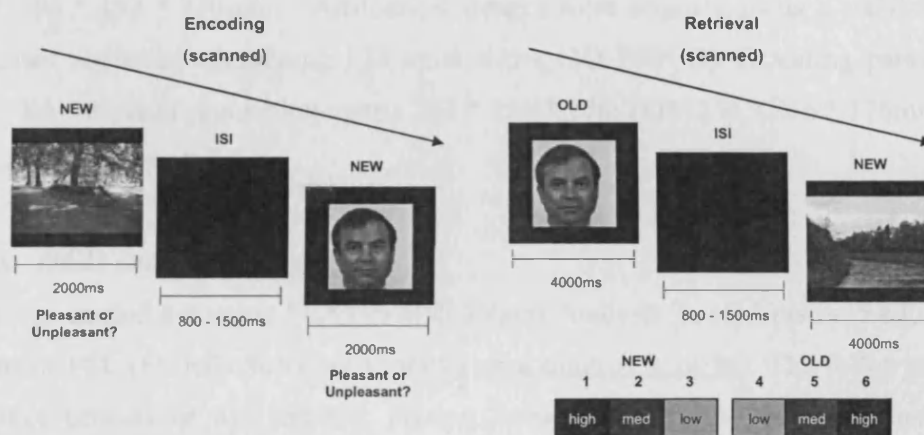


Figure 2.2: Stimuli and procedure. During encoding participants made pleasant and unpleasant judgements about novel faces and scenes. At retrieval participants were presented with previously studied and novel faces and scenes. Participants made memory judgements to stimuli at retrieval using a 6-point scale (1 = high confidence new, 2 = medium confidence new, 3 = low confidence new, 4 = low confidence old, 5 = medium confidence old, and 6 = high confidence old).

Prior to entering the MRI suite, participants carried out a practice task. They saw 6 faces and 6 scenes at study, and 12 faces and 12 scenes at test (an equal number of old and new faces and scenes). They were also asked to explain the reason for each of their responses at test, to ensure they understood the task and the confidence scale.

2.2.4. Scanning parameters

For functional imaging, a gradient-echo, echo-planar imaging (EPI) sequence was used. The same scanning protocol was used in all runs. Forty-five slices were collected per image volume covering the whole-brain. Scanning parameters were: repetition time/echo time (TR/TE) 2750ms/35ms; flip angle (FA) 90°; slice thickness 2.4mm (3.4 * 3.4 * 2.4mm voxel) with a 1mm inter-slice gap; data acquisition matrix GE-EPI 64 * 64; field of view (FOV) 220 * 220mm; and ASSET (acceleration factor). In addition to this, the first frames were dropped to allow for signal equilibrium. Slices were acquired with a 30° oblique axial tilt relative to the anterior-posterior commissure line (posterior downward). To correct for geometrical distortions in the EPI data due to magnetic-field in-homogeneity, a map of the magnetic field was produced from two 3D SPGR images acquired during the scanning session (Jezzard & Balaban, 1995). The SPGR acquisitions were prescribed using the same slice orientation as the EPI data to be unwarped. Parameters for the SPGR acquisitions were: TE 7ms and 9ms; TR 20ms; FA 10°; data acquisition matrix 128 * 64 * 70; FOV 384 * 192 * 210mm. Anatomical images were acquired using a standard T1-weighted sequence comprising 178 axial slices (3D FSPGR). Scanning parameters were: FA 20°; data acquisition matrix 256 * 256 * 176; FOV 256 * 256 * 176mm, and 1mm isotropic resolution.

2.2.5. fMRI data pre-processing

This was carried out using FEAT (FMRI Expert Analysis Tool) Version 5.63, which is part of FSL (FMRIB Software Library, www.fmrib.ox.ac.uk/fsl). The following pre-statistics processing was applied; motion correction using MCFLIRT (Jenkinson, Bannister, Brady, & Smith, 2002); non-brain removal using BET (Smith, 2002); spatial smoothing using a Gaussian kernel of FWHM 5mm; mean-based intensity normalisation of the entire 4D data set by the same multiplicative factor; high pass temporal filtering (Gaussian-weighted least-squares straight line fitting, with sigma = 50s). Phase information from the two SPGR images was unwarped using PRELUDE

(Jenkinson, 2003). The unwarped phase images were then subtracted and the resulting fieldmap was used to unwarped the EPI data using FUGUE (Jenkinson, 2003). Time-series statistical analysis was carried out using FILM with local autocorrelation correction (Woolrich, Ripley, Brady, & Smith, 2001). Registration to high resolution 3D anatomical T1 scans (per participant) and to a standard Montreal Neurological Institute (MNI-152) template image (for group average) was carried out using FLIRT (Jenkinson et al., 2002; Jenkinson & Smith, 2001).

2.3. Data analysis

2.3.1. Behavioural receiver operating characteristic (ROC) analysis

Hit and false alarm pairs for each level of confidence for faces and for scenes were plotted, and ROC curves were fitted to these points using a sums-of-squares search algorithm (Yonelinas et al., 1998), which provided a means of estimating the contributions of recollection and familiarity to recognition memory (see Section 1.4.1.3).

2.3.2. Whole-brain fMRI data analysis

The data were submitted to a (random effects) general linear model, with one predictor that was convolved with a standard model of the haemodynamic response function (HRF) for each event-type. Separate regressors were modelled for each event-type at encoding. These were determined by stimulus (face/scene), and subsequent memory response (high, medium and low confidence old or new). Levels of response accuracy and the distributions of confidence responses guided the formation of 4 encoding regressors for each stimulus category. These were: (a) subsequent miss (sM) - study items that subsequently received high, medium or low confidence new responses, (b) subsequent probably old (sPO) - study items that subsequently received medium and low confidence old responses, (c) subsequent sure old (sSO) - study items that subsequently received high confidence old responses and (d) a regressor for study items that received no response at test.

Retrieval event-types were determined by stimulus type, item status (old/new) and participant response (high, medium and low confidence old or new). There were 5 retrieval regressors for each stimulus type: (a) correct rejection (CR) - high, medium

and low confidence new responses to new items, (b) miss (M) - high, medium and low confidence new responses to old items, (c) probably old (PO) - medium and low confidence old responses to old items, (d) sure old (SO) - high confidence old responses to old items, and finally (e) a regressor of no interest that comprised false alarms (all old responses to new items) and trials where participants failed to make a response.

Parameter estimates relating the height of the HRF response to each event-type were calculated, on a voxel by voxel basis, via a multiple linear regression of the response time-course, to create one beta image for each event-type per run, per participant. Individual runs were then concatenated for each participant in a fixed effects analysis using FEAT. The subsequent parameter estimate images were then combined in a higher-level (group) FLAME analysis (FMRIB's Local Analysis of Mixed Effects: Beckmann, Jenkinson, & Smith, 2003; Woolrich, Behrens, Beckmann, Jenkinson, & Smith, 2004). To examine significant encoding and retrieval memory effects for the two stimuli at the whole-brain level, categorical contrasts between memory regressors were performed separately for faces and scenes. For encoding, whole-brain contrasts were between the face/scene subsequent sure old and miss regressors (scene sSO > scene sM; face sSO > face sM), whereas at retrieval, the contrasts were between face/scene sure old, correct rejection and miss regressors (scene SO > scene CR; scene CR > scene SO; scene SO > scene M; face SO > face CR; face CR > face SO; face SO > face M). FEAT group (gaussianised) t-statistics were then converted to z-statistics and thresholded at $p < 0.001$, uncorrected for multiple comparisons; significant activations involving contiguous clusters of at least 9 voxels are reported. A voxelwise approach was employed as there is evidence that functional differences between faces and scenes can occur within MTL regions (e.g. anterior vs. posterior hippocampus for faces and scenes, respectively; Lee et al., 2008) and because it was expected that significant effects may be evident in smaller MTL regions (e.g. perirhinal cortex). A probability of $p < 0.001$ with an extent threshold of > 9 voxels is equivalent to a mapwise false-positive rate for the MTL (encompassing the hippocampus, parahippocampal gyrus and perirhinal cortex) of $p < 0.05$ (estimated using the Monte Carlo procedure implemented in the AlphaSim program in Analysis of Functional NeuroImages (AFNI)). The locations of significant effects were

identified using the Harvard-Oxford sub-cortical structural atlas in FSLView; coordinates (x, y, z) of significant effects are reported in MNI space (see Section 2.2.5).

2.3.3. *Functional region of interest (fROI) fMRI analysis*

Due to the specific aims of this experiment a functional region of interest (fROI) analysis was conducted. This involved identifying stimulus-specific voxels within different subregions of the MTL and investigating memory effects for faces and scenes within each of these. This analysis strategy was driven by observations of stimulus-specific processing within the MTL (Awipi & Davachi, 2008; Barense, Henson et al., 2010; Lee, Bandelow et al., 2006; Lee et al., 2008; Litman et al., 2009), and by accounts which suggest that areas of the MTL that process different types of complex visual stimuli will also support memory for these (Graham et al., 2010; Lee, Barense et al., 2005; see also Bussey & Saksida, 2005; Saksida & Bussey, 2010). To create *unbiased* stimulus-specific fROIs, group-level contrasts² were performed between the regressors for novel faces and scenes³ (CR faces > CR scenes and the reverse). These orthogonal correct rejection contrasts between faces and scenes were undertaken within three anatomically-defined MTL ROIs in MNI space (Fig. 2.3); perirhinal cortex, hippocampus and parahippocampal gyrus. The perirhinal cortex was defined using a probabilistic map taken from Devlin and Price (2007) (available at <http://joedevlin.psychol.ucl.ac.uk/perirhinal.php>), which was restricted to an area that comprised a > 50% likelihood of being the perirhinal cortex in their participants (N = 12). The hippocampus and parahippocampal gyrus were defined using the Automated Anatomical Labelling (AAL) brain atlas (Tzourio-Mazoyer et al., 2002). Any voxels from the parahippocampal gyrus or hippocampal masks that overlapped with the probabilistic map of the perirhinal cortex were removed. The resulting FEAT t-statistics were converted to z-statistics and a liberal (uncorrected) voxel threshold of $p < 0.025$ was applied to the data to ensure stimulus-specific voxels associated with the

² As there is high consistency across experiments for extrastriate fROIs derived at the group level (Duncan, Pattamadilok, Knierim, & Devlin, 2009).

³ Novel items were used to derive these fROIs as one can then make inferences about memory effects by observing the differences in activity between hit and miss categories, which in some cases may be preferable due to incidental memory encoding activity associated with correct rejections (Stark & Okado, 2003).

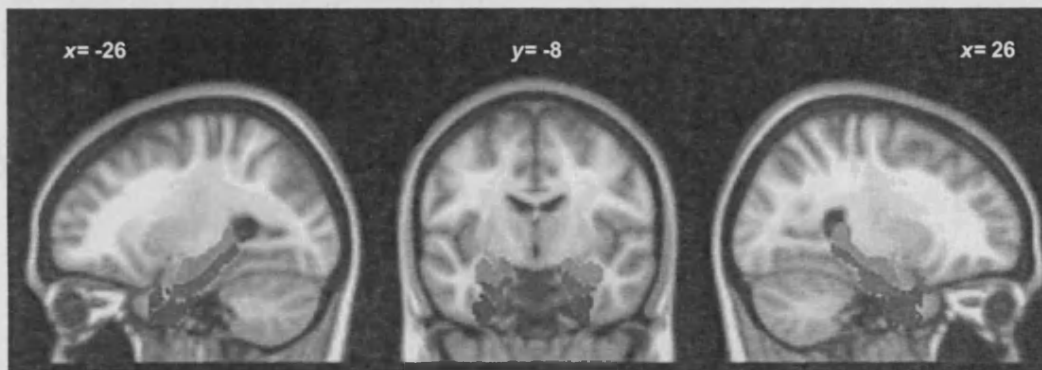


Figure 2.3: Left sagittal (left), coronal (middle) and right sagittal (right) views of the hippocampal (green), parahippocampal gyrus (pink) and perirhinal cortex (blue) masks used to create fROIs in all 3 experiments in this thesis. Images are rendered on a MNI-152 T1 2mm standard brain.

task were identified within each anatomical region. Data are reported for functional ROIs that comprised 10 or more activated voxels. This produced left and right hemisphere fROIs for faces (Fig. 2.4) within anterior hippocampus (left peak: -22, -8, -24, $z = 5.31$, 237 voxels; right peak: 18, -4, -16, $z = 4.99$, 289 voxels), anterior parahippocampal gyrus (left peak: -20, -10, -24, $z = 5.00$, 247 voxels; right peak: 20, 0, -20, $z = 5.43$, 349 voxels) and perirhinal cortex (left peak: -32, -4, -34, $z = 3.77$, 74 voxels; right peak: 24, 0, -28, $z = 3.89$, 248 voxels), and for scenes (Fig. 2.4) within posterior hippocampus (left peak: -18, -34, 4, $z = 3.75$, 125 voxels; right peak: 20, -32, 2, $z = 3.74$, 134 voxels) and posterior parahippocampal gyrus (left peak: -24, -34, -8, $z = 3.34$, 107 voxels; right peak: 16, -40, -8, $z = 4.37$, 177 voxels).

fROI analyses were conducted on the data from the encoding and retrieval phases, which are summarised in separate sections. Using Featquery from the FSL toolkit, the following mean parameter estimate values were extracted from each of the stimulus-specific fROIs for the sSO, sPO and sM face and scene regressors from encoding, and the CR⁴ SO, PO and M face and scene regressors from retrieval. Parameter estimate values were scaled by the height of the effective regressor and mean voxel intensity in order to convert them into percent signal change.

⁴ For demonstration purposes values for CR have been plotted alongside SO, PO and M in the results. To ensure that the contrasts used to identify stimulus-specific voxels were orthogonal to the investigation of memory-related activity, CRs were not included in the analyses.

Individual percent signal change values were entered into a 2*2*3 ANOVA with factors of ‘hemisphere’⁵ (right vs. left), ‘stimulus’ (face vs. scene) and ‘memory’ (encoding: sSO, sPO and sM; retrieval: SO, PO and M) for each fROI. These were conducted separately for the data from encoding and retrieval phases. If there was no significant hemisphere*memory or hemisphere*stimuli*memory interaction, effects were collapsed across hemisphere for the purposes of follow-up analyses. Memory effects were also considered separately for each stimulus type within each fROI (and hemisphere where necessary), by conducting one-way ANOVAs with levels of sSO, sPO and sM (encoding) and SO, PO and M (retrieval). When a significant main effect or linear trend (as indicated by within-subject contrasts) was obtained in these one-way ANOVAs, subsequent planned pairwise comparisons were conducted to identify the reason for the reliable effects.

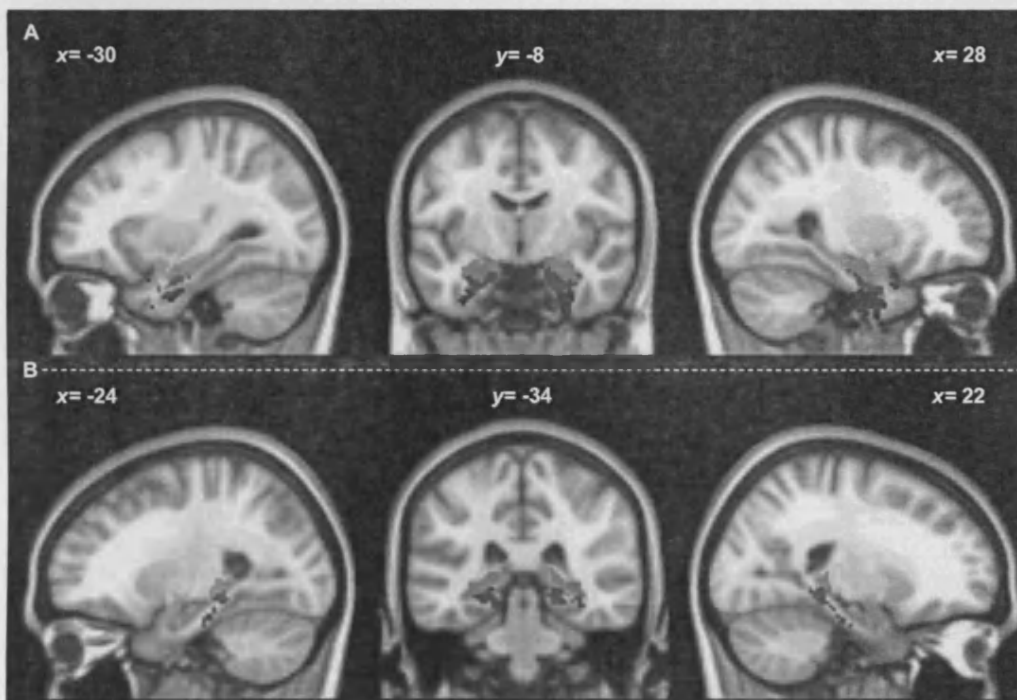


Figure 2.4: Left sagittal (left), coronal (middle) and right sagittal (right) views of functional ROIs located within the hippocampus (green), parahippocampal gyrus (pink) and perirhinal cortex (blue) derived from the (A) CR face > CR scene and the (B) CR scene > CR face contrasts, rendered on a MNI-152 T1 2mm standard brain.

⁵Hemisphere was included as a factor because of reports of right-lateralised effects within the MTL for different types of complex visual stimuli (Awipi & Davachi, 2008; Lee, Bandelow et al., 2006; O'Neil et al., 2009; Rudebeck & Lee, 2010).

2.4. Behavioural results

Old/new discrimination as measured by $p(\text{hit}) - p(\text{false alarm})$ collapsed across confidence ratings did not vary with stimulus type (faces: 0.53, SE = 0.04; scenes: 0.55, SE = 0.03; $t(17) = 0.37$), and was reliably above chance for both stimulus categories (faces: $t(17) = 16.62$; $p < 0.01$, scenes: $t(17) = 17.81$, $p < 0.01$). ROCs for faces and scenes are displayed in Fig. 2.5, which indicates more asymmetry and a higher y-intercept for the scenes than the faces. Using a sums-of-squares search algorithm (Yonelinas et al., 1998), the estimate for recollection was significantly greater for scenes than faces (scenes: 0.48, SE = 0.04; faces: 0.33, SE = 0.05; $t(17) = 2.55$, $p < 0.05$). The familiarity estimate was numerically, but not statistically, higher for faces (faces: 1.06, SE = 0.11; scenes: 0.93, SE = 0.10; $t(17) = 0.97$).

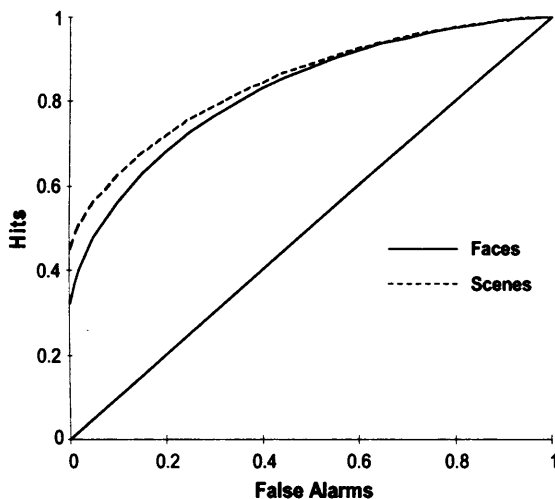


Figure 2.5: Receiver operating characteristics (ROCs) for faces and scenes.

Reaction times to faces were faster than to scenes at encoding (faces: 1083ms, SE = 28ms; scenes: 1131ms, SE = 20ms; $t(17) = 2.94$, $p < 0.01$) and retrieval (faces: 1887ms, SE = 53ms; scenes: 1988ms, SE = 46ms; $t(17) = 3.33$, $p < 0.01$), regardless of memory accuracy. The mean response proportions and reaction times for each type of memory confidence judgement are displayed in Table 2.1. Consistent with previous studies that have utilised similar confidence judgment tasks, mean responses were quicker for high, than for low, confidence judgements for both old and new items (Ranganath et al., 2004; Ratcliff & Murdock, 1976; Yonelinas et al., 2005).

Table 2.1: Mean proportion of responses and reaction times across the confidence scale for old and new faces and scenes⁶

Faces	Recognition judgements					
	1	2	3	4	5	6
<i>Proportion of responses</i>						
Old	0.08 (0.04)	0.12 (0.01)	0.12 (0.01)	0.17 (0.03)	0.23 (0.02)	0.32 (0.05)
New	0.27 (0.05)	0.33 (0.03)	0.21 (0.03)	0.10 (0.01)	0.07 (0.02)	0.02 (0.01)
<i>Mean reaction time (ms)</i>						
Old	1581 (66)*	1933 (86)	2032 (82) ⁺	2097 (86)	1848 (56)	1510 (58)
New	1668 (54)	1823 (55)	2064 (79)	2078 (87)	1964 (136)	1943 (91) [•]
Scenes						
	1	2	3	4	5	6
<i>Proportion of responses</i>						
Old	0.05 (0.01)	0.10 (0.01)	0.09 (0.02)	0.11 (0.01)	0.18 (0.02)	0.47 (0.04)
New	0.33 (0.03)	0.30 (0.03)	0.15 (0.02)	0.08 (0.01)	0.07 (0.01)	0.07 (0.01)
<i>Mean reaction time (ms)</i>						
Old	1765 (61)*	2117 (65)	2302 (105)	2225 (85)	1943 (56)	1505 (48)
New	1688 (41)	2003 (67)	2276 (97)	2139 (80)	2037 (88)	1847 (114)

⁶The values shown are across-participant means with standard error in brackets. As some participants did not make all types of response to old, as well as new items, mean reaction times for *, ⁺ and [•] are based on 17, 14, and 10 participants, respectively. Abbreviations: (1) high confidence new, (2) medium confidence new, (3) low confidence new, (4) low confidence old, (5) medium confidence old, (6) high confidence old.

2.5. Encoding

2.5.1. Results from whole-brain analysis

Significant patterns of activity associated with subsequent memory success for faces and scenes were identified via contrasts between items later remembered with high confidence and items later forgotten (scenes sSO > scenes sM; faces sSO > faces sM). Results from the encoding whole-brain analysis are displayed in Fig. 2.6, and summarised in Tables 2.2 and 2.3. Both faces and scenes activated a variety of occipitotemporal/extrastriate brain regions that form the visual processing streams (e.g. fusiform cortex and occipital fusiform cortex, Haxby et al., 1991). There was also activity in the inferior aspect of the lateral occipital cortex (LOC), which is associated with processing complex visual stimuli (Kanwisher, Chun, McDermott, & Ledden, 1996; Kanwisher, Woods, Iacoboni, & Mazziota, 1997; Malach et al., 1995).

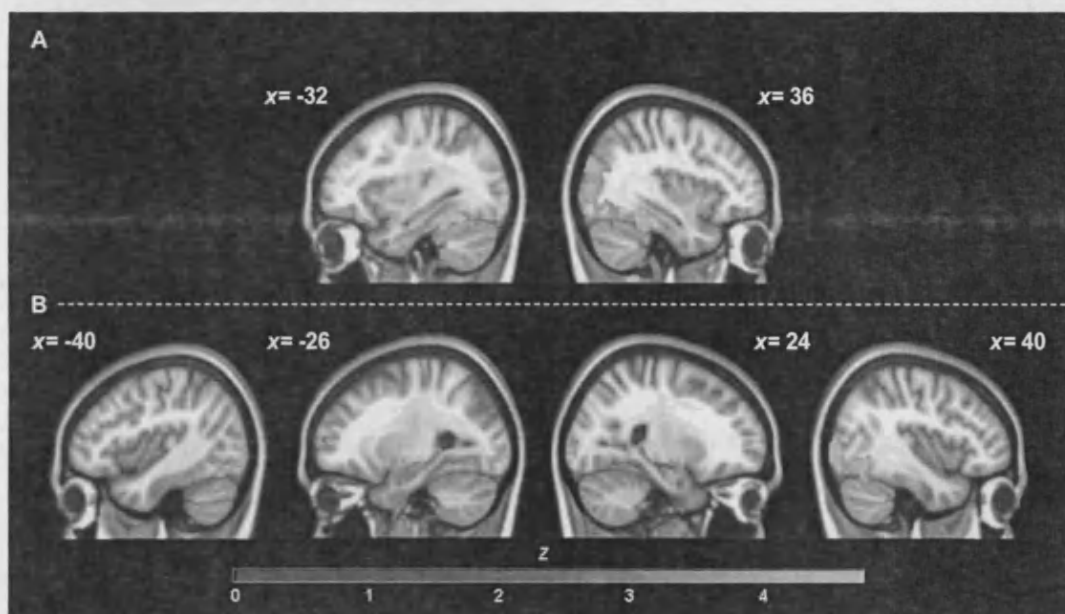


Figure 2.6: Significant memory encoding activity from the (A) scene sSO > sM and (B) face sSO > face sM contrasts. Images are overlaid onto a MNI-152 T1 2mm standard brain.

Table 2.2: Local maxima and corresponding regions according to the Harvard-Oxford sub-cortical structural atlas observed for the subsequent sure old > miss contrast for scenes ($p < 0.001$, cluster > 9 voxels).

Region				
	Z	x	y	z
<i>Right lateral occipital cortex, inferior division</i>	4.73	40	-86	2
<i>Left temporal occipital fusiform cortex</i>	4.35	-32	-56	-20
<i>Right temporal occipital fusiform cortex</i>	4.36	32	-42	-24
<i>Left temporal fusiform cortex, posterior division</i>	3.89	-34	-40	-26
<i>Right temporal fusiform cortex</i>	4.62	26	-38	-26

Table 2.3: Local maxima and corresponding regions according to the Harvard-Oxford sub-cortical structural atlas observed for the subsequent sure old > miss contrast for faces ($p < 0.001$, cluster > 9 voxels).

Region				
	Z	x	y	z
<i>Left lateral occipital cortex, inferior division</i>	3.85	-36	-86	-4
<i>Right lateral occipital cortex, inferior division</i>	4.77	44	-66	-14
<i>Left occipital pole</i>	3.77	-26	-90	-6
<i>Right occipital pole</i>	4.51	36	-90	4
<i>Left occipital fusiform gyrus</i>	3.70	-42	-68	-16
<i>Right occipital fusiform gyrus</i>	4.34	44	-66	-22
<i>Right hippocampus</i>	4.06	24	-8	-22

2.5.1.1. MTL effects

For the MTL, there was significant activity for subsequent sure old faces, relative to subsequently forgotten faces, in the right anterior hippocampus (see Table 2.3, Fig. 2.6B). For all other whole-brain contrasts there were no significant effects in the MTL. Using an ROI mask based on these significant right hippocampal voxels, percent signal change values for the sSO sPO and sM faces and scenes were extracted to further investigate patterns of memory-related activity (Fig. 2.7). The individual percent signal change values for memory confidence responses for old items were entered in a 2*3 ANOVA (2 levels of 'stimuli'; and 3 levels of 'memory'). There was a significant main effect of stimuli ($F(1,17) = 51.48$, $p < 0.01$), and a significant main effect of memory ($F(2,34) = 8.76$, $p < 0.01$). Although the interaction between

stimuli and memory was non-significant ($F(2,34) = 2.12$), due to the specific focus of the current experiment, memory effects were considered separately for the faces and scenes. For faces there was a significant main effect of memory ($F(2,34) = 8.50$, $p < 0.01$) and a significant linear trend ($F(1,17) = 14.05$, $p < 0.01$). Planned pairwise comparisons revealed greater encoding activity for sure old relative to probably old and missed faces (sSO > sPO: $t(17) = 2.95$, $p < 0.01$; sSO > sM: $t(17) = 3.75$, $p < 0.01$). There was also a significant main effect of memory and a linear trend for scenes ($F(2,34) = 3.75$, $p < 0.05$; $F(1,17) = 5.91$, $p < 0.05$, respectively), reflecting greater activity for sSO relative to sM scenes, and sPO than sM that was marginal (sSO > sM: $t(17) = 2.43$, $p < 0.05$; sPO > sM: $t(17) = 1.85$, $p = 0.06$).

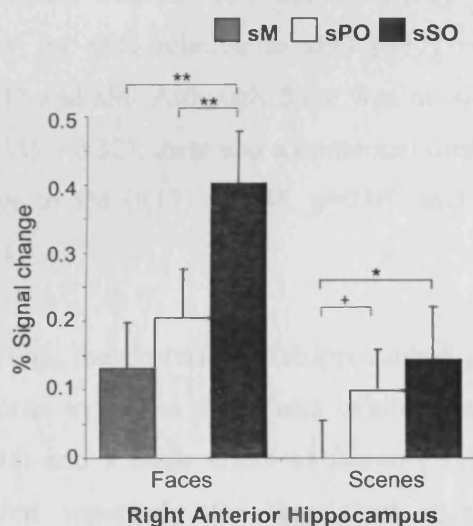


Figure 2.7: Patterns of memory encoding activity for faces and scenes revealed by the face sSO > face sM contrast within the right anterior hippocampus. Abbreviations: (sM) subsequent miss (grey), (sPO) subsequent probably old (white) and (sSO) subsequent sure old (black). + $p \leq 0.06$; * $p < 0.05$, ** $p < 0.01$.

2.5.2. Results from the functional region of interest analysis

2.5.2.1. Scene-sensitive regions

Results from the fROI analysis in scene-sensitive regions are summarised in Fig. 2.8. The scene-sensitive fROI within the posterior hippocampus demonstrated a main effect of memory ($F(2,34) = 3.27$, $p < 0.05$) and a significant hemisphere*memory interaction ($F(2,34) = 4.34$, $p < 0.05$). Further analysis separately within each hemisphere revealed a marginal main effect of stimuli in the left hemisphere only

($F(1,17) = 4.00, p=0.06$; Fig. 2.8A). Separate analyses for faces and scenes revealed no main effects of memory. There was, however, a significant linear trend for the scenes within this region ($F(1,17) = 5.25, p<0.05$), and planned paired comparisons revealed greater activity for sSO than sM ($t(17) = 2.29, p<0.05$); while activation for sPO was intermediate, it did not significantly differ from either sSO or sM.

Voxels within the right posterior hippocampus (Fig. 2.8B) exhibited a main effect of memory ($F(2,34) = 5.30, p<0.01$). When faces and scenes were considered separately, there was a significant main effect of memory for scenes ($F(2,34) = 5.24, p<0.01$), that showed a linear relationship ($F(1,17) = 12.48, p<0.01$). Pairwise comparisons revealed a reliable difference between sSO and sM ($t(17) = 3.53, p<0.01$), a trend towards greater activity for sSO relative to sPO ($t(17) = 1.93, p=0.07$) and no differences between sPO and sM. Although there was no significant main effect of memory for faces ($F(2,34) = 2.32$), there was a numerical increase in encoding-related activity for sSO relative to sM ($t(17) = 1.88, p=0.08$) and a marginal linear trend ($F(1,17) = 3.50, p=0.08$).

The group of voxels within the posterior parahippocampal gyrus (Fig. 2.8C) which showed a greater response to scenes than faces exhibited a main effect of stimuli ($F(1,17) = 9.66, p<0.01$) and a main effect of memory ($F(2,34) = 4.72, p<0.05$). Effects were considered separately for faces and scenes with the posterior parahippocampal gyrus, which revealed a marginal main effect of memory for scenes ($F(2,34) = 3.09, p=0.06$), and a significant linear trend ($F(1,17) = 4.72, p<0.05$). Pairwise comparisons indicated that there was an increase in encoding-related activity for sSO relative to sM only ($t(17) = 2.17, p<0.05$). These scene selective voxels within posterior parahippocampal gyrus did not exhibit a main effect of memory for faces ($F(2,34) = 2.53$), but there was a linear trend and an increase in activity for sSO relative to sM that approached significance ($F(1,17) = 3.90, p=0.06$; $t(17) = 1.98, p=0.06$, respectively).

2.5.2.2. Face-sensitive regions

Results from the fROI analysis in face-sensitive regions are summarised in Fig. 2.8. For voxels that processed faces over scenes within the anterior hippocampus (Fig. 2.8D) there was a significant main effect of stimuli ($F(1,17) = 32.18, p<0.01$) and a

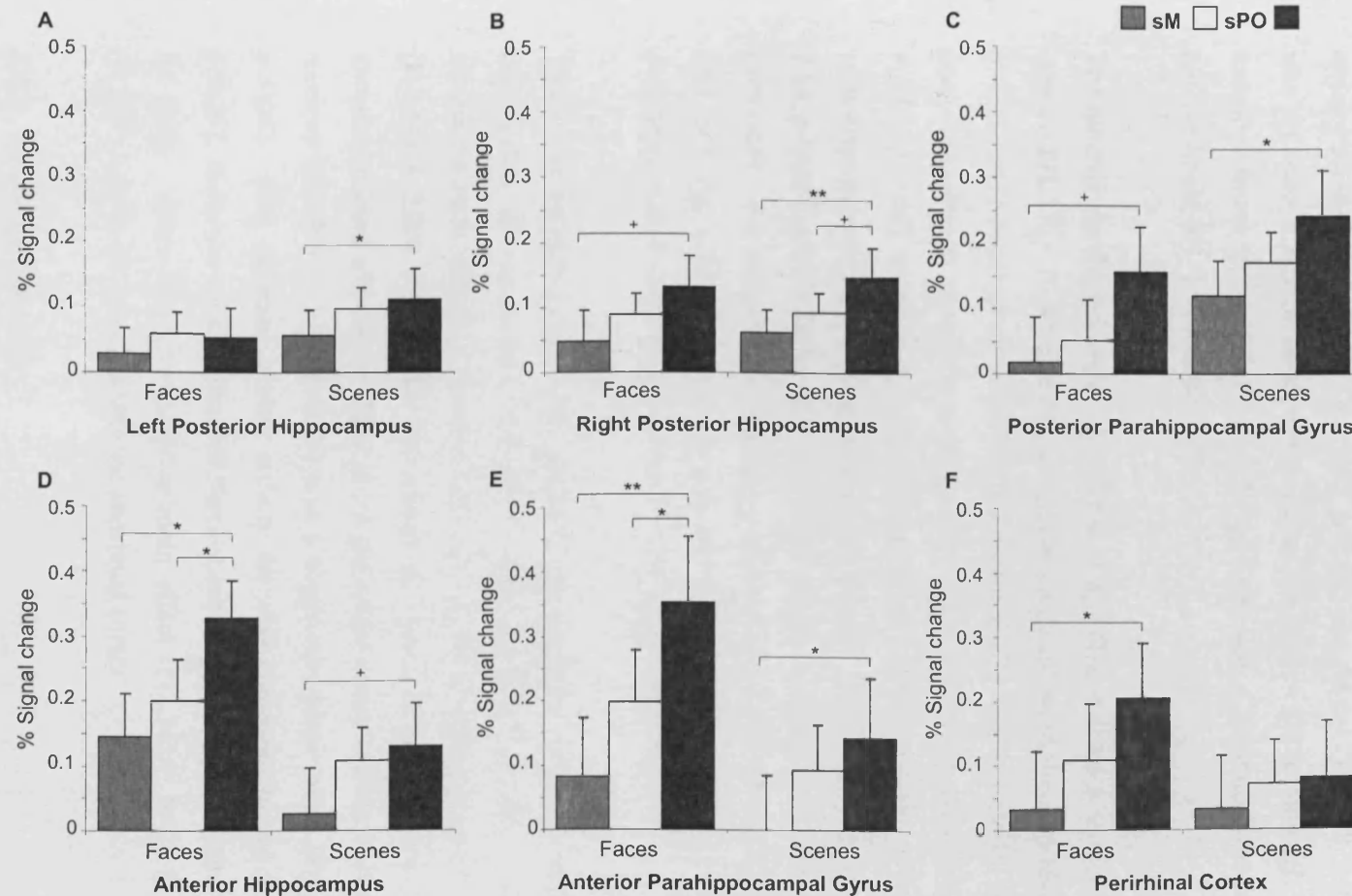


Figure 2.8: Memory encoding activity for faces and scenes in functionally defined MTL regions of interest from (A, B, C) CR scenes > CR faces and (D, E, F) CR faces > CR scenes. Percent signal change (arbitrary units) in the (A) left posterior hippocampus, (B) right posterior hippocampus, (C) posterior parahippocampal gyrus, (D) anterior hippocampus, (E) anterior parahippocampal gyrus, and (F) perirhinal cortex. Abbreviations: (sM) subsequent miss (grey), (sPO) subsequent probably old (white) and (sSO) subsequent sure old (black). + $p \leq 0.09$; * $p < 0.05$.

main effect of memory ($F(2,34) = 4.76, p < 0.05$). A separate analysis for faces revealed that in the anterior hippocampus there was a significant main effect of memory ($F(2,34) = 4.53, p < 0.05$), a linear trend ($F(1,17) = 7.16, p < 0.05$), and greater activity for sSO than sPO ($t(17) = 2.22, p < 0.05$) and sM ($t(17) = 2.68, p < 0.05$). There was no main effect of memory for scenes ($F(2,34) = 2.07$), although there was a marginal linear trend ($F(1,17) = 3.52, p = 0.08$) and a numerical increase for sSO relative to sM ($t(17) = 1.88, p = 0.08$).

The anterior parahippocampal gyrus (Fig. 2.8E) also showed a significant effect of stimuli ($F(1,17) = 15.80, p < 0.01$), as well as a main effect of memory ($F(2,34) = 6.02, p < 0.01$) and a hemisphere*stimuli interaction ($F(1,17) = 5.20, p < 0.05$). When broken down according to stimulus type there was a main effect of memory for faces ($F(2,34) = 5.93, p < 0.01$), which also showed a linear trend ($F(1,17) = 8.16, p < 0.01$). Pairwise comparisons revealed that there was greater activity for sSO relative to sPO ($t(17) = 2.86, p < 0.01$) and sM ($t(17) = 2.61, p < 0.05$), whereas sPO and sM did not differ from each other. For the scenes there was a marginal main effect of memory ($F(2,34) = 2.61, p = 0.09$), a linear increase in memory-related activity ($F(1,17) = 5.08, p < 0.05$) and greater activity for sSO than sM ($t(17) = 2.25, p < 0.05$).

Within the perirhinal cortex face-sensitive voxels (Fig. 2.8F) there was a marginal main effect of stimuli only ($F(1,17) = 3.44, p = 0.08$). Although there were no significant main effects of memory ($F(2,34) = 2.42$) or stimuli*memory interactions ($F(2,34) = 2.20$) within these face-sensitive voxels, follow up tests revealed that encoding-related activity for faces in the perirhinal cortex exhibited a main effect of memory ($F(2,34) = 3.86, p < 0.05$) and a significant linear trend ($F(1,17) = 6.66, p < 0.05$). This reflected greater activity for sSO compared to sM ($t(17) = 2.58, p < 0.05$); there was no significant difference between sSO and sPO and sPO and sM for faces. There was no significant main effect ($F(2,34) = 0.42$) or linear trend ($F(1,17) = 1.04$) for scenes within the perirhinal cortex.

2.5.3. *Encoding summary*

Results from the encoding phase revealed stimulus-specific memory for faces in face voxels within the perirhinal cortex, and stimulus-specific memory for scenes in the left posterior hippocampus. In contrast, memory effects were present for both faces

and scenes in the anterior hippocampal (also observed in the whole-brain face sSO > face sM contrast) and parahippocampal gyrus face-fROIs, and in the scene-sensitive fROIs in the right posterior hippocampus as well as the posterior parahippocampal gyrus.

Dual-process accounts of MTL function posit that the hippocampus is critical for recollection and the perirhinal cortex for familiarity (Aggleton & Brown, 1999; Brown & Aggleton, 2001; see Section 1.4). As outlined in the previous chapter, according to the dual-process signal detection (DPSD) model proposed by Yonelinas (1994; 2002; see Section 1.4.1.3), recollection is a high-threshold process, whereas familiarity is a graded memory strength signal. It follows from this distinction that while recollection-based recognition memory judgments are generally indexed by high confidence responses, familiarity-based judgments can be associated with a wider range of confidence responses (Yonelinas, 2001b). In light of this model, brain regions involved in recollection have been proposed as those that exhibit greater activity for the most confidently recognised items, relative to low confidence old and new or missed items (SO > PO = M/CR: Cohn et al., 2006; Daselaar et al., 2006; Yonelinas et al., 2005). By contrast, regions supporting familiarity-based decisions are those that show an overall hit versus miss effect (SO = PO > M; Davachi et al., 2003; Kensinger & Schacter, 2006), often exhibiting a graded response according to response confidence (SO > PO > M: Daselaar et al., 2006; Ranganath et al., 2004).

Memory encoding activity that fitted the profile for recollection described above (sSO > sPO = sM) was observed for faces in the anterior hippocampus and anterior parahippocampal gyrus and there was a trend for this pattern for scenes within the right posterior hippocampus. No brain regions showed a pattern of activity that fitted the graded familiarity profile (sSO > sPO > sM), although there was a trend for an overall hit vs. miss effect (sSO = sPO > sM) for scenes in the right anterior hippocampus (identified using the face sSO > face sM contrast in the whole-brain analysis). From the fROI analyses, linear gradations in activity were identified in the anterior hippocampus, anterior parahippocampal gyrus, posterior parahippocampal gyrus and left posterior hippocampus for scenes; and the posterior parahippocampal gyrus, perirhinal cortex and right posterior hippocampus for faces. Within these regions, however, the encoding activation for sPO items was not reliably different

from either sSO or sM items (sSO > sM; sSO = sPO; sPO = sM). These effects, therefore, cannot be reliably attributed to recollection or familiarity.

2.6. Retrieval

2.6.1. Results from whole-brain analysis

To identify regions involved in memory processing for faces and scenes at retrieval, three categorical contrasts were performed between memory regressors for each stimulus type (scene SO > scene CR; scene CR > scene SO; scene SO > scene M; face SO > face CR; face CR > face SO; face SO > face M). Results from these whole-brain contrasts are summarised in Tables 2.4-2.9 and Figs. 2.9 and 2.10, which display a variety of significant memory effects in frontal, parietal, occipital and temporal brain regions, replicating the observations from previous fMRI studies that have investigated memory retrieval using confidence judgements (Daselaar et al., 2006; Montaldi et al., 2006; Yonelinas et al., 2005).

Specifically, there were significant memory effects for scenes (Tables 2.4-2.6) in the superior frontal gyrus, middle frontal gyrus, insula cortex, angular gyrus, posterior cingulate, precuneus, caudate, middle temporal gyrus and lingual gyrus (Daselaar et al., 2006; Montaldi et al., 2006; Yonelinas et al., 2005). Likewise, significant memory effects for faces (Tables 2.7-2.9) occurred within these regions (excluding the insula), with the addition of activity in the inferior temporal gyrus, superior parietal lobule and thalamus (Daselaar et al., 2006; Montaldi et al., 2006; Yonelinas et al., 2005). For the scenes there was also significant activation for the scene correct rejection > scene sure old contrast (Table 2.5) that was proximal to reported coordinates for the left parahippocampal place area (PPA: defined using mean Talairach coordinates [-23, -44, 9] from Peelen & Downing, 2005, converted to MNI space [-26, -42, -8]; see also Downing, Chan, Peelen, Dodds, & Kanwisher, 2006; Epstein et al., 2006; Epstein & Kanwisher, 1998; Epstein & Ward, 2010; Park & Chun, 2009) which has been documented as important for spatial processing. For the face sure old > face miss contrast (Table 2.9), however, there was significant activity proximal to reported coordinates for an area of the left temporal occipital fusiform cortex, known as the fusiform face area (FFA: mean Talairach coordinates [41, -47, -17] from Peelen

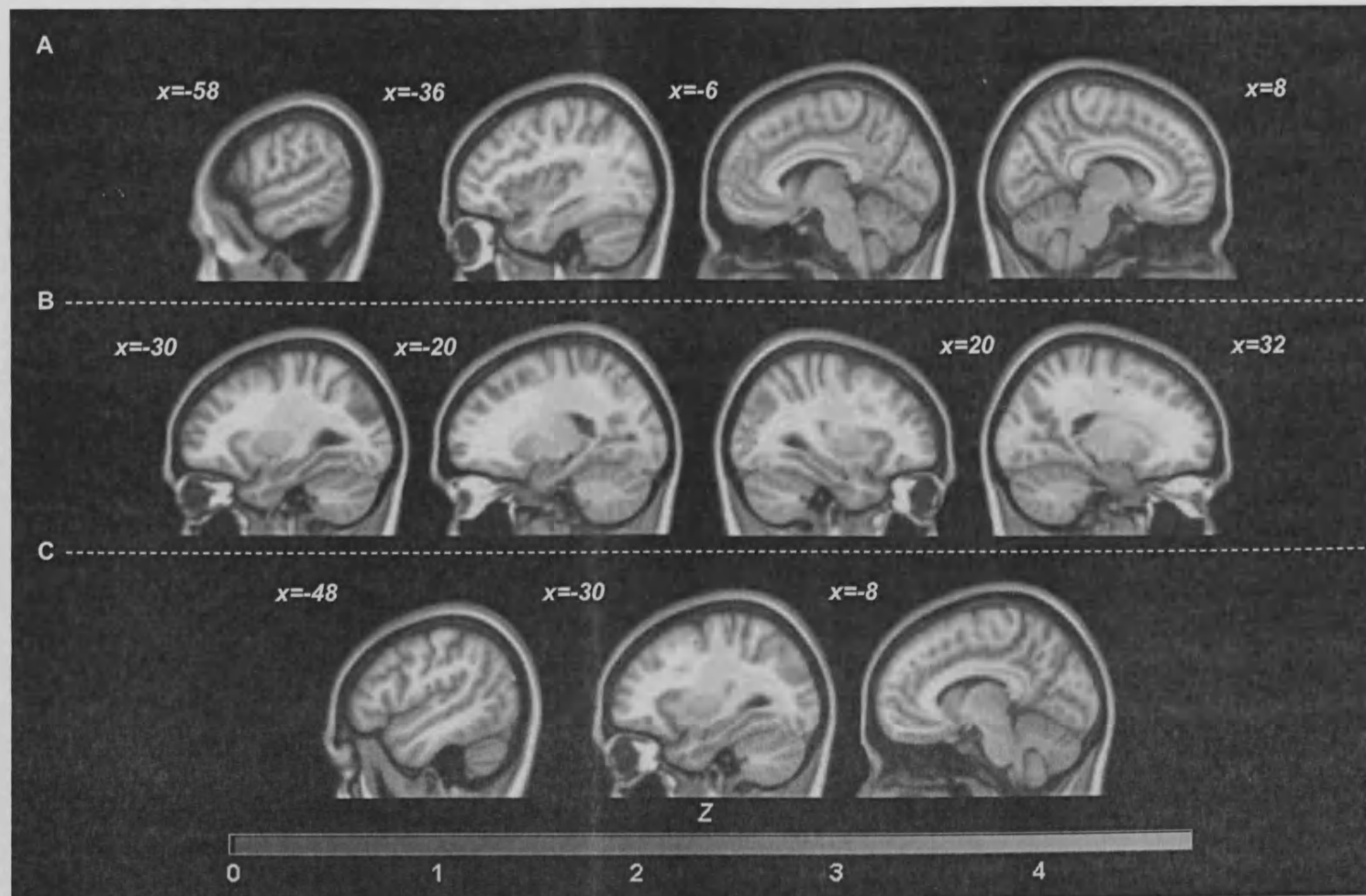


Figure 2.9: Significant memory retrieval-related activity from the (A) scene SO > scene CR, (B) scene CR > scene SO and (C) scene SO > scene miss contrasts. Images are overlaid onto a MNI-152 T1 2mm standard brain.

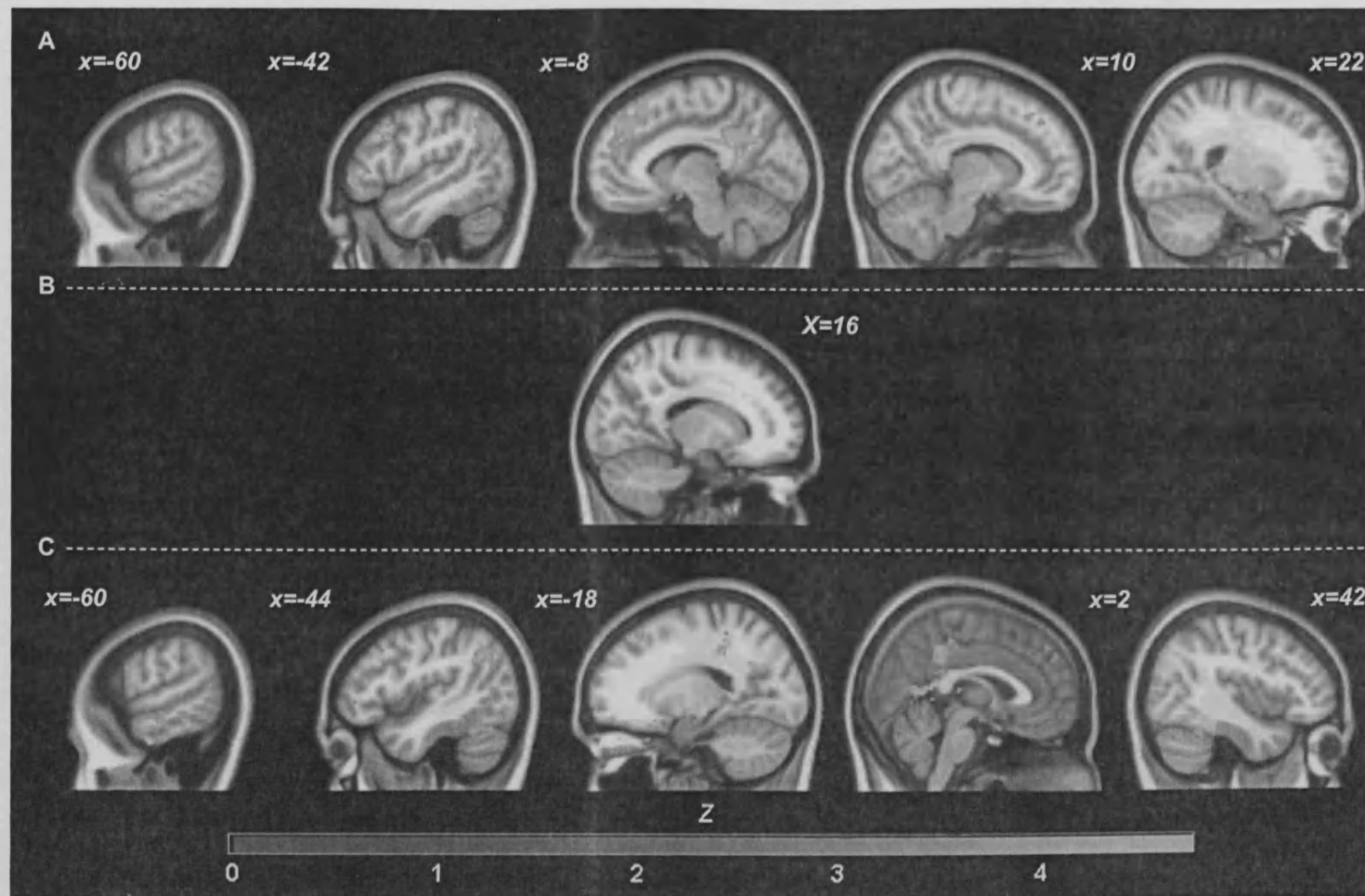


Figure 2.10: Significant memory retrieval-related activity from the (A) face SO > face CR, (B) face CR > face SO and (C) face SO > face miss contrasts. Images are overlaid onto a MNI-152 T1 2mm standard brain.

& Downing, 2005; converted to MNI space [47, -45, -16]; see also Downing et al., 2006; Kanwisher et al., 1996; Kanwisher, McDermott, & Chun, 1997). There was also activation for faces and scenes in occipitotemporal/extrastriate brain regions, including the inferior LOC (Kanwisher et al., 1996; Kanwisher, Woods et al., 1997; Malach et al., 1995), that are similar to those identified by the encoding whole-brain analysis (Tables 2.2 and 2.3).

Table 2.4: Local maxima and corresponding regions according to the Harvard-Oxford sub-cortical structural atlas observed for the sure old > correct rejection contrast for scenes ($p < 0.001$, cluster > 9 voxels).

Region				
	Z	x	y	z
<i>Left frontal pole</i>	4.37	-2	62	10
<i>Left superior frontal gyrus</i>	4.29	-4	46	32
<i>Right superior frontal gyrus</i>	4.06	6	46	34
<i>Left orbital frontal cortex</i>	3.75	-34	18	-12
<i>Left insula cortex</i>	3.73	-32	20	-8
<i>Left paracingulate gyrus</i>	3.34	-6	44	26
<i>Left angular gyrus</i>	4.05	-56	-58	34
<i>Left cingulate gyrus, posterior division</i>	4.95	-8	-44	32
<i>Left precuneus cortex</i>	4.53	-4	-56	30
<i>Right precuneus cortex</i>	3.75	10	-62	28
<i>Left caudate</i>	4.00	-8	14	-4
<i>Right caudate</i>	3.98	10	16	0
<i>Left lateral occipital cortex, superior division</i>	4.46	-54	-68	28
<i>Left middle temporal gyrus, posterior division</i>	4.27	-64	-40	-14
<i>Right middle temporal gyrus, posterior division</i>	3.42	70	-26	-8

Table 2.5: Local maxima and corresponding regions according to the Harvard-Oxford sub-cortical structural atlas observed for the correct rejection > sure old contrast for scenes ($p < 0.001$, cluster > 9 voxels).

Region				
	Z	x	y	z
<i>Right frontal pole</i>	3.66	32	38	20
<i>Left superior frontal gyrus</i>	4.00	-20	2	50
<i>Right superior frontal gyrus</i>	3.86	24	4	56
<i>Left middle frontal gyrus</i>	3.60	-32	-2	50
<i>Right middle frontal gyrus</i>	3.63	28	4	54
<i>Left paracingulate gyrus</i>	3.81	-8	16	40
<i>Left lateral occipital cortex, superior division</i>	3.65	-20	-66	50
<i>Right lateral occipital cortex, superior division</i>	3.93	32	-80	14
<i>Right lateral occipital cortex, inferior division</i>	3.85	30	-84	4
<i>Left occipital fusiform gyrus</i>	4.33	-20	-84	-16
<i>Right occipital fusiform gyrus</i>	4.06	32	-72	-18
<i>Left temporal occipital fusiform cortex (PPA)</i>	3.56	-28	-56	-16
<i>Left lingual gyrus</i>	4.30	-10	-82	-6
<i>Right lingual gyrus</i>	3.16	14	-84	-12

Table 2.6: Local maxima and corresponding regions according to the Harvard-Oxford sub-cortical structural atlas observed for the sure old > miss contrast for scenes ($p < 0.001$, cluster > 9 voxels).

Region				
	Z	x	y	z
<i>Left frontal pole</i>	3.50	-32	34	44
<i>Left superior frontal gyrus</i>	3.74	-26	30	52
<i>Left middle frontal gyrus</i>	3.61	-26	34	46
<i>Left paracingulate gyrus</i>	3.37	-8	44	36
<i>Left lateral occipital cortex, superior division</i>	3.82	-48	-80	24

Table 2.7: Local maxima and corresponding regions according to the Harvard-Oxford sub-cortical structural atlas observed for the sure old > correct rejection contrast for faces ($p < 0.001$, cluster > 9 voxels).

Region				
	Z	x	y	z
<i>Left frontal pole</i>	4.18	-44	44	-4
<i>Left superior frontal gyrus</i>	4.52	-12	30	48
<i>Right superior frontal gyrus</i>	4.26	22	28	44
<i>Left middle frontal gyrus</i>	4.00	-46	18	44
<i>Left inferior frontal gyrus, pars opercularis</i>	3.15	-50	14	24
<i>Right inferior frontal gyrus, pars opercularis</i>	3.72	50	22	24
<i>Left inferior frontal gyrus, pars triangularis</i>	3.49	-52	36	2
<i>Left paracingulate cortex</i>	4.87	-2	46	30
<i>Left angular gyrus</i>	3.99	-46	-58	42
<i>Left cingulate gyrus, posterior division</i>	4.66	-10	-46	32
<i>Right cingulate gyrus, posterior division</i>	3.84	10	-52	28
<i>Left precuneus cortex</i>	4.24	-12	-60	26
<i>Left lateral occipital cortex, superior division</i>	4.27	-40	-76	42
<i>Left temporal occipital fusiform cortex</i>	3.19	-48	-64	-26
<i>Left inferior temporal gyrus, posterior division</i>	3.86	-58	-36	-18
<i>Left middle temporal gyrus, posterior part</i>	3.44	-66	-20	-20
<i>Right middle temporal gyrus, posterior part</i>	3.87	66	-18	-22
<i>Left middle temporal gyrus, temporooccipital part</i>	4.06	-60	-52	-10

Table 2.8: Local maxima and corresponding regions according to the Harvard-Oxford sub-cortical structural atlas observed for the correct rejection > sure old contrast for faces ($p < 0.001$, cluster > 9 voxels).

Region				
	Z	x	y	z
<i>Right superior parietal lobule</i>	3.19	22	-60	60
<i>Right lateral occipital cortex, superior division</i>	3.52	16	-62	60

Table 2.9: Local maxima and corresponding regions according to the Harvard-Oxford sub-cortical structural atlas observed for the sure old > miss contrast for faces ($p < 0.001$, cluster > 9 voxels).

Region				
	Z	x	y	z
<i>Left frontal pole</i>	3.77	-8	60	18
<i>Left frontal orbital cortex</i>	3.56	-22	26	-18
<i>Left inferior frontal gyrus, pars triangularis</i>	3.62	-52	36	2
<i>Left superior frontal gyrus</i>	4.28	-8	26	56
<i>Left middle frontal gyrus</i>	3.40	-32	22	48
<i>Left superior parietal lobule</i>	3.36	-22	-50	42
<i>Left angular gyrus</i>	4.13	-48	-56	32
<i>Left postcentral gyrus</i>	3.31	-18	-38	52
<i>Left cuneal cortex</i>	3.15	-8	-74	26
<i>Left cingulate gyrus, posterior division</i>	4.46	-4	-38	36
<i>Right cingulate gyrus, posterior division</i>	4.09	2	-48	12
<i>Left precuneus cortex</i>	4.13	-14	-62	26
<i>Right precuneus cortex</i>	3.90	6	-60	10
<i>Left lateral occipital cortex, superior division</i>	3.78	-42	-74	42
<i>Left lateral occipital cortex, inferior division</i>	3.36	-44	-80	14
<i>Right lateral occipital cortex, inferior division</i>	3.33	42	-82	6
<i>Left occipital fusiform gyrus</i>	3.94	-46	-64	-22
<i>Right occipital fusiform gyrus</i>	3.48	32	-66	-14
<i>Left temporal occipital fusiform cortex</i>	4.05	-50	-62	-26
<i>Right temporal occipital fusiform cortex (FFA)</i>	3.73	44	-48	-24
<i>Left temporal fusiform cortex, posterior division</i>	3.30	-34	-24	-26
<i>Left inferior temporal gyrus, temporooccipital part</i>	3.81	-54	-52	-22
<i>Right inferior temporal gyrus, temporooccipital part</i>	3.56	52	-50	-24
<i>Left inferior temporal gyrus, posterior division</i>	4.06	-58	-38	-16
<i>Left inferior temporal gyrus, anterior division</i>	3.92	-60	-10	-32
<i>Left middle temporal gyrus, posterior division</i>	3.84	-62	-18	-16
<i>Left middle temporal gyrus, temporooccipital part</i>	3.27	-60	-54	-8
<i>Left lingual gyrus</i>	3.56	-18	-48	-8
<i>Right lingual gyrus</i>	3.52	20	-74	-4
<i>Left thalamus</i>	3.33	-2	-24	10
<i>Right thalamus</i>	3.23	2	-26	10

2.6.1.1. MTL effects

There were no significant MTL activations at the whole-brain level for the retrieval phase of the current experiment.

2.6.2. Results from functional region of interest analysis

2.6.2.1. Scene-sensitive regions

The fROI approach (CR scenes > CR faces) identified two areas within the MTL that showed greater activation for scene than for face stimuli (posterior hippocampus and posterior parahippocampal gyrus). All of these regions showed a significant effect of stimulus type in subsequent analyses (see Figs. 2.11 A and B, all $F(1,17) > 12.15$, $p < 0.01$). As none of these regions showed any significant main effects of memory or interactions between memory and stimuli (all $F(2,34) < 1.33$), they will not be discussed further in the results.

2.6.2.2. Face-sensitive regions

Voxels sensitive to faces in anterior hippocampus (Fig. 2.11C) exhibited a significant main effect of stimuli ($F(1,17) = 18.04$, $p < 0.01$) and a marginally significant hemisphere*memory*stimuli interaction ($F(2,34) = 3.26$, $p = 0.05$). Further analysis revealed that this three-way interaction reflected a main effect of memory for faces in left anterior hippocampus ($F(2,34) = 4.22$, $p < 0.05$), which showed a significant linear trend ($F(1,17) = 6.29$, $p < 0.05$). Pairwise comparisons revealed greater activation in left anterior hippocampus for SO relative to PO ($t(17) = 2.13$, $p < 0.05$) and M ($t(17) = 2.50$, $p < 0.05$). There were no main effects of memory for scenes in left anterior hippocampus, and no memory effects for faces or scenes nor any memory*stimuli interactions in the fROI for the right anterior hippocampus.

Face-sensitive voxels in anterior parahippocampal gyrus (see Fig. 2.11D) exhibited a main effect of stimuli ($F(1,17) = 17.16$, $p < 0.01$), a marginal main effect of memory ($F(2,34) = 3.10$, $p = 0.06$), a hemisphere*stimuli interaction ($F(1,17) = 23.32$, $p < 0.01$) and a hemisphere*memory*stimuli interaction ($F(2,34) = 3.00$, $p = 0.07$) that approached significance. As for the anterior hippocampus, there was a main effect of memory for faces that was marginal in the left anterior parahippocampal gyrus ($F(2,34) = 2.75$, $p = 0.08$), a pattern that was accompanied by a significant linear trend ($F(1,17) = 4.83$, $p < 0.05$). Pairwise comparisons from the left parahippocampal gyrus indicated that activity for SO faces was greater M faces only ($t(17) = 2.20$, $p < 0.05$). Memory effects for scenes were not significant in the left anterior parahippocampal

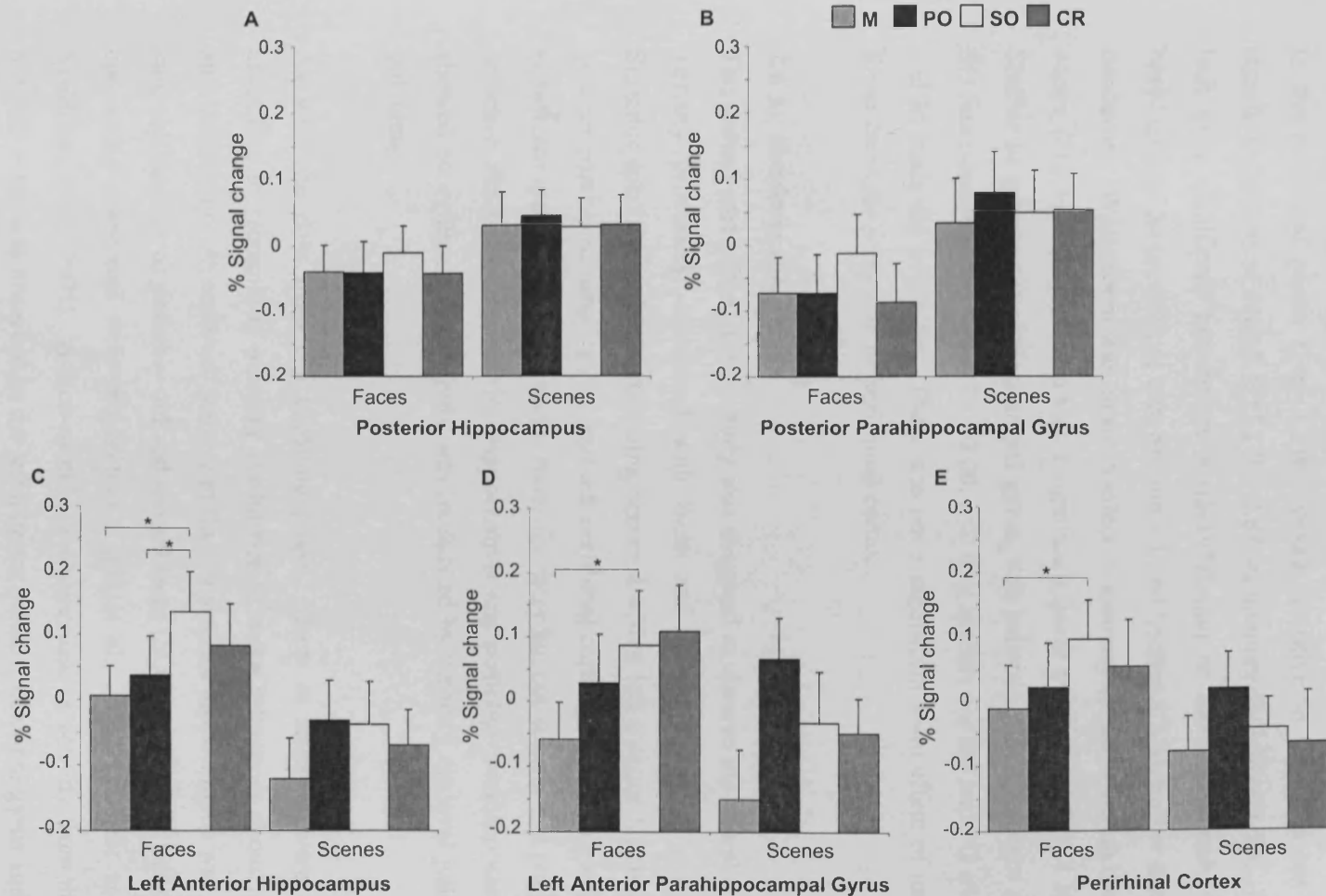


Figure 2.11: Memory retrieval activity for faces and scenes in functionally defined MTL regions of interest from (A, B) CR scenes > CR faces and (C, D, E) CR faces > CR scenes. Percent signal change (arbitrary units) in the (A) posterior hippocampus, (B) posterior parahippocampal gyrus, (C) left anterior hippocampus, (D) left anterior parahippocampal gyrus, and (E) perirhinal cortex. Abbreviations: (M) miss (light grey), (PO) subsequent probably old (black), (SO) subsequent sure old (white) and (CR) correct rejections (dark grey). On all graphs 0 on the y-intercept represents the mean level of activity across all conditions, * $p < 0.05$.

gyrus, and no memory effects were present for faces or scenes in the right anterior parahippocampal gyrus face voxels.

In the perirhinal cortex (Fig. 2.11E), voxels sensitive to faces did not show any significant effects of stimuli ($F(1,17) = 2.87$) or memory ($F(2,34) = 1.50$). Despite the lack of a significant hemisphere*memory*stimuli or memory*stimuli interaction, based on a priori predictions (see Section 2.1 and Section 2.3.3), further analyses were conducted. While there was no main effect of memory for faces within the perirhinal cortex ($F(2,34) = 1.84$), there was a significant linear trend ($F(1,17) = 4.38, p < 0.05$). Similar to anterior parahippocampal gyrus, this pattern reflected greater activity for SO faces compared to M ($t(17) = 2.09, p < 0.05$); activity for SO and PO trials and PO and M trials did not differ. There was not a significant main effect of memory or a linear trend for scenes in the perirhinal cortex.

2.6.3. Retrieval summary

The second part of the current study was designed to observe the neural correlates of memory processing associated with faces and scenes at the time of retrieval. Stimulus-specific memory processing occurred within left anterior hippocampus, left anterior parahippocampal gyrus and left perirhinal cortex; all these regions exhibited significant memory-related brain activity for faces but not scenes. In contrast, scene selective fROIs in the posterior hippocampus and posterior parahippocampal gyrus showed no evidence that activity was modulated by memory retrieval judgements to old items.

As with the data from the encoding phase, effects at retrieval were considered according to recognition memory confidence to make inferences about recollection and familiarity. At retrieval, activity in the left anterior hippocampus was greater for sure old, relative to probably old and missed faces ($SO > PO = M$), a pattern that is commonly associated with recollection (Cohn et al., 2009; Daselaar et al., 2006; Yonelinas et al., 2005). A face-specific linear increase in activity from miss to sure old ($SO > M$) was observed in the left anterior parahippocampal gyrus and perirhinal cortex; activity for sPO was intermediate but did not differ significantly from sSO and/or sM. As with the encoding data, it is unclear whether the pattern within these regions is $SO > PO = M$ (recollection), $SO > PO > M$ (familiarity) or $SO = PO > M$

(familiarity), and thus effects cannot be confidently attributed to recollection or familiarity.

2.7. Discussion

Surprisingly few functional neuroimaging studies have attempted to observe how the MTL contributes to long-term memory for different kinds of complex visual information, such as scenes or faces (Awipi & Davachi, 2008; Prince et al., 2009; Preston et al., 2010) despite recent evidence that subregions may make functionally different contributions depending upon the material to be employed (Graham et al., 2010; Lee, Barense et al., 2005; see also Bussey & Saksida, 2005; Saksida & Bussey, 2010). Predictions guided by previous fMRI investigations (Awipi & Davachi, 2008; Barense, Henson et al., 2010; Lee, Bandelow et al., 2006; Lee et al., 2008; Litman et al., 2009; Pihlajamaki et al., 2004; Rudebeck & Lee, 2010), region of interest analyses were conducted to investigate patterns of memory-related brain activity for faces and scenes within functionally-derived subregions of the MTL. The creation of fROIs, identified from contrasts between novel faces and scenes, revealed that the anterior hippocampus, anterior parahippocampal gyrus and perirhinal cortex showed a larger neural response to faces than scenes. In contrast, activity in posterior parahippocampal gyrus and posterior hippocampus was greater for scenes. These fROIs reflect a body of recent fMRI research that has demonstrated differing profiles of activation, across a variety of cognitive tasks, for objects (including faces) and scenes within the perirhinal cortex, hippocampus and posterior parahippocampal gyrus (Awipi & Davachi, 2008; Barense, Henson et al., 2010; Lee, Bandelow et al., 2006; Lee et al., 2008; Litman et al., 2009; Pihlajamaki et al., 2004; Rudebeck & Lee, 2010).

The fROI analyses revealed significant patterns of memory-related activity within the hippocampus, parahippocampal gyrus and perirhinal cortex. In the first instance these effects are in keeping with fMRI studies that have implicated subregions of the MTL for successful memory encoding and retrieval using functional imaging (encoding or DM effects: Awipi & Davachi, 2008; Brewer et al., 1998; Davachi et al., 2003; Henson et al., 1999; Johnson & Rugg, 2007; Otten et al., 2001, 2002; Paller & Wagner, 2002; Ranganath et al., 2004; Wagner et al., 1998; and retrieval: Cansino et

al., 2002; Daselaar et al., 2006; Daselaar et al., 2001; Diana et al., 2010; Dobbins et al., 2003; Donaldson et al., 2001; Eldridge et al., 2000; Gonsalves et al., 2005; Montaldi et al., 2006; Yonelinas et al., 2005). The implications of the fact that some of these patterns show a trend towards stimulus-specificity (at both encoding and retrieval), will be expanded upon in the following sections.

2.7.1. MTL effects at encoding

Results from the fROI analyses revealed a trend towards memory encoding for faces and scenes in the anterior hippocampus, anterior parahippocampal gyrus and right posterior hippocampus. As patterns of memory-related activity within the anterior hippocampus, anterior parahippocampal gyrus and right posterior hippocampus were not consistent across the two stimulus types, and were accompanied by limited statistical support, it is unclear whether they are domain-general. As such, these effects will not be discussed further. There was a reliable domain-general memory encoding effect that was equivalent across stimuli, however, in the posterior parahippocampal gyrus. In contrast, encoding effects in the perirhinal cortex and left posterior hippocampus were specific to faces and scenes, respectively.

In a recent imaging study that also directly compared recognition memory for faces and scenes, encoding effects within the hippocampus and perirhinal cortex were domain-general, whereas memory-related activity within the parahippocampal gyrus was specific to scenes (Preston et al., 2010; see Section 1.6.3 and 2.1). In the current experiment, therefore, domain-general encoding effects in the anterior hippocampus and right posterior hippocampus replicate the findings from Preston et al. (2010; see also Prince et al., 2009 for domain-general face/scene encoding effect in the hippocampus, which is discussed in the following section). The current data set diverges, however, as memory effects within the posterior parahippocampal gyrus were domain-general rather than specific to scenes, and there were trends towards stimulus-specific memory effects within the left posterior hippocampus (scenes) and perirhinal cortex (objects), both of which were domain-general in Preston et al. (2010).

A profile of stimulus-specific responding in the posterior hippocampus and perirhinal cortex is similar to the findings from Awipi & Davachi (2008, detailed in the

Introduction of this chapter and in Section 1.6.3). Awipi & Davachi (2008) observed brain activity that related to subsequent memory for objects in the perirhinal cortex that was not evident for scenes. In contrast, activity in the hippocampus predicted memory success for scenes, but not objects. The concordance of stimulus-specific encoding activity within the perirhinal cortex between the current study and Awipi & Davachi (2008) is an encouraging finding. As discussed in the Introduction, Preston et al. (2010) may have observed memory effects for faces *and* scenes within the perirhinal cortex because their novel scenes also contained numerous salient objects and the target-detection encoding task they employed could have encouraged participants to encode visuo-object as well visuo-spatial information within the scenes (see Section 2.1 and Fig. 2.1). By the authors' own admission (Preston et al., 2010), memory-related activity for scenes within the perirhinal cortex could 'reflect encoding of the visual objects in scenes, rather than of visuo-spatial information per se' (pp. 168). This notion is expanded upon in the following section, alongside a discussion of retrieval effects for scenes.

2.7.2. MTL effects at retrieval

At retrieval, all significant effects of memory were evident only for faces; these were located in the left anterior hippocampus, left anterior parahippocampal gyrus and perirhinal cortex. Notably, there were no memory effects for scenes in the MTL. Significant patterns of memory-related activity for faces in the perirhinal cortex and the anterior parahippocampal gyrus mirrored findings from a previous fMRI memory investigation that employed faces (Gonsalves et al., 2005). In fact, in an experiment that simultaneously assessed long-term memory retrieval and perception of faces, O'Neil et al. (2009) observed greater activity for correct versus incorrect responses from the perceptual and mnemonic tasks in the perirhinal cortex only (see Section 1.6.3, Fig. 1.24). There is, however, a previous report of domain-general memory encoding and retrieval effects for faces and scenes within the hippocampus (Prince et al., 2009). It is difficult, however, to extrapolate the memory effects from Prince and colleagues paper to the current data set due to discrepancies in the analysis approach; the former identified significant effects within the hippocampus using a contrast that tracked overall memory success collapsed across stimulus type (hit > miss), which could reflect a combination of face- and scene- sensitive hippocampal voxels (the size of the cluster is not reported). If Prince et al. (2009) had identified stimulus-specific

hippocampal voxels, using an unbiased fROI approach, memory effects may have been scene-specific in the scene voxels and face-specific in face voxels.

Alternatively, the present study may have failed to replicate the effects from Prince et al. (2009) because face-specific memory processing within the hippocampus could reflect an insensitivity of the current paradigm to detect MTL memory effects for scenes. The whole-brain analysis, however, indicated memory effects for scenes in regions outside the MTL (posterior cingulate, angular gyrus, insula, lingual gyrus, middle temporal gyrus, caudate and precuneus) that are consistent with previous studies that have investigated brain regions associated with memory retrieval for words (Daselaar et al., 2006; Yonelinas et al., 2005) and scenes using recognition confidence (Montaldi et al., 2006; Prince et al., 2009). There were also patterns of memory-related activity for faces and scenes throughout the lateral occipital cortex, fusiform cortex, temporal fusiform cortex (FFA and PPA, respectively) and inferior temporal cortex, which are regions that have been documented as important for processing visual stimuli (Downing et al., 2006; Epstein & Kanwisher, 1998; Haxby et al., 1991; Kanwisher, Woods et al., 1997). Due to the presence of these memory effects, some which appeared to be contingent upon the visual properties of the stimuli (e.g. PPA), it is certainly arguable whether the observed face-specific effects can be explained by a general insensitivity to memory-related activity for scenes in this paradigm.

As lesions to the hippocampus disrupt scene memory (Bird et al., 2007; Bird et al., 2008; Cipolotti et al., 2006; Taylor et al., 2007) and perceptual discrimination of scenes (Lee, Buckley et al., 2005; Lee, Bussey et al., 2005), it was expected that successful memory retrieval of scenes would elicit activity within the hippocampus. During the encoding phase of the current study, and in previous fMRI experiments, significant short-term and long-term memory effects for scenes have been demonstrated in the posterior hippocampus and parahippocampal gyrus (Litman et al., 2009; Montaldi et al., 2006; Preston et al., 2010; Rudebeck & Lee, 2010). While the posterior hippocampus and posterior parahippocampal gyrus exhibited greater activity for scenes than faces at retrieval, profiles of BOLD within these regions were not modulated by recognition memory accuracy.

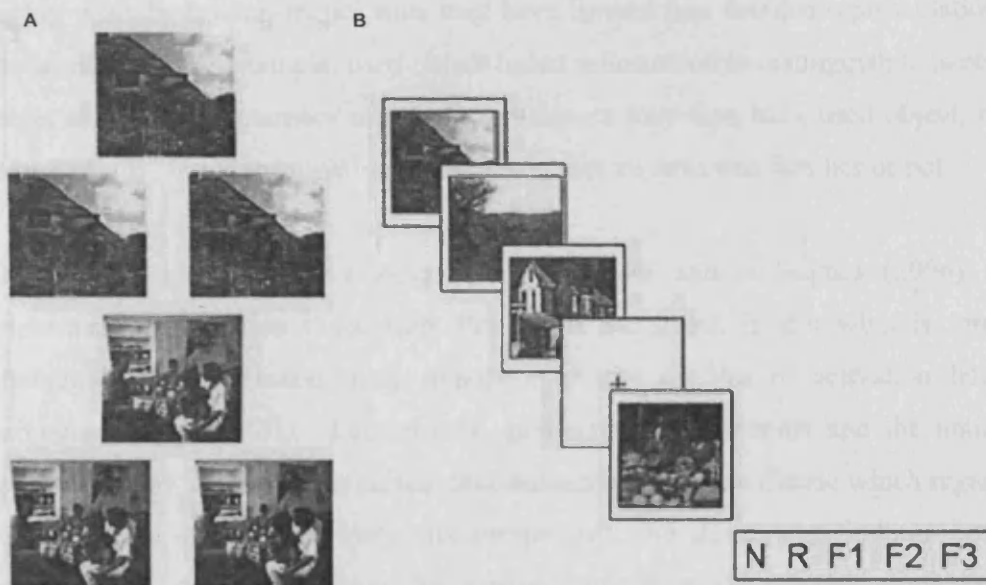


Figure 2.12: Encoding and retrieval phases from Montaldi et al. (2006). (A) Stimuli and the match-to-sample task completed at encoding. For each stimulus, the top scene matches only one of the two lower scenes. The other is shifted vertically or horizontally by a small amount. Participants had to identify the matching lower scene. (B) Stimuli and retrieval task; for each test item participants had to indicate whether they felt the scene was (N) new, (F1) weakly, (F2) moderately, or (F3) strongly familiar or if they effortlessly (R) recollected the item. Figure from Montaldi et al. (2006).

Notably, however, memory retrieval activity for scenes is not restricted to the posterior hippocampus and parahippocampal gyrus (Montaldi et al., 2006; for encoding effects see also Preston et al., 2010). In an experiment that was specifically designed to encourage participants to use familiarity, Montaldi et al. (2006; previously described in Section 1.4.4) observed a pattern of activity for scenes within the perirhinal cortex which increased monotonically with increases in recognition confidence. The stimuli employed in that experiment comprised full colour pictures that contained numerous objects (including people; see Fig. 2.12), and, although these could be described as scenes, they may not be best equipped to *independently* assess memory for visuo-spatial features.

Furthermore, memory effects for scenes could have occurred in the perirhinal cortex due to Montaldi and colleagues (2006) study task. At encoding participants completed a difficult match-to-sample task, where they were required to match one of two visually similar scenes to a sample scene presented above. As foils and targets were

highly visually similar, participants may have formed less detailed representations of the scenes and, for example, used object based information to distinguish between the target and foil. At memory retrieval, participants may then have used object, rather than spatially, based information to judge whether an item was familiar or not.

One interpretation of the findings from Montaldi and colleagues (2006) fMRI experiment (as well as those from Preston et al., 2010) is that what is formally characterised as a 'scene' may impact upon the profiles of activation between subregions of the MTL. Furthermore, processing requirements and the nature of representations formed under certain task demands could also dictate which regions of the MTL are involved. From this perspective, the discordant findings between encoding and retrieval within the current investigation may be explained via differences in tasks demands during the study and test phases.

2.7.3. MTL activation and recognition confidence

During the retrieval phase, participants were required to make memory judgements to old/new test items on a 6-point confidence scale (1 = high confidence new to 6 = high confidence old), which were used to subcategorise encoding and retrieval items into one of three bins; sure old (sSO/SO), probably old (sPO/PO) and miss (sM/M). In this study all significant memory effects at encoding and retrieval comprised increases in activity for old items according to confidence in the old decision. Furthermore, planned pairwise comparisons between memory confidence bins revealed evidence of a face-specific recollection effect at retrieval, as indexed by an increase in brain activity for sure old, relative to probably old and forgotten items (sSO/SO > sPO/PO = sM/M) within the anterior hippocampus (Daselaar et al., 2006; Yonelinas et al., 2005). In contrast, pairwise comparisons failed to reveal any reliable overall hit vs. miss effects (sSO/SO = sPO/PO > sM/M) or linear changes in brain activity across recognition memory confidence regressors (sSO/SO > sPO/PO > sM/M), which are analogous to a parametric modulations in activity that have been previously associated with familiarity (at encoding: Davachi, 2003; Ranganath et al., 2004; and at retrieval: Daselaar et al., 2006; Montaldi et al., 2006). Finally, graded increases in activity (sSO/SO > sM/M) were observed in the posterior parahippocampal gyrus (domain-general) and left posterior hippocampus (scene-specific) at encoding, left perirhinal cortex (face-specific) during encoding and retrieval, and anterior parahippocampal

gyrus (face-specific) at retrieval only. As these effects showed increases in activity for sure old items compared to missed items, and no difference between sure old and probably old, or probably old and missed items, these effects could not be attributed to either recollection or familiarity.

In the current study there were no significant linear changes in BOLD relating to item familiarity at encoding or retrieval in any of the fROIs. Notably, previous experiments that have revealed parametric fluctuations in familiarity strength have done so across a greater number of confidence response categories (Daselaar et al., 2006; Montaldi et al., 2006; Ranganath et al. 2004; Yonelinas et al., 2005). For example, Ranganath et al. (2004) observed linear changes in brain activity across 5 confidence bins, ranging from high confidence miss to medium confidence hit, within the perirhinal cortex. Likewise, Montaldi et al. (2006) demonstrated similar effects by conducting a parametric analysis across miss and 3 levels of familiarity strength (Fig. 2.12). In the current experiment the number of study trials was restricted (relative to previous experiments) because two stimulus types were employed and fMRI scanning was conducted during the encoding and retrieval phases. Due to low trial numbers, low and medium confidence old responses were concatenated into a single 'probably old' regressor. While the aforementioned studies merely accepted linear changes across confidence groups as an index of familiarity, here, due to the low number of response categories, a conservative approach was adopted, whereby sure old had to be significantly different from probably old, and probably old from miss. It is likely that the creation of a single probably old regressor may have masked changes in activity that could have driven a significant parametric modulation using a more liberal approach. This, therefore, could account for the number of instances for which activity for probably old was intermediate between, but did not significantly differ from, sure old or miss.

As discussed in the previous chapter, dual-process accounts of MTL function posit that the hippocampus and perirhinal cortex support recollection and familiarity, respectively (see Section 1.4). Similarly, informational accounts (see Section 1.5), such as binding of item and context (BIC: Diana et al., 2007; see also Davachi, 2006) propose that, while context is processed by the parahippocampal cortex, item-based information is supported by the perirhinal cortex. Item and context information

converges in the hippocampus, where domain-general item-context representations are formed, and reinstated during memory retrieval (Diana et al., 2007; Davachi, 2006). Behavioural estimates of recollection, which requires the recovery of contextual information, should, therefore, correlate with activity in the hippocampus and, according to BIC, in the parahippocampal cortex. Likewise, measures of familiarity, which is supported by item-based information, should be associated with perirhinal cortex activity. Previous functional neuroimaging investigations have revealed that activity in the hippocampus and parahippocampal cortex consistently correlates with correct source, remember and high confidence memory judgements, whereas activity in the anterior MTL and perirhinal cortex is generally associated with memory for single items, know judgements and linear modulations based on item memory (or familiarity) strength (Daselaar et al., 2006; Davachi et al., 2003; Henson et al., 1999; Johnson & Rugg, 2007; Montaldi et al., 2006; Ranganath et al., 2004)

In the current study, although there was activity that pointed to recollection at retrieval in the anterior hippocampus, this was only evident for faces. As noted in the Introduction, however, dual-process and BIC accounts do not make explicit theoretical predictions about stimulus-specificity. As such, it is unclear whether the absence of memory effects for scenes within the anterior hippocampus can be accommodated by dual-process and BIC accounts of MTL function. Furthermore, although there was a significant domain-general encoding effect (posterior parahippocampal gyrus at encoding), the pattern of data could not be ascribed confidently to recollection or familiarity. These data, therefore, provide limited support for dual-process and information-based theories of MTL function.

2.7.4. *Stimulus-specific MTL memory effects*

In this experiment there was a trend towards stimulus-specific memory encoding-related activity for scenes in scene-sensitive voxels in the left posterior hippocampus. Likewise, there were significant memory effects for faces in voxels that process faces in the anterior MTL, including perirhinal cortex (at both encoding and retrieval), which were not evident for scenes. In part, these effects are consistent with neuropsychological studies demonstrating that MTL lesions that include the perirhinal cortex, but not those that are restricted to the hippocampus, lead to impairments in long term memory for faces (Bird et al., 2008; Cipolotti et al., 2006; Taylor et al.,

2007). As there is significant overlap between voxels that signal accuracy for memory retrieval and oddity judgements in the perirhinal cortex (O'Neil et al., 2009), these stimulus-specific memory effects are also in keeping with the observation that damage to the perirhinal cortex can impair higher-level perception of faces (Lee, Buckley et al., 2006; Lee, Buckley et al., 2005; Lee, Bussey et al., 2005).

According to a representational account of MTL function (EMA: Graham et al., 2010), the division of labour between MTL subregions is guided by the properties of the stimulus materials employed in a task (see Section 1.6 and 1.7). The formation of these representational accounts has been guided by observations that complex representations of objects and scenes are processed and stored in discrete MTL regions, which are necessary for long-term memory, as well as short-term memory and higher-level perception (Awipi & Davachi, 2008; Barense et al., 2005; Barense et al., 2007; Barense, Henson et al., 2010; Lee, Bandelow et al., 2006; Lee, Buckley et al., 2005; Lee, Bussey et al., 2005; Lee et al., 2008; Taylor et al., 2007). As such, for regions that show differential sensitivity to processing objects and scenes, memory effects should be stimulus-specific.

One dual-process explanation for stimulus-specific processing, and disproportionate impairments in face and scene memory in hippocampal amnesics, such as those observed in Taylor et al. (2007), is that face and scene memory differentially rely on recollection and familiarity. For example, it has been proposed that faces are processed holistically (Tanaka & Farah, 1991), which may increase reliance of face recognition memory on familiarity-based memory in the perirhinal cortex (Yonelinas et al., 1999). In the current study, confidence ratings collected at test were used to infer the contributions of recollection and familiarity to memory performance. Overall memory accuracy for faces and scenes was comparable, with no difference between familiarity estimates, and a higher recollection estimate for the scenes. If there had been a higher familiarity estimate in the condition that showed greater activation in perirhinal cortex, and/or a higher recollection estimate for the condition that showed greater activation in the hippocampus, this would have permitted nothing other than the claim that the perirhinal cortex and hippocampus are associated with the processes of familiarity and recollection, respectively. The key results here, however, are that (a) for both stimulus types, there were comparable estimates for

familiarity but activation related to memory in the perirhinal cortex for one stimulus type only, and (b) activation at retrieval within the hippocampus for the stimulus type for which the recollection estimate was reliably lower. These patterns of face-specific memory encoding and retrieval-related activity in the hippocampus and the perirhinal cortex, therefore, are unlikely to reflect greater dependence on recollection and/or familiarity, or that the face stimuli were more memorable than the scenes.

In terms of the BIC model, an alternative possibility is that faces and scenes disproportionately rely on item or context based information, respectively. Importantly, according to BIC, although measures of recollection are most commonly associated with encoding/retrieval of context, and familiarity is associated with encoding/retrieval of items, as information is the overruling factor, patterns of activity within the perirhinal cortex and parahippocampal gyrus/hippocampus will not always reflect recollection and familiarity. For example, recollection of item features can be supported by the perirhinal cortex (Awipi & Davachi, 2008; Diana et al., 2010; Staresina & Davachi, 2006; 2008). As both estimates could reflect the recovery of item-based information, the absence of deficits in recollection *and* familiarity for faces in hippocampal amnesia (e.g. Cipolotti et al., 2006) is not sufficient to discount the BIC account of MTL function (Diana et al., 2007). Measures of recollection and familiarity based on confidence ratings, therefore, are not adequate to disambiguate the relative contributions of item and context memory processing for faces and scenes. Using an item-context associative memory paradigm (or source memory), however, the recollection of contextual information can be experimentally observed, and dissociated from instances where only item information is recovered (providing the context does not comprise an item feature). To date there has not been an experiment published which has *directly* compared the neural basis of item and context memory (independently from recollection and familiarity measures) for different stimulus types.

2.8. Conclusions

A number of regions within the MTL showed stimulus-specific responding; the posterior hippocampus and posterior parahippocampal gyrus exhibited greater activity for novel scenes versus novel faces, whereas the anterior hippocampus, anterior

parahippocampal gyrus and perirhinal cortex were more active for novel faces. The locations of these face- and scene-sensitive regions are consistent with the findings from a number of previous neuroimaging studies (Awipi & Davachi, 2008; Barense, Henson et al., 2010; Lee, Bandelow et al., 2006; Lee et al., 2008; Litman et al., 2009; O'Neil et al., 2009; Pihlajamaki et al., 2004; Rudebeck & Lee, 2010). Within each of these stimulus-specific regions, excluding the perirhinal cortex and left posterior hippocampus, memory effects at encoding were largely domain-general. In contrast, significant memory retrieval effects within the anterior hippocampus, anterior parahippocampal gyrus and perirhinal cortex were stimulus-specific, which, in light of the specific aims of this thesis, is an encouraging trend. The data from the memory confidence decisions revealed that face-specific memory activity in the hippocampus at retrieval could be attributed to recollection (Cohn et al., 2009; Daselaar et al., 2006; Yonelinas et al., 2005). While these data do not necessarily challenge a dual-process or informational account of MTL function, they are also consistent with some features of a representational view (Graham et al., 2010) in which material is an important predictor of activity in MTL regions.

In the current study there were no patterns of activity within the MTL that conclusively pointed to familiarity-based memory processing. In fact, for the majority of memory effects, the relationship between recognition confidence conditions could not be distinguished in terms of recollection or familiarity. The presence of these ambiguous memory effects is likely to have arisen from the adoption of a reasonably conservative analysis strategy, conducted over a small number of memory response categories (necessary due to trial numbers, a limitation imposed by using two stimulus types). One of the key aims for Experiment 2 was to increase the number of study items, and, therefore, the number of recognition confidence categories with which to identify neural markers of recollection and familiarity (Montaldi et al., 2006; Ranganath et al., 2004; Yonelinas et al., 2005). Furthermore, to disambiguate memory effects for items versus context, responses at test comprised a 6-point recognition memory confidence judgement (sure new to sure old), followed by a source memory judgement. In Experiment 2, fMRI scanning was restricted to the encoding phase so that it was possible to include the increased number of study trials required for linear trend analyses across a greater number of response categories.

For clearer investigation of stimulus-specificity in the MTL, it may be more informative to make comparisons between memory-related activity for objects and scenes, rather than faces and scenes. Previous functional imaging investigations that have compared the neural correlates of face and scene processing have also observed face-specific effects in the anterior hippocampus, as well as the perirhinal cortex (Barens, Henson et al., 2010; Lee et al., 2008). This indicates that there may be a face versus scene division of labour between the anterior and posterior hippocampus (Lee, Bandelow et al., 2006; Lee et al., 2008). It has been demonstrated that the amygdala, which is superior to the anterior hippocampus, is involved in processing faces (Adolphs, Tranel, Damasio, & Damasio, 1994; Haxby, Hoffman, & Gobbini, 2000). As a result, memory effects for faces in the current study could reflect a network of face processing regions that extend across the anterior MTL (encompassing the perirhinal cortex, anterior hippocampus and amygdala). Notably, significant stimulus-specific effects for objects are generally evident in the perirhinal cortex only (Awipi & Davachi, 2008; Devlin & Price, 2007; Kohler et al., 2005; Lee, Bandelow et al., 2006; Litman et al., 2009; although see Pihlajamaki et al., 2004). With a view to observing whether object mnemonic processing would elicit similar diverse anterior MTL effects to faces (e.g. anterior hippocampus, anterior parahippocampal gyrus and perirhinal cortex), or if these would be restricted to the perirhinal cortex, Experiment 2 was designed made direct comparisons between item and context memory for objects and scenes.

Chapter 3

Dissociable MTL correlates of item and context memory for objects and scenes

3.1. Introduction

The data described in the previous chapter provided some evidence for stimulus-specific memory processing within the MTL. At retrieval there were memory effects for faces in the left anterior hippocampus, left anterior parahippocampal gyrus and perirhinal cortex. There were no significant memory retrieval effects for scenes in the MTL. While there was a numerical trend towards subsequent memory effects for faces in the perirhinal cortex and scenes in the left posterior hippocampus, as well as a domain-general effect in the posterior parahippocampal gyrus, all other encoding effects could not be reliably labelled as domain-general or stimulus-specific. Confidence ratings collected at test were used to infer whether patterns of memory-related activity could be linked to recollection or familiarity (Aggleton & Brown, 1999; Yonelinas, 2002). The face-specific retrieval effect in the left anterior hippocampus followed a pattern that has been previously linked to recollection (Cohn et al., 2009; Daselaar et al., 2006; Yonelinas et al., 2005). For all other memory effects, both at retrieval and encoding, the pattern across confidence response categories was inconclusive; activity was greater for sure old, relative to miss, and although probably old was intermediate, it did not significantly differ from sure old or miss.

The strength of the claim that the findings in the previous experiment provide evidence for stimulus-specificity in the MTL is bolstered by the fact that (a) overall memory accuracy for faces and scenes was comparable, (b) there were no differences between familiarity estimates, and (c) recollection estimates were higher for the scenes. If memory accuracy was greater for faces than scenes, face-specific memory effects could reflect differences in how memorable one stimulus type was over another and/or disproportionate dependence on different processes that support accurate memory judgments. The stimulus-specific effects in the previous study,

therefore, provide some support for representational accounts, which suggest the MTL subregions process and store complex representations of different types of visual information (Graham et al., 2010; see also Saksida et al., 2010).

An alternative explanation of the findings from Experiment 1 comes from consideration of information-based theories of MTL function (BIC: Diana et al., 2007; see Section 1.5). It is possible that stimulus-specific memory deficits (Bird et al., 2007; Bird et al., 2008; Cipolotti et al., 2006; Taylor et al., 2007) and patterns of stimulus-specific memory-related effects arise because certain types of complex visual stimuli differentially depend upon item- versus contextually-based mnemonic information. This explanation is similar to a dual-process account, as item information processed by the perirhinal cortex supports familiarity-based recognition, whereas recollection is associated with the recovery of contextual information processed by the parahippocampal cortex and hippocampus. Informational accounts, however, also stipulate that the perirhinal cortex can support recollection of item feature details (Awipi & Davachi, 2008; Diana et al., 2010; Staresina & Davachi, 2006; 2008).

One way to determine whether patterns of stimulus-specific brain activity differentially reflect item or context processing, which was not possible in the previous experiment, is to separate memory for items and item details from the recollection of contextual details. This can be achieved using a source memory paradigm, providing the diagnostic source information comprises contextual information, rather than an item feature. Ranganath et al. (2004) investigated activity at the time of encoding in the perirhinal cortex and hippocampus based on subsequent memory for items versus contextual information (Fig. 3.1). Participants studied nouns presented in red or green. To ensure they remembered the associated colour they were instructed to indicate if the study item referred to an object that would fit into a shoebox (size condition) if presented in green or, if in red, whether the word referred to a living or non-living object (animacy condition). Following this, participants performed a recognition memory test where they had to make a two-stage memory judgement for each test item. First, using a 6-point confidence scale, they were required to indicate how confident they were that the test item was old or new. They were then asked for the colour the word was originally presented in. The first stage of

this judgement is not dissimilar from the procedure used in the previous study. The second, however, was specifically designed to assess context memory. Using this method, Ranganath et al. (2004) observed a parametric increase in memory-related activity based on subsequent recognition memory confidence in the perirhinal cortex, which did not vary according to the recovery of contextual information (see Section 1.4.4, Fig. 1.15). Activity in the hippocampus and posterior parahippocampal gyrus, however, predicted subsequent memory for the associated contextual details (see also Davachi et al., 2003; and for retrieving source details Cansino et al., 2002; Dobbins et al., 2003; Kahn et al., 2004).

In relation to the specific aims of this thesis, the data from Ranganath et al. (2004) offers little insight as to whether there would be dissociable hippocampal and perirhinal cortex contributions to item and context memory (respectively) for complex visual stimuli, such as objects and scenes. As it stands, no study has directly measured and compared neural activity relating to the recovery of contextual source details for different stimulus types. The aim of the current experiment was to accomplish this, adopting the design used by Ranganath et al. (2004), and employing objects and scenes as stimuli. Guided by the Ranganath paper, separate analyses were conducted to interrogate item and source memory effects in the MTL. In the first instance, whole-brain contrasts were performed to identify brain regions associated with (a) familiarity, as indicated by linear changes in activity based on increases in subsequent recognition confidence, (b) recollection, by observing differences between subsequent high confidence hits compared to medium confidence hits, and (c) successful encoding of contextual source details for objects and scenes (based on

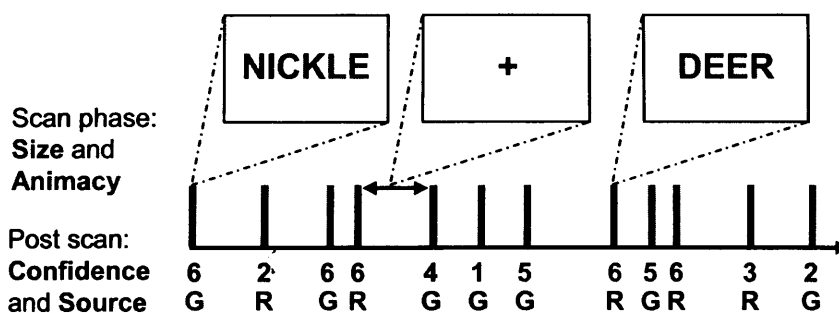


Figure 3.1: A schematic depiction of the scanned encoding phase from Ranganath et al. (2004). At test subjects made recognition confidence and source memory judgments for each test word, and fMRI results during encoding were analysed as a function of these measures.

analyses from Daselaar et al., 2006; Ranganath et al., 2004). Second, MTL functional ROIs for objects and scenes were identified in the hippocampus, parahippocampal gyrus and perirhinal cortex, and item confidence/source memory effects were investigated within these (as reported in the previous study). As this is an encoding study, there were no experimental trials available (e.g. correct rejections) with which to make unbiased fROIs. Functional ROIs, therefore, were created from a separate functional localiser task comprising objects and scenes, which was run for every subject in the scanning session.

Based on representational accounts of MTL function (see Section 1.7) and tentative findings from Experiment 1 (see also Awipi & Davachi, 2008), it is predicted that patterns of memory-related activity will be stimulus-specific in regions that show a greater response to objects or scenes (perirhinal cortex for objects, and hippocampus and parahippocampal gyrus for scenes). Moreover, separate item and source memory analyses should reveal stimulus-specific brain activity relating to item memory (familiarity) or source recollection. Alternatively, in terms of informational accounts, patterns of activity in MTL subregions will differentially reflect successful domain-general item or source memory encoding (perirhinal cortex for item memory, and hippocampus and parahippocampal gyrus for source memory). The same prediction holds for dual-process accounts.

Notably, instances of stimulus-specific MTL activity could still be accommodated by dual-process and informational accounts if there were significant differences between behavioural measures of recollection and familiarity, and/or overall item and source memory accuracy, for objects and scenes (e.g. a stimulus-specific source memory effect for scenes in the parahippocampal gyrus, coupled with greater source memory accuracy for scenes than objects or a pattern that reflects familiarity for objects in the perirhinal cortex and a higher familiarity estimate for objects). Without these behavioural differences, however, the presence of stimulus-specific memory effects would be difficult to reconcile with dual-process and informational accounts of MTL function.

3.2. *Materials and methods*

3.2.1. *Participants*

Twenty-four volunteers (11 females) took part. According to self-report, all were right-handed native-English speakers with normal or corrected to normal vision and no neurological and/or psychiatric disorders. The data from two participants (both male) were removed from the analyses due to poor behavioural performance; one participant had a level of item memory performance ($p(\text{hit})-p(\text{false alarm})$) for objects = 0.15) that was significantly poorer than the overall group ($z = -2.93$), and the other had source memory accuracy (0.51) that was below the threshold for inclusion (≥ 0.55 ; 0.50 equals chance). The mean age of the remaining 22 participants was 23.4 years (range = 19-30). All participants gave written informed consent prior to the experiment and were paid £10/hr for their participation. The experiment received ethical approval from the Cardiff University School of Psychology Ethics Committee.

3.2.2. *Materials*

Stimuli comprised a set of 397 black and white images of everyday objects from the Hemera Photo Objects database (Volumes I, II and III), 397 full colour images of buildings and landscapes (scenes), and two greyscale images of arrows, one pointing left and the other right, for the active-baseline task (Fig. 3.2). The scenes overlapped with the stimuli used in the previous study, with any scenes that contained distinctive and/or numerous objects removed. Additional scene stimuli were collected from the LabelMe Matlab toolbox (Russell, Torralba, Murphy & Freeman, 2008). Scenes were presented in colour, and objects black and white, in an attempt to match scene and object memory performance (following extensive piloting)⁷. Ten items from each set were used in a practice session, with the remaining items separated into 258 objects

⁷Similar dissociable MTL effects have been demonstrated in functional imaging and neuropsychological experiments that have used greyscale (Barens, Henson et al., 2010; Lee, Bandelow et al., 2006; Lee, Buckley et al., 2006; Lee, Buckley et al., 2005; Lee, Bussey et al., 2005) and full colour stimuli (Awipi & Davachi, 2008; Barens et al., 2005; Barens et al., 2007; Pihlajamaki et al., 2004). Moreover, as colour oddity is often used as a baseline in neuroimaging and human/animal lesion studies that investigated stimulus-specific processing within the MTL (Buckley et al., 2001; Devlin & Price, 2007; Lee, Buckley et al., 2005), differences in colour information are unlikely to explain the incidence of any stimulus-specific effects in the current experiment.

and 258 scenes presented at study and test, and 129 objects and 129 scenes presented at test only ('new' stimuli).

3.2.3. Tasks and procedure

The experiment was run using the same programme (E-prime), laptop, General Electric 3-T HDx MRI system and MR compatible equipment as described previously (see Section 2.2.3):

Participants were scanned at encoding only, and a surprise test phase was administered immediately after the scanning session (Fig. 3.2). The experiment consisted of 3 separate study runs, with an equal number of objects and scenes shown in each. In each scanned study run there were 86 novel object trials, 86 novel scene trials and 33 active-baseline trials. These objects and scenes were re-presented in the test phase, alongside unstudied objects and scenes, in three separate runs. No stimuli were encountered in more than one study or test run, and the presentation order of object/scene and baseline trials at study, as well as test, was randomised for each participant.

The event-related fMRI paradigm for the current experiment was designed to improve signal-to-noise (relative to Experiment 1) by means of increasing the stimulus presentation time and ISI, including active-baseline trials and scanning more participants. Study items were presented in the centre of the screen against a black background for 3000ms, separated by a jittered inter-stimulus interval (ISI: 500-3500ms, mean = 2000ms), during which the screen remained black. During the study phase participants were either asked if the displayed object/scene was common or uncommon, or pleasant/unpleasant, with the prompt for the judgement appearing beneath each study item. Within a given run, half of the objects and scenes were presented in the common/uncommon task, and half in the pleasant/unpleasant task (43:43 per run) in a random order. Throughout each study run a baseline task was intermixed with the object/scene trials. During baseline trials an arrow was presented and participants were prompted to indicate whether the arrow pointed to the left or right. Participants responded using their right index and middle fingers to indicate right/common/pleasant and left/uncommon/unpleasant, respectively. In the current experiment the (a) old/new status of the stimulus materials, (b) encoding task items

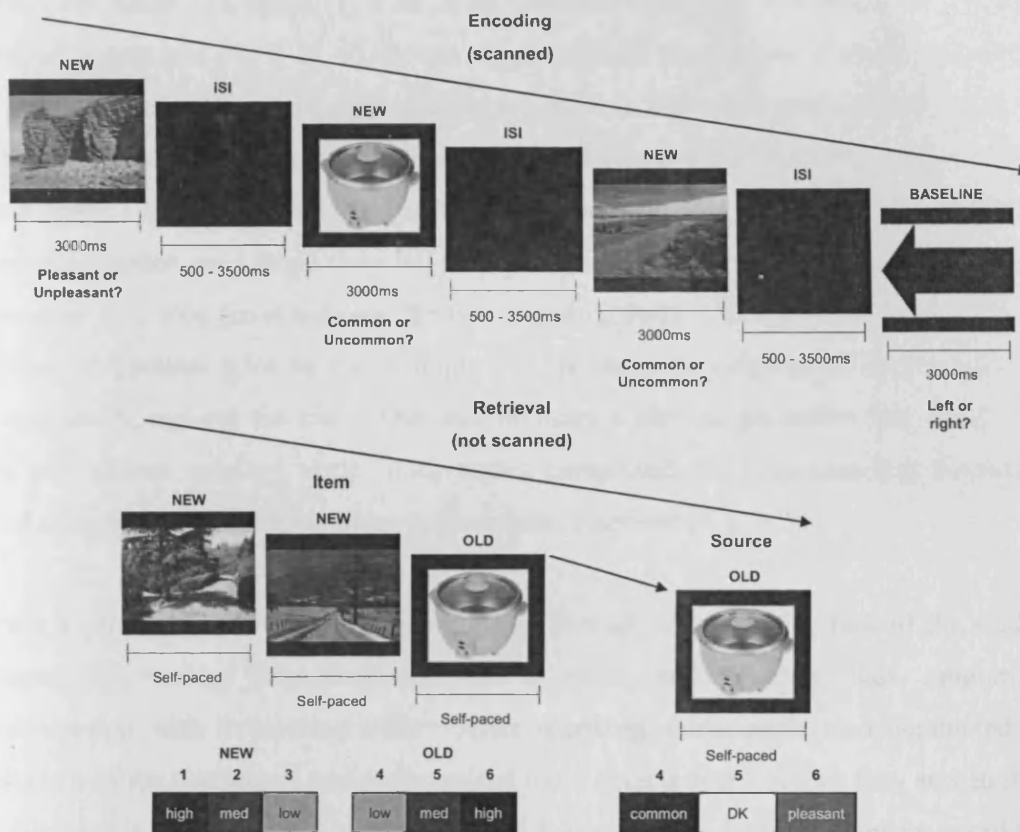


Figure 3.2: Stimuli and procedure. At encoding participants made pleasant/unpleasant or common/uncommon judgements about novel objects and scenes. At retrieval participants were presented with previously studied and new objects and scenes and made memory judgements to stimuli using a 6-point scale. If participants made an old judgement they then had to indicate which of the two tasks the item was originally presented in (source memory).

were presented in, and (c) finger used to signal common/pleasant and uncommon/unpleasant were fully counterbalanced across participants.

Following the study phase (Fig. 3.2), participants were presented with a surprise self-paced recognition memory test, which comprised studied and new items split across three runs (516 old: 258 new; $\frac{1}{2}$ objects: $\frac{1}{2}$ scenes). For each test item participants were prompted to indicate, using a 6-point scale, their confidence that the item was studied or new (1: high confidence new, 2: medium confidence new, 3: low confidence new, 4: low confidence old, 5: medium confidence old, 6: high confidence old). As with previous experiments where a 6-point confidence scale was used, participants were encouraged to make use of the entire scale (Yonelinas et al., 2005). Following this, if the participant responded new (1, 2 or 3), they were instructed to

press the same key again (1, 2 or 3) to continue on to the next test trial. If the response was old (4, 5 or 6), however, participants then made a source memory judgement, indicating if the item initially appeared in the common/uncommon (button 4) or the pleasant/unpleasant task (button 6), or if they did not remember the encoding task ('don't know': button 5). Participants were instructed to use the 'don't know' response option only when they felt they had no mnemonic information on which to make an educated guess between the two encoding tasks. Test items were presented for a set 2500ms prior to the prompts for the memory judgements, and remained onscreen throughout the trial. The item memory scale was presented first, followed by the source memory scale; both scales comprised the corresponding response keys/numbers and disappeared upon participant response (Fig. 3.2).

Prior to entering the MRI suite, participants carried out a practice task of the study phase, where they were presented with 5 object and 5 scene trials, randomly interspersed with 4 baseline trials. After scanning, participants also conducted a practice of the test phase, which comprised the 5 objects and 5 scenes they saw in the study practice, along with 5 new objects and 5 new scenes. Participants were asked to explain the reason for each of their responses during the test practice, to ensure they understood the task and the use of the confidence scale.

3.2.4. Functional localiser task and procedure

To create unbiased fROIs, the scanning protocol also included a 1-back functional localiser task (see Fig. 3.3) that comprised mini blocks containing scenes, objects and scrambled images of objects (scrambles), which was run using Presentation (Neurobehavioral Systems, Albany, California, USA). The design for this was based upon previously employed functional localiser tasks, in which contrasts across conditions are used to locate stimulus-specific areas of the extrastriate cortex (Downing et al., 2006; Epstein et al., 2006; Mundy et al., 2009; Peelen & Downing, 2005). The functional localiser consisted of 3 groups of 12-16s blocks, with each group separated by a 16s fixation only block. Within each group of 12, there were 4 object (OB), 4 scene (SN), and 4 scramble (SR) blocks. For group one blocks 1, 4, 7, 10 were objects, 2, 5, 8, 11 were scenes and 3, 6, 9, 12 were scrambles; for group two blocks 1, 4, 7, 10 were scrambles, 2, 5, 8, 11 were scenes and 3, 6, 9, 12 were objects; and for group three blocks 1, 4, 7, 10 were scenes, 2, 5, 8, 11 were objects and 3, 6, 9,

12 were scrambles. Within every 16s block, 16 pictures were presented for 300ms, each with a 450ms ISI. To ensure attention was paid to each stimulus, participants indicated when the same stimulus appeared twice in succession (1-back task). The experiment was programmed so that the presentation of stimuli within blocks was random, but consecutive repeats of stimuli had to occur at least twice in a block. Responses were made with the right index finger.

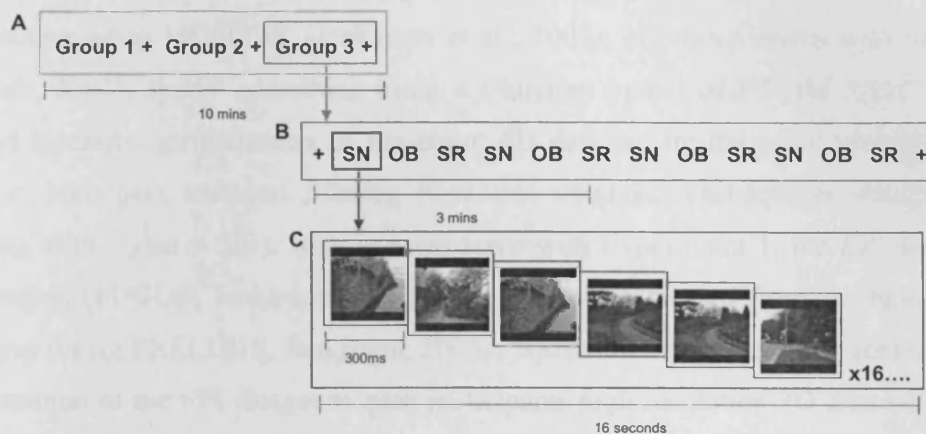


Figure 3.3: The functional localiser 1-back task. (A) There were 3 3 min groups separated by a 16s crosshair. (B) Within each group there were 4 16s SN, FL and SR blocks. (C) Each block comprised 16 stimuli, present for 300ms (ISI: 450ms). Participants responded to consecutive repetitions of stimuli. Abbreviations: (SN) scenes, (OB) objects, (SR) scrambles.

3.2.5. Scanning parameters

Within subjects, the same scanning protocol was used in all sessions. An identical EPI sequence was adopted for the subsequent memory task and the 1-back functional localiser. Forty-five slices were collected per image volume covering the whole-brain. Scanning parameters for the EPI sequence were identical to the previous experiment (see Section 2.2.4) with the exception of the TR, which was increased from 2750ms to 3000ms to allow for longer EPI runs (19 mins). To correct for geometrical distortions in the EPI data due to magnetic-field in-homogeneity, a map of the magnetic field was produced from two 3D SPGR images acquired during each scanning session. The SPGR acquisitions were prescribed based on the same slice orientation as the EPI data to be unwarped. Anatomical images were acquired using a standard T1-weighted sequence comprising 178 axial slices (3D FSPGR). As with

the EPI sequences, scanning parameters for the SPGR and FSPGR acquisition mirrored those from Experiment 1 (see Section 2.2.4).

3.2.6. *fMRI data pre-processing*

The same pre-processing steps were carried out on the current data set as Experiment 1 (see Section 2.2.6) using FEAT (FMRI Expert Analysis Tool) Version 5.63, in FSL (FMRIB Software Library, www.fmrib.ox.ac.uk/fsl). These included motion correction using MCFLIRT (Jenkinson et al., 2002); non-brain removal using BET (Smith, 2002); spatial smoothing using a Gaussian kernel of FWHM 5mm; mean-based intensity normalisation of the entire 4D data set by the same multiplicative factor; high pass temporal filtering (Gaussian-weighted least-squares straight line fitting, with $\sigma = 50$ s). Also in accordance with Experiment 1, the EPI data was unwarped (FUGUE, Jenkinson, 2003) using fieldmaps created from the two SPGR images (using PRELUDE, Jenkinson, 2003). Spatial normalisation was achieved via registration of the EPI images to each participants high resolution 3D anatomical T1 scans, and then to a standard Montreal Neurological Institute (MNI-152) template image, using FLIRT (Jenkinson et al., 2002; Jenkinson & Smith, 2001).

3.3. *Data analysis*

3.3.1. *Behavioural receiver operating characteristic (ROC) analysis*

ROC curves for scenes and objects were estimated using a sums-of-squares search algorithm (Yonelinas et al., 1998), which also derived behavioural estimates for recollection and familiarity (see Section 1.4.1.3 and 2.3.1).

3.3.2. *Whole-brain fMRI data analysis*

After pre-processing the three object/scene memory encoding runs for each fMRI time series for each participant, the data were submitted to a (random effects) general linear model, with one predictor that was convolved with a standard model of the haemodynamic response function (HRF) for each event-type. The encoding trials were analysed both as a function of subsequent recognition memory confidence (item memory) and source memory performance (source memory) for both stimulus types. Separate regressors were, therefore, modelled for each event-type, for objects and scenes, in the item and source memory analysis, alongside a regressor for the active-

baseline trials (baseline). For the item memory analysis, there were 5 regressors based on subsequent recognition memory confidence for each stimulus type: (a) subsequent high confidence hit (s6), (b) subsequent medium confidence hit (s5), (c) subsequent low confidence hit (s4), (d) subsequent low confidence miss (s3) and (e) subsequent high + medium confidence miss (s1+2)⁸.

In the source memory analysis there were 4 source memory regressors for each stimulus type (objects and scenes). These were: (a) subsequent miss (sMM) - items labelled as new, (b) subsequent hit-miss (sHM) - items identified as old, but for which the source judgement was incorrect, (c) subsequent hit-hit (sHH) - items identified as old for which the source memory judgement was correct and (d) subsequent hit-don't know (sHDK) - study items subsequently identified as old that received a don't know response for the source judgement. Due to the conservative use of the don't know response option, sHDK trial numbers were low (see Table 3.2) and will not be discussed further.

Parameter estimates relating the height of the HRF response to each regressor were calculated on a voxel by voxel basis, via a multiple linear regression of the response time-course, to create one beta image for each regressor per run, per participant. Individual runs were then concatenated for each participant in a fixed effects analysis using FEAT. Resulting parameter estimate images were then combined in a higher-level (group) FLAME analysis (FMRIB's Local Analysis of Mixed Effects; Beckmann et al., 2003; Woolrich et al., 2004). To examine the relationship between encoding activity and graded increases in subsequent item familiarity for objects and scenes, a linear contrast was performed separately for each stimulus type using the recognition memory confidence regressors (s5 = +3, s4 = +1, s3 = -1, s1+2 = -3; Ranganath et al., 2004). Brain regions sensitive to subsequent recollection were investigated by performing a contrast between high confidence hit and medium confidence hit, for both stimulus types (s6 > s5). To identify regions that were associated with successful source/context memory encoding for objects and scenes,

⁸ High and medium confidence miss were combined to form a single regressor due to low trial numbers for the former.

subsequent hit-hit objects/scenes were contrasted with subsequent hit-miss objects/scenes (sHH > sHM). For the above contrasts, FEAT group (gaussianised) t-statistics were then converted to z-statistics and thresholded using a voxel significance level of $p < 0.001$, uncorrected for multiple comparisons. Only significant activations involving contiguous clusters of at least 9 voxels are reported. These probability and extent thresholds are equivalent to a mapwise false-positive rate for the MTL (encompassing the hippocampus, parahippocampal gyrus and perirhinal cortex) of $p < 0.05$ (estimated using the Monte Carlo procedure implemented in the AlphaSim program in AFNI). Co-ordinates (x, y, z) of significant effects are reported in MNI space.

3.3.3. *Functional region of interest (fROI) fMRI analysis*

Based on a priori predictions for memory effects in the MTL, functional regions of interest (fROIs) were created by performing group-level contrasts between the object and scene blocks (object > scene; scene > object) from the orthogonal 1-back functional localiser task. This contrast was undertaken within three anatomically-defined MTL ROIs; perirhinal cortex, hippocampus and parahippocampal gyrus (see Section 2.3.3; Fig. 2.3). The resulting FEAT (gaussianised) t-statistics were converted to z-statistics and a liberal (uncorrected) voxel threshold of $p < 0.025$ was applied to the data to ensure all stimulus-specific voxels were identified within each anatomical region. Data are reported for functional ROIs with ten or more activated voxels (Fig. 3.4). Voxels that processed objects over scenes were identified in the perirhinal cortex only (left peak: -32, -2, -40, $z = 3.88$, 190 voxels; right peak: 32, -10, -40, $z = 3.99$, 131 voxels). For the scenes over objects contrast, significant functional ROIs were identified in the hippocampus (left peak: -22, -20, -18, $z = 4.81$, 284 voxels; right peak: 24, -12, -22, $z = 4.02$, 255 voxels) and parahippocampal gyrus (left peak: -32, -42, -8, $z = 5.58$, 503 voxels; right peak: 18, -38, -10, $z = 5.37$, 581 voxels).

Separate analyses for the subsequent item and source memory effects were conducted within each of the fROIs. Each of the item and source memory regressors was contrasted with the active-baseline regressor. Using Featquery from the FSL toolkit, mean parameter estimate values relative to baseline were extracted for the 5 item memory confidence object and scene regressors (s1+2 to s6), and the 3 object and scene source memory regressors (sHH, sHM, sMM), within each of the object- and

scene-sensitive MTL fROIs. Parameter estimate values were scaled by the height of the effective regressor and mean voxel intensity in order to convert them into percent signal change.

For each fROI, to identify linear increases in brain activity according to subsequent recognition memory confidence, the individual percent signal change values from the 10 item memory confidence regressors (5 per stimulus type) were entered into a $2 \times 2 \times 5$ ANOVA (SPSS) with factors of 'hemisphere' (right vs. left), 'stimuli' (objects vs. scenes) and 'memory' (s6, s5, s4, s3, s1+2). Even in the absence of significant stimuli*memory interactions, due to a priori predictions, item memory effects were considered separately for each stimuli within each fROI (and hemisphere where necessary) by conducting 2 one-way ANOVAs, with 5 levels of memory (s6, s5, s4, s3, s1+2). As well as interrogating main effects of memory within stimulus category, these one-way ANOVAs also indicated the presence of polynomial trends (linear, quadratic and cubic).

For the source memory analysis, percent signal change values for the 6 source memory regressors from each fROI were entered into a $2 \times 2 \times 3$ ANOVA, with factors of 'hemisphere' (right vs. left), 'stimuli' (objects vs. scenes) and 'memory' (sHH, sHM and sMM). Memory effects within each fROI were also considered separately for each stimulus category in one way ANOVAs.

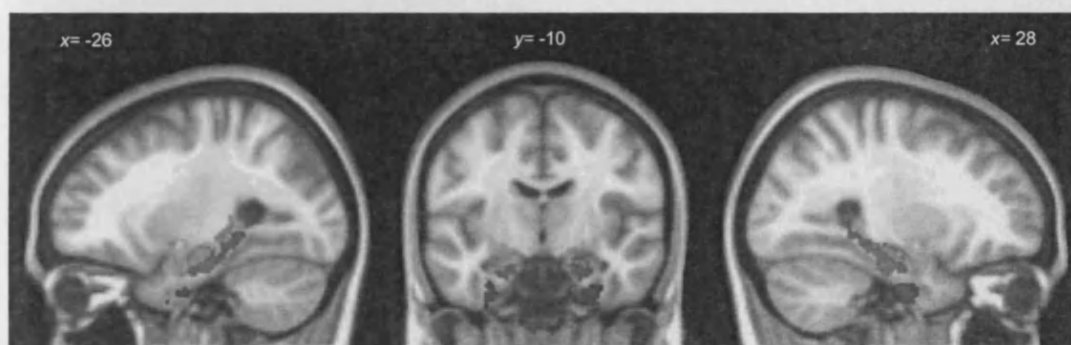


Figure 3.4: Left sagittal (left), coronal (middle) and right sagittal (right) views of functional ROIs located within the hippocampus (green), parahippocampal gyrus (pink) and perirhinal cortex (blue) derived from the object > scene (perirhinal cortex) and scene > object (hippocampus and parahippocampal gyrus) contrasts from the functional localiser.

3.4. Behavioural results

Overall old/new discrimination, as measured by $p(\text{hit}) - p(\text{false alarm})$, was significantly above chance for the objects and scenes (objects: 0.55, SE = 0.02; $t(21) = 25.82$, $p < 0.01$; scenes: 0.44, SE = 0.03; $t(21) = 17.22$, $p < 0.01$). Discrimination accuracy was reliably higher for objects than scenes ($t(21) = 3.98$, $p < 0.01$). ROCs for objects and scenes are displayed in Fig. 3.5. This shows that compared to the ROC for scenes, the ROC for the objects was more asymmetric with a higher y-intercept. The recollection estimate, derived using Yonelinas et al. (1998) sum-of-squares search algorithm, was greater for objects than scenes (objects: 0.42, SE = 0.04; scenes: 0.26, SE = 0.03; $t(21) = 6.69$, $p < 0.01$), whereas the familiarity estimates for objects and scenes did not reliably differ (objects: 1.01, SE = 0.07; scenes: 0.89, SE = 0.06; $t(21) = 1.77$). Notably, there were also behavioural differences in Experiment 1, but there the recollection estimate for *scenes* was greater than the estimate for faces (scenes: 0.48, SE = 0.04; faces: 0.33, SE = 0.05; $t(17) = 2.55$, $p < 0.05$).

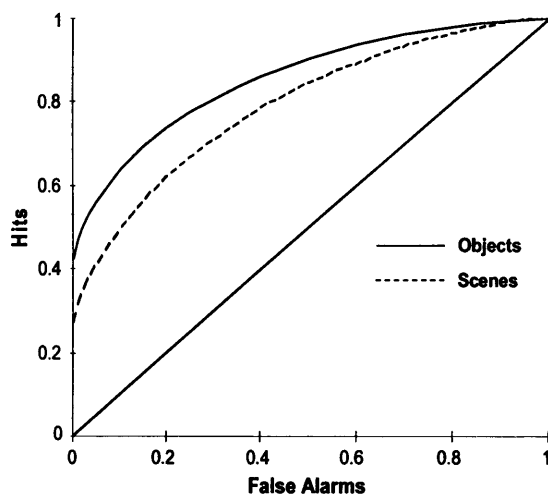


Figure 3.5: Average receiver operating characteristics (ROCs) for objects and scenes.

Reaction times at encoding were faster for scenes than objects (objects: 1696, SE = 50; scenes: 1524, SE = 52; $t(21) = 9.89$, $p < 0.01$). For test items, there was no difference between reaction times to objects and scenes (objects: 1404, SE = 186; scenes: 1365, SE = 191; $t(21) = 0.36$). The mean response proportions and reaction times for each type of memory confidence judgement to old and new test items are

Table 3.1: Mean proportion of responses and reaction times across the confidence scale for old and new objects and scenes⁹

Objects	Recognition judgements					
	1	2	3	4	5	6
<i>Proportion of responses</i>						
Old	0.04 (0.01)	0.07 (0.01)	0.10 (0.01)	0.14 (0.02)	0.23 (0.02)	0.42 (0.04)
New	0.33 (0.04)	0.23 (0.02)	0.19 (0.02)	0.11 (0.01)	0.07 (0.01)	0.07 (0.01)
<i>Mean reaction time (ms)</i>						
Old	786 (110)	1081 (152)	1609 (373)	1686 (303)	1433 (221)	920 (85)
New	678 (62)	1249 (217)	1465 (188)	2175 (462)	1929 (438)	1865 (530)
Scenes	Recognition judgements					
	1	2	3	4	5	6
<i>Proportion of responses</i>						
Old	0.07 (0.02)	0.13 (0.01)	0.17 (0.02)	0.18 (0.01)	0.18 (0.02)	0.26 (0.03)
New	0.25 (0.04)	0.32 (0.02)	0.25 (0.02)	0.13 (0.02)	0.05 (0.01)	0.01 (0.00)
<i>Mean reaction time (ms)</i>						
Old	912 (133)*	1152 (175)	1677 (260)	2079 (336)	1631 (217)	1097 (103)
New	885 (106)	1101 (177)	1334 (193)	2156 (438)	2167 (605)	1205 (233) ⁺

⁹The values shown are across-participant means with standard error in brackets. As some participants did not make all types of response to old, as well as new items, mean reaction times for * and ⁺ are based on 18 and 21 participants, respectively. Abbreviations: (1) high confidence new, (2) medium confidence new, (3) low confidence new, (4) low confidence old, (5) medium confidence old, (6) high confidence old.

displayed in Table 3.1. Similar, to Experiment 1, the proportion of responses for old and new items increased monotonically with confidence, and responses were quicker for high confidence (1 or 6) judgements compared to low confidence judgements (3 or 4) for both stimulus types (Ratcliff & Murdock, 1976; Ranganath et al., 2004; Yonelinas et al., 2005).

Overall source memory responses for objects and scenes are displayed in Table 3.2. Source memory accuracy, which was calculated by dividing the number of source hits (HH) by the number of overall hits with the don't know (HDK) responses removed ($p(\text{HH}) / (p(\text{HH}) + p(\text{HM}))$), was above chance for both stimuli (objects: 0.71 SE = 0.01, $t(21) = 15.65$, $p < 0.01$; scenes: 0.71, SE = 0.01, $t(21) = 11.52$, $p < 0.01$) and these did not reliably differ from each other ($t(21) = 0.39$). Reaction times for HH, HM and HDK responses were entered into a 2*3 ANOVA, with factors of 'stimuli' (object vs. scene) and 'source response' (HH, HM, HDK), which revealed no significant differences.

Table 3.2: Mean proportions and reaction times of source responses for objects and scenes that attracted a correct old judgement¹⁰

Objects	Source judgement		
	HH	HM	HDK
<i>Proportion of responses</i>	0.65 (0.02)	0.26 (0.02)	0.09 (0.03)
<i>Mean reaction time (ms)</i>	1446 (153)	1676 (192)	1608 (328)*
Scenes	Source judgement		
	HH	HM	HDK
<i>Proportion of responses</i>	0.62 (0.03)	0.26 (0.02)	0.11 (0.03)
<i>Mean reaction time (ms)</i>	1572 (209)	1615 (199)	1523 (194) ⁺

¹⁰ The values shown are across-participant means with standard error in brackets. Not all participants pressed the 'don't know' response key for objects and scenes, mean reaction times for * and ⁺ are based on 21 and 19 participants, respectively

3.5. *Functional imaging results*

3.5.1. *Whole-brain analysis*

For the first stage of fMRI analysis contrasts were performed between subsequent item and source memory regressors to identify regions, at the whole-brain level, involved in memory processing for objects and scenes. In keeping with the Ranganath et al. (2004) study, brain regions associated with familiarity were investigated via linear contrasts across recognition confidence regressors ($s5 = +3$, $s4 = +1$, $s3 = -1$, $s1+2 = -3$). To identify brain regions relating to source recollection, contrasts were performed between remembered items that elicited a correct source judgement and those for which the source judgement was incorrect ($sHH > sHM$). As there are previous studies where differences in recognition memory confidence judgements have been employed to index recollection (Yonelinas et al., 2005; Daselaar et al., 2006), there was also a contrast between items later identified with high confidence, compared to items subsequently remembered with medium confidence ($s6 > s5$).

Results from these whole-brain contrasts are displayed in Figs. 3.6 and 3.7, and summarised in Tables 3.3-3.8. There were significant memory effects in a number of frontal, parietal and temporal brain regions. Replicating Ranganath et al. (2004), there were patterns of memory-related activity in the superior frontal gyrus, inferior frontal gyrus, superior parietal lobule, precentral gyrus, lingual gyrus, fusiform gyrus, inferior temporal gyrus, and precuneus. Effects were detected in the parahippocampal place area (PPA) for the linear item (left only) and source (bilaterally) memory contrasts for the scenes (established using the mean Talairach coordinates [-23, -44, 9 and 27, -40, -7] from Peelen & Downing, 2005, converted to MNI space [-26, -42, -8 and 31, -37, -5]; see also Downing et al., 2006; Epstein et al., 2006; Epstein & Kanwisher, 1998; Epstein & Ward, 2010; Park & Chun, 2009). There was also significant activity in the left retrosplenial cortex for the scene linear item memory contrast, which, like the PPA, is thought to be highly specialised for spatial processing (Park & Chun, 2009), as well as being involved in memory for scenes at retrieval (Montaldi et al., 2006). Both objects and scenes activated a variety of occipitotemporal/extrastriate brain regions that form the visual processing streams (fusiform cortex and occipital fusiform cortex, Haxby et al., 1991), as well as the

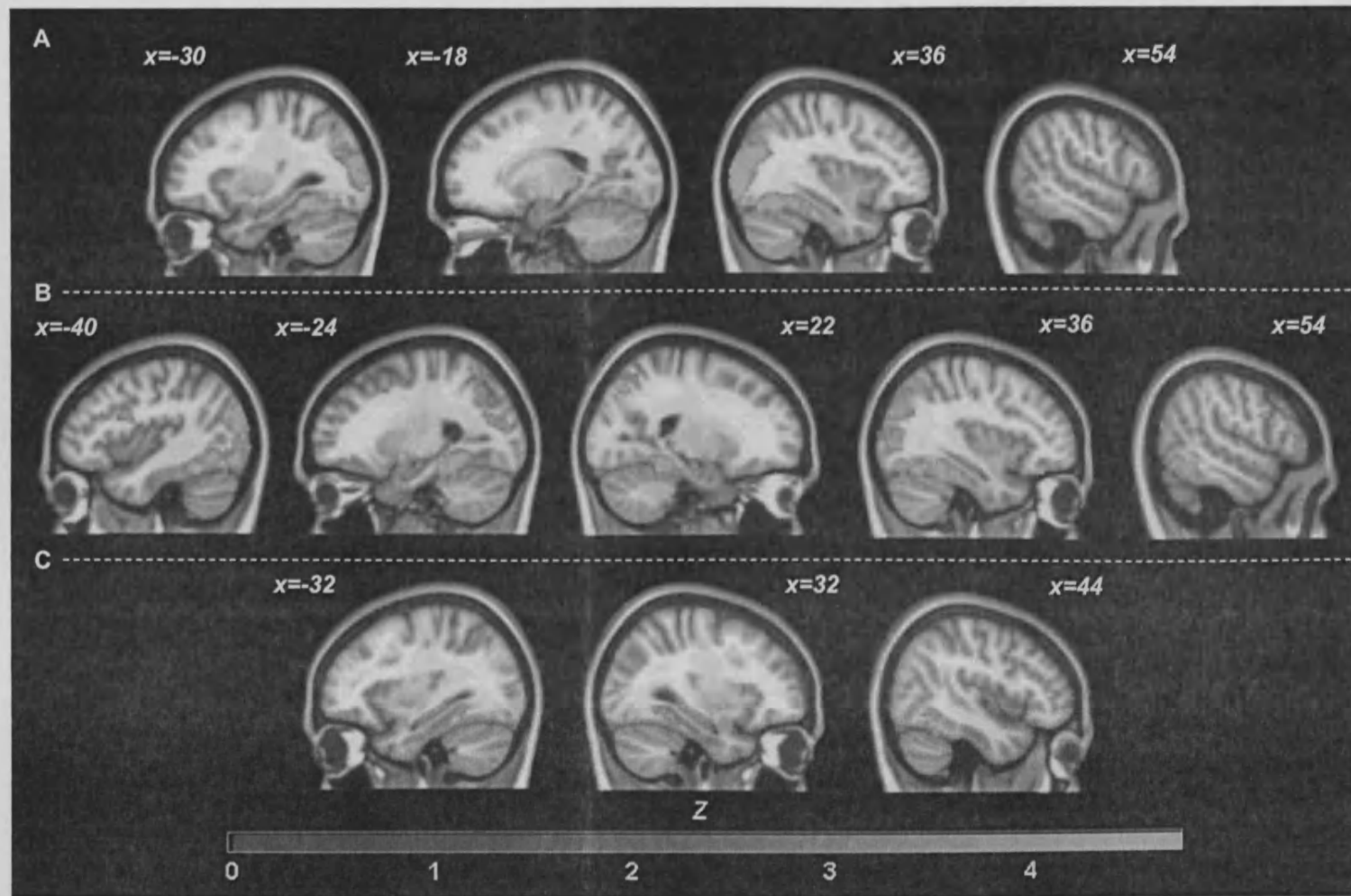


Figure 3.6: Significant memory encoding activity for scenes from the (A) linear contrast across recognition memory confidence regressors, (B) high confidence hit > medium confidence hit contrast, and (C) subsequent hit-hit > hit-miss contrast. Images are overlaid onto a MNI-152 T1 2mm standard brain.

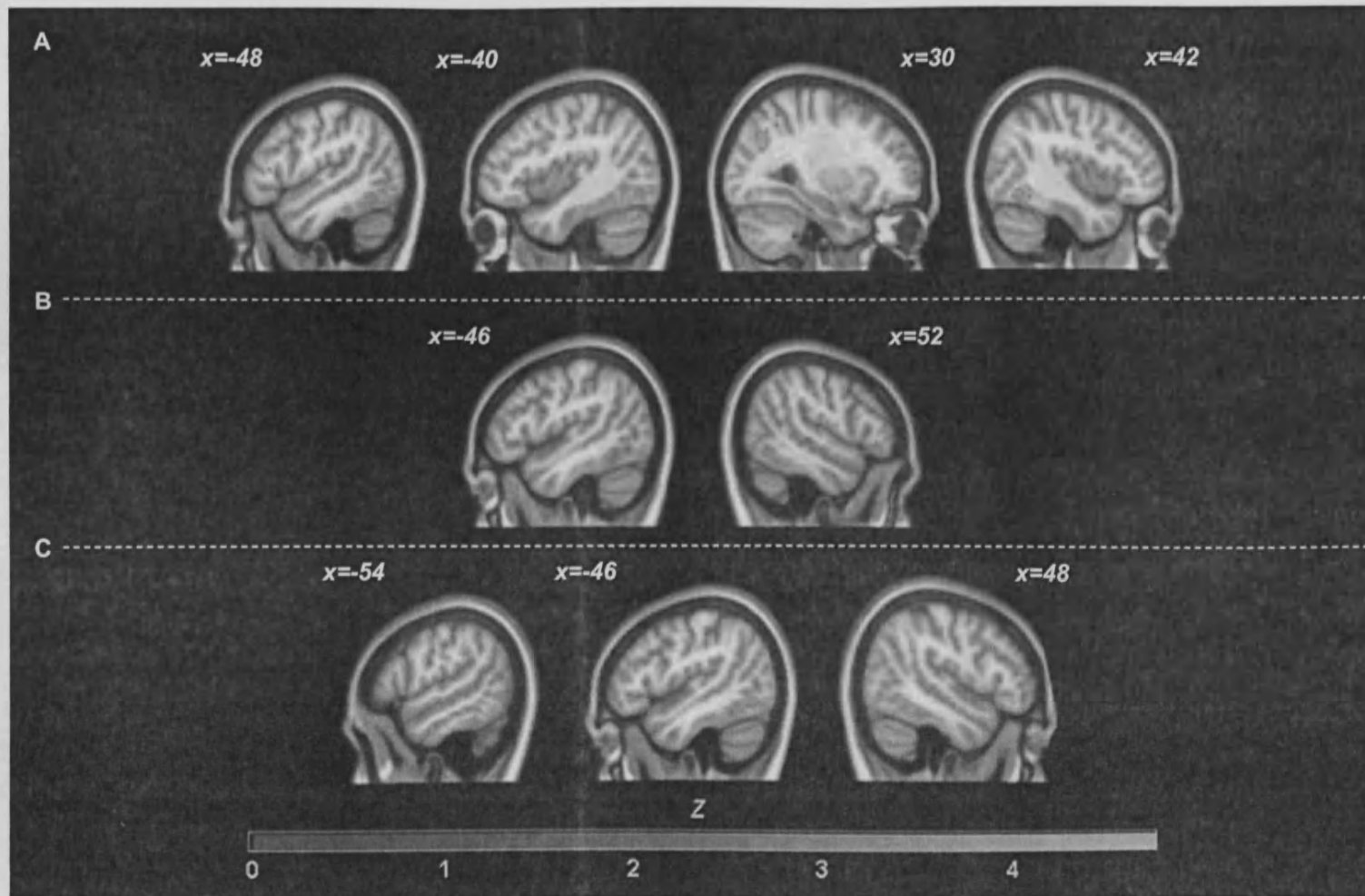


Figure 3.7: Significant memory encoding activity for objects from the (A) linear contrast across recognition memory confidence regressors, (B) high confidence hit > medium confidence hit contrast, and (C) subsequent hit-hit > hit-miss contrast. Images are overlaid onto a MNI-152 T1 2mm standard brain.

inferior aspect of the lateral occipital cortex (LOC), which, in contrast to PPA, is thought to be specialised for object processing (Kanwisher et al., 1996; Kanwisher, Woods et al., 1997; Malach et al., 1995). As with Experiment 1, due the specific focus of this thesis, only significant activations in the MTL are discussed below.

Table 3.3: Local maxima with regions according to the Harvard-Oxford sub-cortical structural atlas observed for the linear contrast across subsequent memory confidence for scenes ($p < 0.001$, cluster > 9 voxels).

Region				
	Z	x	y	z
<i>Right frontal pole</i>	3.35	54	36	14
<i>Right precentral gyrus</i>	3.65	44	8	26
<i>Left cuneal cortex</i>	3.89	-20	-76	24
<i>Left retrosplenial cortex</i>	3.42	-18	-68	14
<i>Left precuneus cortex</i>	3.29	-16	-62	10
<i>Right precuneus cortex</i>	4.22	16	-56	10
<i>Left occipital pole</i>	4.09	-34	-92	-2
<i>Right occipital pole</i>	5.59	36	-92	6
<i>Left lateral occipital cortex, superior division</i>	3.96	-28	-72	28
<i>Right lateral occipital cortex, superior division</i>	5.15	34	-80	18
<i>Left lateral occipital cortex, inferior division</i>	4.49	-30	-90	6
<i>Right lateral occipital cortex, inferior division</i>	4.62	36	-88	-8
<i>Left occipital fusiform gyrus</i>	3.28	-30	-80	-18
<i>Right occipital fusiform gyrus</i>	5.18	32	-64	-12
<i>Left temporal occipital fusiform cortex (PPA)</i>	4.73	-30	-46	-14
<i>Right temporal occipital fusiform cortex</i>	4.87	32	-58	-16
<i>Right inferior temporal gyrus, temporooccipital part</i>	4.80	48	-60	-12
<i>Right temporal fusiform cortex, posterior division</i>	4.53	28	-36	-20

Table 3.4: Local maxima with regions according to the Harvard-Oxford sub-cortical structural atlas observed for the subsequent high confidence hit > medium confidence hit contrast for scenes ($p < 0.001$, cluster > 9 voxels).

Region				
	Z	x	y	z
<i>Right frontal pole</i>	3.39	54	40	4
<i>Left superior frontal gyrus</i>	3.42	-22	10	42
<i>Left middle frontal gyrus</i>	3.23	-28	6	46
<i>Right inferior frontal gyrus, pars triangularis</i>	4.23	54	32	14
<i>Left frontal orbital cortex</i>	4.15	-44	32	-18
<i>Left precentral gyrus</i>	5.02	-46	6	26
<i>Right precuneus cortex</i>	3.66	24	-58	8
<i>Right cingulate gyrus, posterior division</i>	3.35	12	-48	2
<i>Right occipital pole</i>	3.88	28	-96	8
<i>Left lateral occipital cortex, superior division</i>	5.52	-42	-84	22
<i>Right lateral occipital cortex, superior division</i>	4.96	24	-76	48
<i>Right lateral occipital cortex, inferior division</i>	5.25	42	-68	-14
<i>Left occipital fusiform gyrus</i>	5.14	-36	-78	-12
<i>Left temporal occipital fusiform cortex</i>	5.23	-42	-60	-14
<i>Right temporal occipital fusiform cortex</i>	5.36	44	-58	-16
<i>Left temporal fusiform cortex, posterior division</i>	5.31	-28	-38	-16
<i>Right inferior temporal gyrus, temporooccipital part</i>	5.18	56	-54	-14
<i>Right lingual gyrus</i>	5.02	26	-38	-12
<i>Right amygdala</i>	3.78	32	-4	-20
<i>Left hippocampus</i>	3.21	-24	-20	-12
<i>Right hippocampus</i>	3.68	22	-14	-24

Table 3.5: Local maxima with regions according to the Harvard-Oxford sub-cortical structural atlas observed for the subsequent hit-hit > hit-miss contrast for scenes ($p < 0.001$, cluster > 9 voxels).

Region				
	Z	x	y	z
<i>Right lateral occipital cortex, superior division</i>	3.35	40	-86	12
<i>Left lateral occipital cortex, inferior division</i>	3.41	-30	-88	6
<i>Right lateral occipital cortex, inferior division</i>	3.63	48	-62	-10
<i>Left temporal occipital fusiform cortex (PPA)</i>	3.64	-34	-46	-12
<i>Right temporal occipital fusiform cortex (PPA)</i>	3.81	30	-48	-10
<i>Left temporal fusiform cortex, posterior division</i>	3.37	-32	-36	-18
<i>Right temporal fusiform cortex, posterior division</i>	3.54	32	-38	-22

Table 3.6: Local maxima with regions according to the Harvard-Oxford sub-cortical structural atlas observed for the linear contrast across subsequent memory confidence for objects ($p < 0.001$, cluster > 9 voxels).

Region				
	Z	x	y	z
<i>Right frontal pole</i>	3.87	30	38	-20
<i>Left inferior frontal gyrus, pars triangularis</i>	3.50	-50	28	10
<i>Right superior parietal lobule</i>	3.55	28	-56	54
<i>Right precentral gyrus</i>	3.56	44	6	26
<i>Left lateral occipital cortex, superior division</i>	3.37	-34	-86	8
<i>Right lateral occipital cortex, superior division</i>	4.19	32	-68	28
<i>Left lateral occipital cortex, inferior division</i>	4.26	-42	-68	-10
<i>Right lateral occipital cortex, inferior division</i>	4.01	50	-72	-6
<i>Left temporal occipital fusiform cortex</i>	4.23	-42	-62	-12
<i>Right temporal occipital fusiform cortex</i>	3.89	42	-56	-18
<i>Right temporal fusiform cortex, posterior division</i>	3.65	26	-38	-22
<i>Right inferior temporal gyrus, temporooccipital part</i>	3.87	44	-60	-10

Table 3.7: Local maxima with regions according to the Harvard-Oxford sub-cortical structural atlas observed for the subsequent high confidence hit $>$ medium confidence hit contrast for objects ($p < 0.001$, cluster > 9 voxels).

Region				
	Z	x	y	z
<i>Left frontal pole</i>	3.64	-50	40	0
<i>Right frontal pole</i>	3.34	52	42	6
<i>Left inferior frontal gyrus, pars triangularis</i>	3.17	-52	32	8
<i>Left inferior temporal gyrus, temporooccipital part</i>	3.61	48	-60	-12

Table 3.8: Local maxima with regions according to the Harvard-Oxford sub-cortical structural atlas observed for the subsequent hit-hit $>$ hit-miss contrast for objects ($p < 0.001$, cluster > 9 voxels).

Region				
	Z	x	y	z
<i>Left lateral occipital cortex, inferior division</i>	3.69	-46	-68	-8
<i>Right lateral occipital cortex, inferior division</i>	3.33	48	-62	-10
<i>Left inferior temporal gyrus, temporooccipital part</i>	3.46	-54	-46	-22

3.5.1.1. MTL effects

There was a significant cluster in the left and right hippocampus for the subsequent high confidence scene hit > subsequent medium confidence scene hit contrast (Table 3.4, Fig. 3.6). For all of the other whole-brain contrasts no significant effects were detected in the MTL. To investigate this hippocampal activation further, ROI masks (left and right) were created based on significant voxels, and values for percent signal change were extracted for the 5 levels of item recognition memory confidence for both objects and scenes (Fig. 3.8). Percent signal change values for each level of item memory confidence (contrasted with baseline) were entered in a 2*5 ANOVA (2 levels of 'stimuli'; and 5 levels of 'memory').

In the left hippocampus (Fig. 3.8A) there was a significant main effect of stimuli ($F(1,21) = 7.12, p < 0.05$) and a stimulus*memory interaction ($F(4,84) = 2.96, p < 0.05$). In follow-up tests there was a main effect of memory for scenes ($F(1,21) = 4.10, p < 0.01$), but not objects ($F(1,21) = 0.01$). The former was accompanied by reliable linear ($F(1,21) = 9.06, p < 0.01$) and quadratic ($F(1,21) = 4.72, p < 0.05$) trends, and planned pairwise comparisons revealed greater activity for high confidence scene hit (s6) relative to all other levels of item memory response (s6 > s5: $t(21) = 2.32, p < 0.05$; s6 > s4: $t(21) = 2.84, p < 0.01$; s6 > s3: $t(21) = 2.50, p < 0.05$; s6 > s1+2: $t(21) = 2.94, p < 0.01$). No other planned pairwise comparisons involving scenes were significant within this region.

In the right hippocampus (Fig. 3.8.B) there was a significant main effect of stimuli ($F(1,21) = 47.45, p < 0.01$), a main effect of memory ($F(4,84) = 5.9, p < 0.01$) and a stimulus*memory interaction ($F(4,84) = 5.35, p < 0.01$). In these voxels, there was a main effect of memory for scenes ($F(1,21) = 4.10, p < 0.05$) and a marginal main effect of memory for objects ($F(4,84) = 2.14, p = 0.08$). For the objects there was a cubic trend ($F(4,84) = 7.30, p < 0.01$), and pairwise comparisons revealed a significant increase in encoding-related activity for high + medium confidence miss (s1+2) and medium confidence hit (s5) relative to low confidence miss (s1+2 > s3: $t(21) = 2.38, p < 0.05$; s5 > s3: $t(21) = 2.23, p < 0.05$), and a marginal increase in activity for low confidence hit (s4), compared to low confidence miss (s4 > s3: $t(21) = 1.83, p = 0.08$). Memory activity for the scenes, by contrast, demonstrated a significant linear trend ($F(1,21) = 23.62, p < 0.01$) and a marginal quadratic trend ($F(1,21) = 3.78, p = 0.07$).

While activity for high confidence hit (s6) was greater than all other levels of confidence (s6 > s5: $t(21) = 2.92$, $p < 0.01$; s6 > s4: $t(21) = 5.10$, $p < 0.01$; s6 > s3: $t(21) = 3.95$, $p < 0.01$; s6 > s1+2: $t(21) = 4.96$, $p < 0.01$), there was also a significant difference between medium confidence hit (s5) and low confidence miss, and a trend towards greater activity for medium confidence hit relative to low confidence hit and high + medium confidence miss (s5 > s4: $t(21) = 1.90$, $p = 0.07$; s5 > s3: $t(21) = 2.25$, $p < 0.05$; s5 > s1+2: $t(21) = 1.98$, $p = 0.06$).

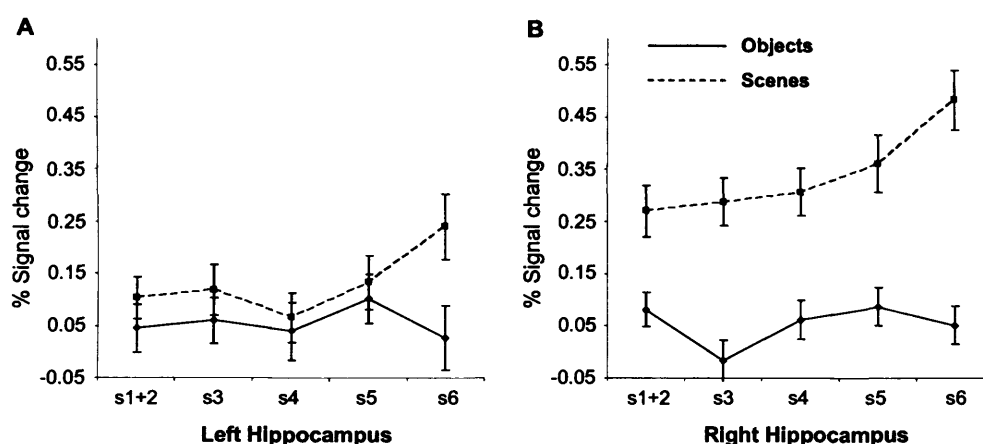


Figure 3.8: Patterns of memory encoding activity separated according to recognition confidence for objects and scenes revealed by the high confidence scene hit > medium confidence scene hit contrast in the (A) left and (B) right hippocampus. Abbreviations: (s1+2) subsequent high + medium confidence miss, (s3) subsequent low confidence miss, (s4) subsequent low confidence hit, (s5) subsequent medium confidence hit, and (s6) subsequent high confidence hit.

3.5.2. Functional region of interest analysis

3.5.2.1. Subsequent item memory effects

FROI analyses of subsequent item recognition confidence are summarised in Fig. 3.9 (within voxels that processed scenes over objects in the hippocampus and parahippocampal gyrus, and objects over scenes in the perirhinal cortex). Within the scene-sensitive voxels in the hippocampus there were main effects of stimuli ($F(1,21) = 11.61$, $p < 0.01$) and memory ($F(4,84) = 2.88$, $p < 0.05$), and three significant interactions: hemisphere*stimuli ($F(1,21) = 8.67$, $p < 0.01$), stimuli*memory ($F(4,84) = 2.7$, $p < 0.05$) and hemisphere*stimuli*memory ($F(4,84) = 2.5$, $p < 0.05$). In the left hippocampus (Fig. 3.9A) there was a main effect of memory for scenes ($F(4,84) = 5.6$, $p < 0.01$), with a linear ($F(1,21) = 13.18$, $p < 0.01$) and a quadratic trend ($F(1,21) =$

5.22, $p < 0.05$). In subsequent pairwise comparisons, encoding-related activity for scenes was greater for high confidence hit (s6) compared to all other levels of recognition memory confidence (s6 > s5: $t(21) = 2.55$, $p < 0.05$; s6 > s4: $t(21) = 3.18$, $p < 0.01$; s6 > s3: $t(21) = 2.98$, $p < 0.01$; s6 > s1+2: $t(21) = 3.46$, $p < 0.01$).

In the right hippocampus (Fig. 3.9B) there was also a significant main effect of memory for scenes, that was accompanied by both a linear and quadratic trend (scenes main effect of memory: $F(4,84) = 4.91$, $p < 0.01$; linear trend: $F(1,21) = 15.44$, $p < 0.01$; and quadratic trend: $F(1,21) = 4.98$, $p < 0.05$). Follow-up pairwise comparisons revealed that activity for high confidence scene hit (s6) was greater than for all other responses (s6 > s5: $t(21) = 2.39$, $p < 0.05$; s6 > s4: $t(21) = 3.77$, $p < 0.01$; s6 > s3: $t(21) = 2.72$, $p < 0.05$; s6 > s1+2: $t(21) = 3.88$, $p < 0.01$). There were no significant memory effects for objects within the left and right hippocampal scene fROIs.

In the scene-sensitive parahippocampal gyrus fROI (Fig. 3.9C) there was a significant main effect of stimuli ($F(1,21) = 44.73$, $p < 0.01$), a main effect of memory ($F(4,84) = 4.09$, $p < 0.01$), a stimuli*hemisphere interaction ($F(1,21) = 20.13$, $p < 0.01$) and a stimuli*memory interaction ($F(4, 84) = 4.82$, $p < 0.01$). Subsequent analyses revealed that there was a main effect of memory for the scenes, which demonstrated a linear and quadratic trend (scenes main effect of memory: $F(4,84) = 9.52$, $p < 0.01$; linear trend: $F(1,21) = 23.66$, $p < 0.01$; and quadratic trend: $F(1,21) = 6.11$, $p < 0.05$). Pairwise comparisons revealed greater encoding-related activity for high confidence scene hit (s6), compared to all other levels of recognition memory confidence (s6 > s5: $t(21) = 3.48$, $p < 0.01$; s6 > s4: $t(21) = 4.12$, $p < 0.01$; s6 > s3: $t(21) = 4.21$, $p < 0.01$; s6 > s1+2: $t(21) = 4.82$, $p < 0.01$), and greater activity for medium confidence scene hit (s5) relative to low confidence scene miss that was marginal (s5 > s3: $t(21) = 1.93$, $p = 0.07$). As with the hippocampus, there were no significant effects for objects within the scene-sensitive parahippocampal fROIs.

Object-sensitive voxels within the perirhinal cortex (Fig. 3.9D) showed significant main effects of stimuli ($F(1,21) = 61.30$, $p < 0.01$) and memory ($F(4,84) = 2.47$, $p < 0.05$) and a hemisphere*stimuli interaction ($F(1,21) = 16.15$, $p < 0.01$). Despite there being no significant stimuli*memory interaction within the perirhinal cortex ($F(4,84) = 1.33$), separate analyses for objects and scenes were conducted based on a

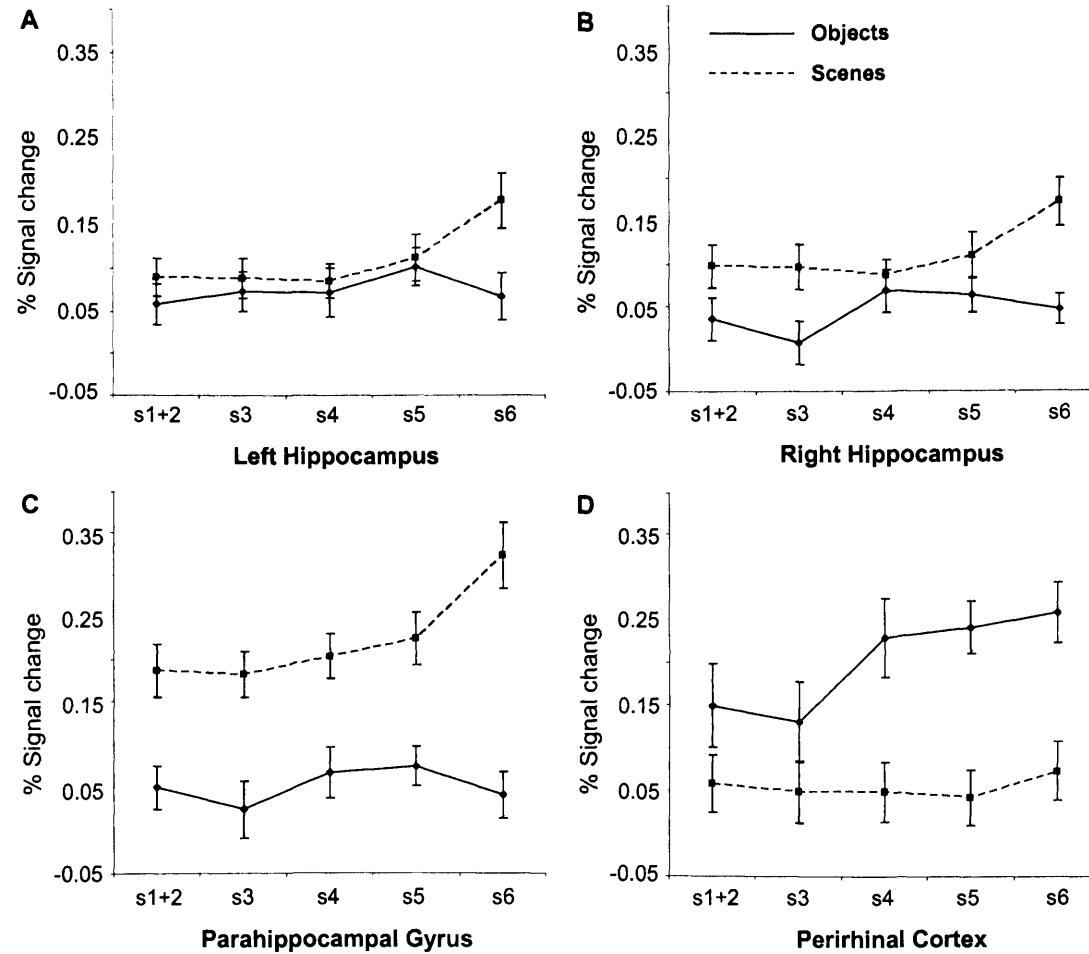


Figure 3.9: Patterns of memory encoding activity separated according to recognition confidence for objects and scenes in functionally defined MTL regions of interest from (A, B, C) scenes > objects and (D) objects > scenes. Percent signal change (arbitrary units) in the (A) left hippocampus, (B) right hippocampus, (C) parahippocampal gyrus, and (D) perirhinal cortex. Abbreviations: (s1+2) subsequent high + medium confidence miss, (s3) subsequent low confidence miss, (s4) subsequent low confidence hit, (s5) subsequent medium confidence hit, and (s6) subsequent high confidence hit.

priori predictions (see Section 3.3.3). The main effect of memory for scenes was not significant in this fROI ($F(4,84) = 0.18$). For objects, however, there was a main effect of memory, which along with a significant linear trend (object main effect of memory: $F(4,84) = 2.97$, $p < 0.05$; linear trend: $F(1,21) = 8.02$, $p < 0.01$), planned pairwise comparisons revealed greater encoding-related activity for: (a) high confidence object hit (s_6) relative to low (s_3) and high + medium confidence (s_1+2) object miss ($s_6 > s_3$: $t(21) = 2.45$, $p < 0.05$; $s_6 > s_1+2$: $t(21) = 2.23$, $p < 0.05$), (b) medium confidence object hit (s_5) relative to low confidence object miss ($s_5 > s_3$: $t(21) = 2.29$, $p < 0.05$), and (c) marginal effects for medium confidence object hit (s_5) compared to high confidence object miss, and low confidence object hit (s_4) compared to high confidence object miss ($s_5 > s_1+2$: $t(21) = 1.96$, $p = 0.06$; $s_4 > s_1+2$: $t(21) = 2.02$, $p = 0.06$). There were no differences between confidence responses for object hits ($s_6 = s_5 = s_4$).

To summarise, in the hippocampus and the parahippocampal gyrus scene-sensitive fROIs memory-related activity was present for the scenes, but not objects. Specifically, memory effects for scenes followed a quadratic pattern and pairwise comparisons revealed greater activity for most confidently recognised scenes (s_6) compared to all other levels of confidence response ($s_6 > s_5 = s_4 = s_3 = s_2 = s_1$). In contrast, within the object-sensitive fROI in the perirhinal cortex memory effects were evident for objects only. Memory-related activity for objects within the perirhinal fROI showed a reliable linear trend, and was greater for subsequently remembered old items, compared to forgotten items ($s_6 = s_5 = s_4 > s_3 = s_2 = s_1$).

3.5.2.2. *Subsequent source memory effects*

Brain activity associated with subsequent source recollection was also investigated within the parahippocampal, hippocampal (scenes) and perirhinal (objects) fROIs (Fig. 3.10). Within the hippocampus there were significant main effects of stimuli ($F(1,21) = 16.61$, $p < 0.01$) and memory ($F(2,42) = 3.73$, $p < 0.05$), a hemisphere*stimuli*memory interaction ($F(2,42) = 4.02$, $p < 0.05$), and an interaction between hemisphere and stimuli that was marginal ($F(1,21) = 3.72$, $p = 0.07$). In both the left and right hippocampus there were main effects of memory for scenes (left: $F(2,42) = 4.30$, $p < 0.05$; right: $F(2,42) = 4.07$, $p < 0.05$). Follow up pairwise comparisons for scenes in the left hippocampus (Fig. 3.10A) revealed greater

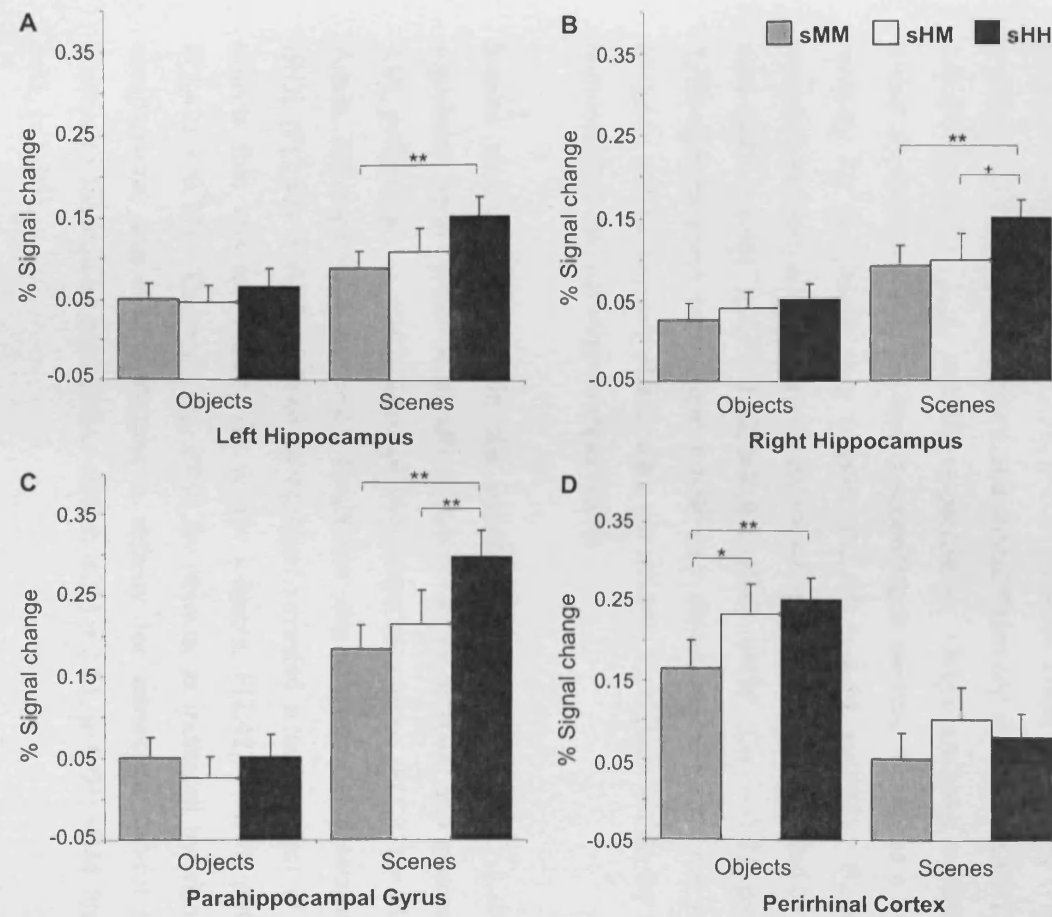


Figure 3.10: Patterns of memory encoding activity separated according to source memory accuracy for objects and scenes in functionally defined MTL regions of interest from (A, B, C) scenes > objects and (D) objects > scenes. Percent signal change (arbitrary units) in the (A) left hippocampus, (B) right hippocampus, (C) parahippocampal gyrus, and (D) perirhinal cortex. Abbreviations: (sMM) subsequent miss (grey), (sHM) subsequent hit-miss (white) and (sHH) subsequent hit-hit (black). + $p \leq 0.06$; * $p < 0.05$; ** $p < 0.01$.

encoding-related activity for subsequent scene hit-hit compared to subsequent scene hit-miss only (sHH > sMM: $t(21) = 3.48$, $p < 0.01$). Within the right hippocampus (Fig. 3.10B), activity was greater for subsequent scene hit-hit compared to scene miss (sHH > sMM: $t(21) = 3.65$, $p < 0.01$), and scene hit-miss (that approached significance; sHH > sHM: $t(21) = 2.04$, $p = 0.06$).

In the parahippocampal gyrus scene-sensitive fROI (Fig. 3.10C) there was a main effect of stimuli ($F(1,21) = 52.58$, $p < 0.01$), a main effect of memory ($F(2,42) = 5.89$, $p < 0.01$), and hemisphere*stimuli and stimuli*memory interactions ($F(1,21) = 16.17$, $p < 0.01$; $F(2,42) = 3.33$, $p < 0.05$, respectively). When analyses were broken down within these scene-sensitive voxels according to stimuli, there was a main effect of memory for the scenes only (scenes: $F(2,42) = 8.74$, $p < 0.01$). Planned pairwise comparisons revealed greater activity for subsequent hit-hit compared to hit-miss, and miss (sHH > sHM: $t(21) = 2.82$, $p < 0.01$; sHH > sMM: $t(21) = 5.21$, $p < 0.01$), but no difference between subsequent hit-hit and hit-miss. As with the item memory analysis, source memory effects were not evident for objects within the left and right hippocampal, and parahippocampal fROIs.

Source memory analyses in the perirhinal cortex fROI (Fig. 3.10D) revealed significant main effects of stimuli ($F(1,21) = 42.84$, $p < 0.01$) and memory ($F(2,42) = 4.01$, $p < 0.05$) and a reliable hemisphere*stimuli interaction ($F(1,21) = 14.02$, $p < 0.01$). Again, although there was not a significant stimuli*memory interaction within this fROI ($F(2,42) = 0.67$), follow up analyses revealed a main effect of memory for objects that was not evident for scenes (objects: $F(2,42) = 4.48$, $p < 0.05$; scenes: $F(2,42) = 0.77$). This memory effect for objects, as indicated by planned pairwise comparisons, was driven by greater activity for subsequent hit-hit and hit-miss, relative to subsequent miss (sHH > sMM: $t(21) = 2.91$, $p < 0.01$; sHM > sMM: $t(21) = 2.43$, $p < 0.05$).

3.6. Discussion

The current experiment was designed to investigate stimulus-specific long-term memory effects within subregions of the MTL, with the aim of elucidating whether stimuli (objects vs. scenes), process (familiarity vs. recollection) or information (item

vs. context) is the overruling factor in how the perirhinal cortex and hippocampus functionally fractionates. Using a similar design to Ranganath et al. (2004), who identified dissociable MTL correlates of item and source memory using words (see Section 1.4.4 and 3.1; Fig. 1.15), it was possible to obtain multiple measurements of successful memory encoding for objects and scenes. As with Experiment 1, and based upon the assumptions made by dual-process signal detection (see Section 1.4.4), recognition confidence judgements made at retrieval (outside the scanner) were used to identify patterns of neural activity associated with recollection and familiarity (Cohn et al., 2009; Daselaar et al., 2006; Montaldi et al., 2006; Ranganath et al., 2004; Yonelinas et al., 2005). In this study, however, participants also made source memory judgements at retrieval to investigate whether patterns of neural activity indexed subsequent contextual source memory success. As a result, this paradigm allowed the separation, and direct comparison, of activity relating to item familiarity, recollection and successful encoding of contextual information for objects and scenes within the hippocampus and perirhinal cortex, as well as the parahippocampal gyrus.

There was a significant stimulus-specific subsequent item memory/familiarity effect for objects within the perirhinal cortex, whereas subsequent memory effects within the hippocampus and parahippocampal gyrus reflected scene-specific contextual source recollection. These stimulus-specific memory effects will be discussed in the following sections, along with how they can be accommodated by current models of MTL function, in light of the predictions laid out in the Introduction.

3.6.1. Summary of findings

3.6.1.1. Whole-brain analysis

The first stage of the analysis approach was to identify significant effects of subsequent familiarity, recollection and contextual source memory encoding at the whole-brain level. Three different fMRI contrasts were performed separately for objects and scenes; regions associated with (a) familiarity were investigated via linear contrasts across recognition confidence regressors ($s_5 = +3$, $s_4 = +1$, $s_3 = -1$, $s_{1+2} = -3$), (b) recollection were identified via a contrast between the high confidence hit and medium confidence hit recognition memory regressors ($s_6 > s_5$) and (c) encoding of contextual source information were elucidated via contrasts between remembered

items that elicited a correct source judgement with those for which the source judgement was incorrect ($s_{HH} > s_{HM}$).

In keeping with previous studies that have used recognition memory confidence to investigate regions relating to recollection at the time of retrieval (Cohn et al., 2009; Daselaar et al., 2006; Yonelinas et al., 2005), there was significant memory encoding activity in the left and right hippocampus for the scene subsequent high confidence hit > scene subsequent medium confidence hit contrast (scene $s_6 > s_5$). Further analyses revealed that for objects there was a marginal main effect of memory in the right hippocampus only. As the memory effect for objects was supported by limited statistical evidence and was driven by a decrease in activity for low confidence miss, relative to all the other confidence groups (as indicated a cubic trend and the following pattern: $s_{1+2} > s_3 < s_4 = s_5 = s_6$; see Fig. 3.8B) it cannot be reliably attributed to a specific memory process. Consequently, the main finding from the whole-brain analysis was that activity in the left and right hippocampus reflected scene-specific recollection. It is notable that, for all of the other whole-brain contrasts, there were no significant effects within the MTL.

3.6.1.2. *Functional region of interest analysis*

Due to the a priori focus of the current study and in keeping with Experiment 1, patterns of memory-related neural activity were investigated within functionally defined MTL regions of interest (fROIs). By performing contrasts between object and scene trials from an orthogonal functional localiser task, unbiased stimulus-specific fROIs were created. Scene-sensitive voxels (scenes > objects) were identified in the hippocampus and parahippocampal gyrus, whereas object-sensitive voxels (objects > scenes) were located in the perirhinal cortex only. Separate analyses were conducted to investigate the relationship between encoding activity and subsequent recognition confidence (item memory analysis) and contextual source memory accuracy (source memory analysis) within each of these fROIs.

In the item memory analyses there were significant stimuli*memory interactions within scene-sensitive voxels in the left and right hippocampus, and the parahippocampal gyrus (bilaterally). Memory-related activity for scenes in the hippocampus was greater for high confidence hit, compared to all other levels of

confidence ($s_6 > s_5 = s_4 = s_3 = s_{1+2}$), whereas for objects there were no significant memory effects. The profile of activity within the left and right hippocampal fROIs reflected scene-specific recollection, therefore mirroring the findings from the whole-brain analysis (detailed earlier). Likewise, activity in the parahippocampal gyrus demonstrated a similar recollection-like pattern for the scenes, and there was no evidence of memory processing for the objects.

As with the item memory analysis, there were interactions between stimulus type and source memory effects within the scene-sensitive hippocampal and parahippocampal fROIs. In the parahippocampal gyrus there was a profile of activity that predicted subsequent contextual source memory for scenes (scene subsequent hit-hit (sHH) > scene subsequent hit-miss (sHM) = scene subsequent miss (sMM)), and a trend for a similar pattern within the right hippocampus. In the left hippocampus, activity for sHH scenes was greater than sMM scenes, and although activity sHM scenes was intermediate, it did not reliably differ from sHH or sM. The pattern for scenes in the left hippocampus was ambiguous and, therefore, cannot reliably be labelled as subsequent item or contextual source memory. There were no significant effects for objects in any of these fROIs.

For the perirhinal cortex object-sensitive fROI, despite the lack of interactions between stimuli and memory, there were significant main effects of memory for the objects that were not present for the scenes in both the item and source memory analyses. Memory-related activity for objects was accompanied by a linear trend without a quadratic component, which comprised greater activity for old relative to forgotten items (subsequent hit (s_6, s_5 and s_4) > subsequent miss (s_3 and s_{1+2})) which did not modulate according to subsequent recovery of contextual source details (sHH=sHM > sMM). Activity within the perirhinal cortex therefore reflected a subsequent object-specific item memory effect, which is a pattern that has been previously associated with familiarity (Davachi et al., 2003; Kensinger & Schacter, 2006).

In general, results from the item confidence and contextual source memory analyses are consistent. For example, in the parahippocampal gyrus fROI there was a non-linear increase in activity for high confidence scene hit, relative to all other levels of

confidence, as well as an increase in activity for scenes remembered with the source detail compared to those for which the source was forgotten. Both of these profiles have been linked with recollection (Cohn et al., 2009; Daselaar et al., 2006; Davachi et al., 2003; Kensinger & Schacter, 2006; Ranganath et al., 2004; Yonelinas et al., 2005).

Notably, the analysis of memory effects within the left and right hippocampus according to recognition confidence indicated patterns of activity for scenes that have been previously linked to recollection (Cohn et al., 2009; Daselaar et al., 2006; Yonelinas et al., 2005). For the source memory analyses, however, there was only a trend towards a source memory effect for scenes in the left hippocampus and an ambiguous pattern in the right hippocampus. This disparity may have come about because of issues associated with using source memory judgements to index recollection. Although one can be confident that participants have recollected the contextual information for a reasonable proportion of subsequent hit-hits, they may also have recollected some *non-criterial* contextual information for hit-misses (Yonelinas & Jacoby, 1996; see also Section 1.4.1.1). As a result, the source memory judgement might not isolate activity related to recollection as well as item recognition confidence.

3.6.2. *Implications for dual-process and informational accounts*

According to the dual-process account, the hippocampus supports recollection, whereas familiarity operates via the perirhinal cortex (Aggleton & Brown, 1999; Brown & Aggleton, 2001). Informational accounts, however, suggest that the perirhinal cortex processes item-based mnemonic information, the parahippocampal cortex processes associated spatial (item and context account: Davachi, 2006) and non-spatial (BIC: Diana et al., 2007) contextual information, and the hippocampus forms domain-general associations between items and contexts. Based on these two accounts and the findings from the Ranganath et al. (2004) paper, in the Introduction it was predicted that activity within the hippocampus should reflect domain-general recollection and the recovery of contextual source information, whereas a domain-general linear pattern of neural activity based on increases in familiarity strength, which is insensitive to the recovery of contextual source information, should be

observed in the perirhinal cortex. In terms of informational accounts, it was also predicted that recollection effects should occur within the parahippocampal gyrus.

Activity within the hippocampus and parahippocampal gyrus in this experiment could be linked to recollection, and a familiarity-like pattern occurred within the perirhinal cortex. As such, the loci of significant memory effects within the MTL are not inconsistent with dual-process and informational accounts. The observations that significant memory effects within the perirhinal cortex and hippocampus were object- and scene-specific (respectively), however, are provocative as neither informational nor dual-process accounts make explicit predictions about stimulus-specificity within these regions. According to the item-context informational account (Davachi, 2006), the parahippocampal cortex is responsible for processing spatial-contextual information (Awipi & Davachi, 2008; Litman et al., 2009). As there was limited spatial information associated with the objects, the item-context account would predict a scene-specific effect in the parahippocampal gyrus. According to the BIC model (Diana et al., 2007), however, as the parahippocampal gyrus is responsible for processing contextual information that is both spatial and non-spatial, significant effects of contextual encoding should have been observed for objects and scenes within this region.

As mentioned in the Introduction, stimulus-specific patterns of memory-related data could reflect differences between the contributions of recollection and familiarity to memory for these different stimulus types. Likewise, informational accounts could accommodate these findings by way of a disproportionate dependence of object and scene processing on item and context mnemonic information (Davachi, 2006). In light of these considerations, stimulus-specific memory effects within each fROI are discussed below alongside important aspects of the behavioural data.

Within the perirhinal cortex object-sensitive fROI there was a significant hit vs. miss item memory effect for objects (Davachi et al., 2003; Kensinger & Schacter, 2006). Memory-related activity was not detected for scenes within these voxels. Behaviourally, item memory accuracy was reliably higher for the objects than the scenes ($p(\text{hit})-p(\text{false-alarm})$). As item memory was not matched for the objects and scenes, stimulus-specific effects within the perirhinal cortex could reflect increased

sensitivity to the more memorable stimulus type. Notably, the ROC analyses indicated that, although the recollection estimate was significantly greater for objects than scenes, familiarity estimates did not reliably differ. This suggests that the mnemonic advantage for objects was driven by recollection and it would be difficult to conclusively argue that, in this experiment, memory for objects was disproportionately supported by familiarity. These findings are consistent with the view that there is some degree of stimulus-specificity within the perirhinal cortex, if it assumed that this region solely supports memory judgements made on the basis of familiarity. The results from the ROC analyses, however, do not rule out the possibility that memory for objects may be more reliant on a neural system (which includes the perirhinal cortex) responsible for processing item-based mnemonic information that can support both recollection- and familiarity-based recognition memory judgements (Davachi, 2006; Diana et al., 2007).

In contrast to the perirhinal cortex, activity within the hippocampus predicted subsequent recollection and a trend toward significant contextual source memory encoding for scenes. Despite there being differences between the memorability of objects and scenes (computed via $p(\text{hit}) - p(\text{false-alarm})$), source memory accuracy was matched and, in fact, the recollection estimate was higher for objects. Mirroring the findings from Experiment 1, therefore, stimulus-specific hippocampal recollection effects in Experiment 2 were detected for the stimulus type for which the recollection estimate was lower. As such, the profile of stimulus-specific mnemonic processing in the hippocampus in Experiments 1 and 2 does not easily reduce to differences in the memorability of one stimulus type compared to another. Likewise, as source memory accuracy was matched across the two stimulus types, the pattern of scene-specific recollection within the parahippocampal fROI cannot be accommodated by appealing to a disproportionate dependence of scene memory on contextual processing.

In sum, although item memory accuracy was higher for objects than scenes, the mnemonic advantage for objects was driven by recollection. In so far as these estimates are accurate, the current findings point strongly toward stimulus-specific MTL processing. The converging findings in this current experiment (as well as those from Experiment 1), therefore indicate the inadequacy of dual-process and

informational models as complete accounts of MTL contributions to recognition memory.

3.6.3. Implications for representational accounts

The key claim in the previous section is that a dual-process view provides an inadequate explanation of the current data. Furthermore, although there are certain aspects of these results that can be accommodated by facets of informational models of MTL function (effects in the parahippocampal cortex and Davachi's (2006) item-context account), no single account can accommodate all of the findings. Representational accounts of MTL function, however, provide an adequate explanation for all of the stimulus-specific effects in the fROIs. According to one representational view (EMA: Graham et al., 2010), stimulus-specific representations are processed and stored discretely within subregions of the MTL. This model is consistent with observations that damage to the perirhinal cortex is associated with impairments in higher-level perception and memory for objects, whereas damage restricted to the hippocampus disrupts memory and perception for scenes as well as performance on spatially demanding tasks (e.g. Bird et al., 2007; Bird et al., 2008; Lee, Buckley et al., 2005; Lee, Bussey et al., 2005; Taylor et al., 2007).

There is also recent neuroimaging evidence for a distinction between perirhinal cortex and hippocampal contributions to object and scene processing, across a number of different cognitive tasks (e.g. Awipi & Davachi, 2008; Barense, Henson et al., 2010; Lee, Bandelow et al., 2006; Lee et al., 2008; Litman et al., 2009; Pihlajamaki et al., 2004). According to EMA, as representations of objects and scenes are formed within the perirhinal cortex and hippocampus, respectively, the recruitment of MTL regions should be guided by the nature of the to-be remembered material, as opposed to the specific process or type of information that supports successful recognition memory (EMA: Graham et al., 2010). By this view, therefore, the stimulus-specific profiles of activity within the hippocampus for scenes and perirhinal cortex for objects in the current experiment complement the findings from previous fMRI and neuropsychological experiments that have tested memory and perception for objects, faces and scenes. Furthermore, the current findings closely relate to the predictions of EMA specifically for memory; stimulus-specific representations were located

discretely in MTL regions and predicted memory performance in a stimulus-specific fashion.

Scene-specific activity was observed within the parahippocampal gyrus in the current experiment, and has been in previous functional imaging investigations (Litman et al., 2009; Awipi & Davachi, 2008; Lee et al., 2008; Preston et al., 2010). The majority of information that projects to the posterior parahippocampal gyrus originates from spatial processing sites that form the dorsal processing stream. In turn, information from the posterior parahippocampal gyrus largely projects to the hippocampus, via the lateral entorhinal cortex (see Sections 1.2.1, 1.5 and 1.6). It is likely, therefore, that the posterior parahippocampal gyrus forms an intermediate processing site for spatial information between the dorsal processing stream and the hippocampus. As such, the posterior parahippocampal gyrus may similarly contribute to long-term memory and perception for scenes (Davachi, 2006). Although EMA only makes explicit predictions about the functional roles of the perirhinal cortex and the hippocampus, it is possible that the formation of spatial representations also requires the posterior parahippocampal gyrus.

3.6.4. The relationship between neural activity and memory strength

Although the overall pattern of effects in the current study is consistent with a representational account, patterns of memory-related activity that could be linked to process (familiarity and recollection) or type of mnemonic information (item and context) occurred within the regions that both the informational and dual-process models predict. It is possible, however, that dissociable patterns of neural activity within the perirhinal cortex and hippocampus are driven by variations in the same memory process, but that the neural response within these two brain regions is not equally responsive to this variation. This could result in the misattribution of neural activity within the perirhinal cortex and hippocampus to item/familiarity and context/recollection mnemonic processing (respectively).

Specifically, according to one such strength-based account, the processes of recollection and familiarity combine to form a single memory strength signal (Wixted, 2004; Wixted, 2007; Squire et al., 2007) and the empirical procedures used to isolate recollection and familiarity (or memory for items vs. context) actually separate strong

memories from weak memories (see Sections 1.4.1 and 1.4.4, Kirwan et al., 2008; Squire et al., 2007; Wais et al., 2010; although see Cohn et al., 2009). Furthermore, according to this account, different profiles of memory-related activation between the hippocampus/parahippocampal cortex and the perirhinal cortex reflect regional differences in the relationship between fluctuations in memory strength and neural activity.

In a recent review, Squire et al. (2007) suggest that a steep increase in activity for recollected items, relative to non-recollected items (consistently observed in the hippocampus: Cohn et al., 2009; Daselaar et al., 2006; Montaldi et al., 2006; Yonelinas et al., 2005) could occur due to a non-linear relationship between neural activity and memory strength. In contrast, patterns of activity within the perirhinal cortex could result from a linear relationship between memory strength and neural activity that plateaus for high strength memories (see Fig. 3.11). If this account is

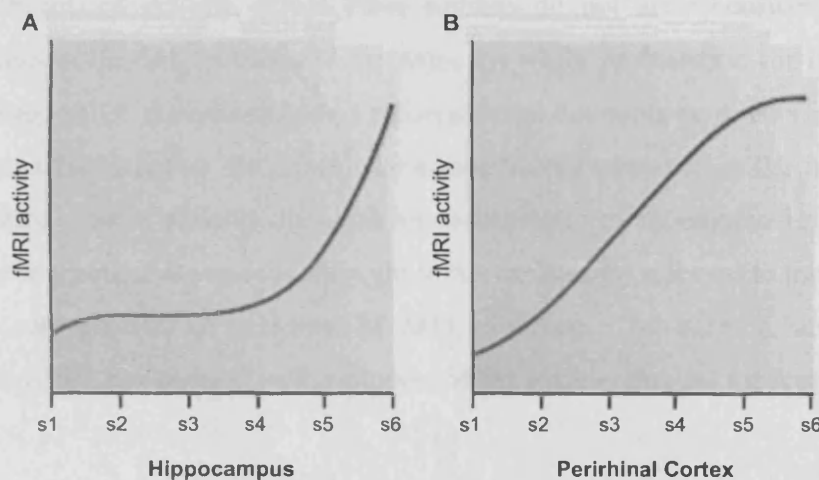


Figure 3.11: Possible non-linear and linear relationships between encoding activation in the (A) hippocampus and (B) perirhinal cortex, respectively. On the x-axis are memory confidence judgements for old items ranging from (s1) high confidence new to (s6) high confidence old, which actually represent increases in memory strength from very weak to very strong. In the hippocampus there is often a relatively a steep increase in fMRI activity for high confidence hits (as well as for remember responses and correct source judgements), with little or no change in response across other confidence response categories. In the perirhinal cortex, however, activity generally increases monotonically across lower confidence response categories, which becomes shallow when confidence is high. According to Squire et al. (2007), therefore, these regional effects can be explained via a differential relationship between the neural response to weak vs. strong memories, and arise for reasons unrelated to the distinction between recollection and familiarity. Figure adapted from Squire et al. (2007).

correct, differences between the linearity and shape of the BOLD response for the hippocampus and perirhinal cortex explain the data from investigations that have formed the basis for claims that there are dissociable correlates of recollection and familiarity within the MTL (e.g. Cansino et al., Cohn et al., 2009; 2002; Daselaar et al., 2006; Davachi et al., 2003; Dobbins et al., 2003; Johnson & Rugg, 2007; Kahn et al., 2004; Montaldi et al., 2006; Yonelinas et al., 2005). It is notable that the different neural signatures of recollection and familiarity are predicted a priori by dual-process signal detection and are subsequently confirmed by imaging experiments. In contrast, Squire's highly speculative strength-based account is an entirely post-hoc explanation of these data points.

One interpretation of the observations in the current study, therefore, is that the hippocampus and perirhinal cortex support memory for objects and scenes in a stimulus-specific manner, but differences between object- and scene-specific patterns of memory-related activity across these regions do not arise because the regions support distinct memory processes. Importantly, while problematic for fMRI studies cited in support of dual-process and informational accounts (e.g. Ranganath et al., 2004), dissecting whether the neural signal commonly observed in the hippocampus and perirhinal cortex reflects different processes/types of mnemonic information or sensitivity to changes in memory strength is not necessarily relevant to the predictions made by representational accounts of MTL function. As such, a strength-based explanation does not undermine the support of the current data set for representational accounts.

3.6.5. Source memory and the perirhinal cortex

One strong prediction from the strength-based account is that it will not be possible to measure a recollection-like non-linear signal that predicts source memory accuracy in the perirhinal cortex ($HH > HM = MM$ or $s_6 > s_5 = s_4 = s_3 = s_2 = s_1$). As discussed in Chapter 1, there are examples of non-linear brain activity within the perirhinal cortex linked to the recovery of item-related source information (hit-hit > hit-miss = miss; see Section 1.5; Awipi & Davachi, 2008; Staresina & Davachi, 2006; 2008; see also Diana et al., 2010). These perirhinal cortex source memory effects somewhat invalidate the assumptions of the strength view, and are problematic for the most

common incarnations of the dual-process account (Aggleton & Brown, 1999; although see Diana et al., 2008; Haskins et al., 2008; Quamme et al., 2008).

These data can be accommodated by, and have been interpreted as support for, informational accounts, which predict perirhinal cortex contributions to the encoding and retrieval of item-based source information (in particular see Section 1.5; Diana et al., 2007; Diana et al., 2010; Staresina & Davachi, 2006; 2008). Neural activity in the perirhinal cortex that reflects contextual source memory encoding, however, would be extremely problematic for all of these models of MTL function. In contrast, due to the focus on stimuli, rather than process/mnemonic information, representational accounts (such as EMA: Graham et al., 2010; see also Bussey & Saksida, 2005; Saksida & Bussey, 2010) can allow for item-feature and contextual source memory processing for objects within the perirhinal cortex. To reiterate, in the current experiment, contextual source memory encoding was only detected for scenes in the hippocampus and parahippocampal cortex; no activity that predicted source memory accuracy for the objects was detected in the MTL. An outstanding question from the current experiment, and in terms of representational accounts, therefore is: what are the circumstances that are likely to influence the detection of object-specific *contextual* source memory encoding effect in the perirhinal cortex?

A key component of representational accounts is that object representations are organised hierarchically along the ventral visual processing stream, ranging from very simple representations in early visual processing regions, to complex and conjunctive representations in the perirhinal cortex (Bussey & Saksida, 2005; Cowell et al., 2010; Graham et al., 2010; Saksida & Bussey, 2010). As the perirhinal cortex houses the most complex representations of objects, this brain region will only be recruited when the task is perceptually demanding or when stimuli are high in ‘feature-ambiguity’ (Barense et al., 2005; Barense et al., 2007; Barense, Henson et al., 2010; Bartko et al., 2007a, 2007b; Bussey et al., 2002, 2003; Devlin & Price, 2007; Lee, Buckley et al., 2005; Lee, Bussey et al., 2005). As discussed in Chapter 1, feature ambiguity refers to situations when discriminanda contain many overlapping visual features (see Section 1.6 and 1.7). It follows from this that source memory effects for objects may have not been detected using the current paradigm because the stimuli employed were not sufficiently featurally ambiguous to require the perirhinal cortex. Furthermore,

the encoding tasks (which provided the criterial source information at retrieval) asked participants to make conceptual judgements about the presented objects. As representational accounts emphasise that MTL regions differentially process visual features of objects vs. scenes (Bussey & Saksida, 2005; Saksida & Bussey, 2010; Graham et al., 2010; Lee, Barense et al., 2005) and there is some evidence that source memory encoding is task-dependent (Otten et al., 2002; Otten & Rugg, 2001; Park, Uncapher, & Rugg, 2008), it may be more appropriate to use an encoding task that encourages participants to process the visual (perceptual) features of the stimuli. These theoretical observations are expanded upon in more detail in the following Chapter.

3.7. Conclusions

In this experiment, subregions within the MTL responded in a stimulus-specific manner, replicating previous fMRI experiments that have shown greater levels of activity for scenes than objects in the hippocampus and parahippocampal cortex, and for objects over scenes in the perirhinal cortex (Awipi & Davachi, 2008; Lee et al., 2008; Litman et al., 2009). Analyses of memory effects for objects and scenes within each of these functional ROIs revealed patterns of memory activation consistent with scene-specific recollection in the hippocampus and parahippocampal gyrus, and object-specific familiarity within the perirhinal cortex. As such, the stimulus-specific memory effects within the hippocampus and perirhinal cortex, although potentially reflecting recollection and familiarity (respectively), challenge a dual-process account of MTL function (Aggleton & Brown, 1999). As there is an informational account which states that the parahippocampal cortex processes spatial-contextual information (item and context account: Davachi, 2006), and item memory accuracy was greater for objects than scenes, stimulus-specific effects within the parahippocampal and perirhinal cortices are not entirely inconsistent with a view that characterises MTL function according to mnemonic information. The finding of a stimulus-specific effect within the hippocampus, however, cannot be encompassed by informational accounts.

All of the stimulus-specific effects in the current experiment can be accommodated by a representational view (EMA: Graham et al., 2010), which states that material is an

important predictor of activity in MTL regions. A stronger argument for a representational account, and against the alternatives, however, would be the demonstration of a significant contextual source memory effect for objects in the perirhinal cortex. The use of more featurally ambiguous stimuli and an encoding task that encourages participants to process object features may result in a pattern of neural activity within the perirhinal cortex that relates to subsequent contextual source memory success.

Chapter 4

Contextual source memory effects for objects in the perirhinal cortex

4.1. *Introduction*

In Experiment 2, activity in the perirhinal cortex showed an overall subsequent hit vs. miss effect (which was supported by a significant linear trend), which is a pattern of activity that is assumed to be characteristic of item memory encoding/familiarity (Davachi et al., 2003; Kensinger & Schacter, 2006). In contrast, within the hippocampus and parahippocampal gyrus, neural activity was significantly greater for scenes recognised with high confidence, compared to all other levels of confidence. In the parahippocampal gyrus, activity was also greater for scenes for which contextual information could be recovered compared to those for which contextual information was not available. This pattern of activity is widely assumed to reflect the process of recollection (Cohn et al., 2009; Daselaar et al., 2006; Yonelinas et al., 2005). For the previous experiment, therefore, the loci of significant item/familiarity and contextual/recollection effects are, at first glance, somewhat consistent with predictions of informational as well as dual-process models (see also Section 3.6.2).

Notably, however, in all of these regions, patterns of memory encoding-related activity were stimulus-specific; no significant changes in activity were detected for scenes within the perirhinal cortex, and for objects in the hippocampus and parahippocampal gyrus, according to the accuracy of memory judgements, or response confidence. Although activity within the perirhinal cortex was object-specific, item memory accuracy was greater for the objects than for the scenes. ROC analyses revealed that although recollection estimates were reliably higher for the objects, familiarity estimates were statistically equivalent. As the mnemonic advantage for objects was primarily driven by recollection, it is unlikely that the pattern within perirhinal cortex reflects an increased sensitivity to familiarity-based recognition for objects, compared to scenes. According to an informational account (BIC: Diana et al., 2007), however, as the perirhinal cortex can support recollection of

item-features (Diana et al., 2010; Staresina & Davachi, 2006; 2008) it cannot be ruled out that this object-specific effect reflects a disproportionate dependence during object processing on item-based mnemonic information. In terms of the scene-specific effects, as there is an informational account (item-context: Davachi, 2006), which states that the parahippocampal gyrus selectively processes spatial-contextual information (and the dual-process account makes no explicit predictions regarding the parahippocampal gyrus), scene-specific activity within this region is also not necessarily inconsistent for these models. By both informational and dual-process accounts, however, memory-encoding activity within the hippocampus should be domain-general. Furthermore, in light of matched memory accuracy for the contextual source information for objects and scenes, stimulus-specific memory processing within the hippocampus is a problematic finding.

As has already been described, however, these findings are not problematic for EMA (Graham et al., 2010). It is notable that, EMA also suggests that item and context memory can be driven by the same representation, so it should be possible to observe activity linked to memory for context for objects in the perirhinal cortex and an item memory effect for scenes within the hippocampus (Graham et al., 2010). This is, in fact, the main area where representational, informational and dual-process models diverge (see Section 1.8). One of the strongest arguments for a representational account, therefore, would be neural activity that tracks memory for context for objects within the perirhinal cortex. In the following sections, the focus is on the circumstances under which specific patterns of activity linked to memory encoding within the perirhinal cortex would support or discount competing accounts of MTL function.

According to proponents of the view that the hippocampus and perirhinal cortex do not make qualitatively different contributions to long-term memory (the strength-based/unitary account: Squire & Zola-Morgan, 1991; Squire et al., 2004; Squire et al., 2004; Squire et al., 2007; see Section 1.3), one explanation for regional dissociations in activity considered supportive of dual-process and informational accounts is that there is a different relationship between the signature of neural activity measured by fMRI and memory strength across MTL regions (see Section 3.6.4; Fig. 3.11: Squire et al., 2007). As such, the patterns of neural activity observed during memory

encoding and retrieval in the hippocampus and perirhinal cortex do not represent recollection and familiarity (respectively), but are indicative of regional variations in the sensitivity to quantitative differences in memory strength. If dissociable patterns of neural activity can easily reduce to regional differences in memory based neural responses, one inevitable conclusion is that the majority of current fMRI findings do not provide conclusive support for dual-process or informational accounts (Kirwan et al., 2008; Wais et al., 2010; although see Cohn et al., 2009).

A key element of this strength account is that parametric modulations in activity commonly observed within the perirhinal cortex, and which have been linked to familiarity (Daselaar et al., 2006; Ranganath et al., 2004), could instead reflect a linear relationship between brain activity and overall memory strength that tapers for high strength judgements, possibly reflecting contributions from both recollection and familiarity (Squire et al., 2007). By this view it should not be possible to detect a recollection-like non-linear signal that predicts source memory success within the perirhinal cortex. There is, however, some evidence of this pattern in the perirhinal cortex (Awipi & Davachi, 2008; Staresina & Davachi, 2006; 2008; see also Sections 1.5; 2.1; 3.6.5). In a recent experiment, Staresina and Davachi (2008) directly compared encoding-related activity within the MTL for associated item and contextual source information. At study, nouns were presented on a red or blue background. For each encoding trial, participants were required to vividly imagine the referent of the noun in the presented colour and were then asked to indicate whether this representation was plausible/implausible or appealing/unappealing (see Section 1.5 and Fig. 1.18). At test, participants were required to identify old items, as well as the colour (red vs. blue) and the task (plausible vs. appealing) in which they had originally encountered old items. In keeping with previous findings, activity within the hippocampus predicted subsequent memory for the colour and task information. A novel finding, however, was that significant source memory processing for the colour information was identified in the perirhinal cortex (colour hit-hit > colour hit-miss = miss; task hit-hit = task hit-miss = miss). As a non-linear recollection-like pattern occurred within the perirhinal cortex, the findings from this study argue against a strength-based account. In contrast, this pattern of source memory activity can be accommodated by informational accounts of MTL function, which propose that perirhinal cortex can form novel associations between an item and

its source, when the source information comprises an item feature (see Section 1.5.; Davachi, 2006; Diana et al., 2007; Diana et al., 2010; Staresina & Davachi, 2006; 2008).

Similarly, Diana et al. (2010) demonstrated that when source information was encoded as an item feature, activity in both the hippocampus and perirhinal cortex was associated with the successful recovery of this information at retrieval. When the same information was encoded as a contextual detail, however, a pattern relating to source memory success was only detected in the hippocampus. Importantly, significant effects within the perirhinal cortex were present between hit-hit and hit-miss contrasts for strong *and* weak memory, which was indexed by an assessment of confidence in the source judgement (e.g. high confidence hit-hit > hit-miss and low confidence hit-hit > hit-miss) and confirmed by differences in source memory accuracy across these two response categories (Wixted et al., 2010). The authors concluded, therefore, that source memory effects within the perirhinal cortex were not sensitive to the strength with which source judgements were made, but rather to the type of source information recovered (an item feature or contextual feature). As differences in patterns of activity across the hippocampus and the perirhinal cortex were qualitative rather than quantitative, these data has also been held to indicate the inadequacy of Squire and colleagues' (2007) strength-based account (Diana et al., 2010).

It has also been suggested that memory for novel associations might be supported by a familiarity signal within the perirhinal cortex if an item and item-related information are configurally bound into a single mnemonic representation (via unitisation; see Section 1.5; Diana et al., 2008; Haskins et al., 2008; Mayes et al., 2007; Quamme et al., 2007; Yonelinas et al., 1999). This account is supported by observations that associative memory impairments in patients with MTL damage can be reduced when these individuals are encouraged to encode pairs of words as a single item (for example, by forming new compound words, Quamme et al., 2007; see also Giovanello et al., 2006). Using a similar conjunction paradigm, activity within the perirhinal cortex was greater during memory encoding for unitised word-pairs compared to non-unitised word pairs (Haskins et al., 2008; see Section 1.5 and Fig. 1.19). Furthermore, source/associative memory ROCs for items encoded under

experimental conditions that encourage unitisation are more curvilinear than conditions that do not (Diana et al., 2008; Haskins et al., 2008; Sauvage et al., 2008). Increases in the curvilinearity of associative memory ROCs is an important observation, as this element supports the notion that memory for unitised novel associations can be supported by familiarity, which according to a dual-process account, operates via the perirhinal cortex. It has been demonstrated that voxels within the perirhinal cortex showing an increased response to unitised vs. non-unitised words pairs significantly overlap with voxels that show a familiarity-like linear increase in encoding activity based on associative memory confidence judgements made at retrieval (Haskins et al., 2008).

There is another proposal regarding familiarity-based perirhinal cortex contributions to associative memory, referred to as the Domain Dichotomy account (DD: Mayes et al., 2007; see Section 1.5). Like dual-process accounts, the DD states that the hippocampus supports recollection and the perirhinal cortex familiarity. As a result, similar to the unitisation view characterised above, the DD states that the perirhinal cortex can support familiarity for single items, as well as unitised associative representations. According to the DD, however, under certain circumstances, the perirhinal cortex can also support familiarity for *non-unitised* associations. Specifically, Mayes et al. (2007) posit that separate elements can converge and interact within the perirhinal cortex when they are represented in close proximity within the perirhinal cortex, making it is easy for them to bind here. This is most probable for information from the same processing domain, since these items are likely to be represented in adjacent cortical neurons. In contrast, information that is distally represented, such as for items from different processing domains, cannot converge sufficiently within the perirhinal cortex. Instead, the formation of associations for between-domain elements (or items and contexts) requires the hippocampus, and memory for which will be supported by recollection. It is notable that, unlike unitised pairs of items (which are characterised as a single configurally bound mnemonic representation), within-domain associations formed within the perirhinal cortex comprise two separate, but related elements.

In keeping with DD, individuals with focal hippocampal damage show intact memory for item-item associations when the memoranda are from the same processing domain

(Mayes et al., 2002; Mayes et al., 2004; Vargha-Khadem et al., 1997). Item-item associative memory that comprises items from different processing domains, however, is significantly impaired in hippocampal amnesia (Holdstock et al., 2002; Holdstock et al., 2005; Mayes et al., 2004; Turriziani et al., 2004; Vargha-Khadem et al., 1997). It is also possible that within-domain associations are more likely to be unitised than between-domain. As such, these disproportionate associative memory impairments in hippocampal amnesia could reflect differences in the degree to which unitisation can support memory for within- compared to between-domain associations. Importantly for this thesis, however, both the unitisation and DD accounts agree that between-domain, or item-context associations, like those in the previous experiment, will be solely dependent upon recollection supported by the hippocampus.

Based upon the above observations there are three factors which might explain why source memory effects were not detected in the perirhinal cortex in Experiment 2. First, because the source information comprised a contextual detail rather than an item feature. Second, because participants were not able to unitise the item and contextual information into a single mnemonic representation. And third, because the item and contextual source information were from different processing domains. In light of these possibilities, two manipulations were used in Experiment 3, which were implemented to revisit perirhinal cortex contributions to source memory for objects with specific reference to the predictions made by representational accounts. In addition to this, in order to clarify the differences between trials where the source detail was subsequently remembered or forgotten, participants made confidence judgements in their source decision so that activity relating to subsequent source guesses (low confidence hit-hit) could be considered separately from subsequent source-hits (high confidence hit-hit).

As discussed in Sections 1.6 and 1.7, there is a developing literature that has guided the formation of representational accounts (Bussey & Saksida, 2005; Cowell et al., 2010; Graham et al., 2010; Saksida & Bussey, 2010), which suggests that perirhinal cortex contributions to object memory and perception are influenced by increasing perceptual demands (Buckley et al., 2001; Buckley & Gaffan, 1997; 1998; Eacott et al., 1994). Specifically, there is recent research that has indicated that damage to the

perirhinal cortex interrupts memory and perception for objects when the experimental materials contain many overlapping visual features, as well as greater activity within the perirhinal cortex under similar conditions during memory and perceptual tasks (Barens et al., 2005; Barens et al., 2007; Barens, Henson et al., 2010; Bartko et al., 2007a, 2007b; Bussey et al., 2002, 2003; Devlin & Price, 2007; Lee, Buckley et al., 2005; Lee, Bussey et al., 2005). It has been inferred from these data that the perirhinal cortex is likely to be recruited when complex or highly configural representations of objects are required by the task; when stimuli are less configural, or there is minimal feature overlap between objects, memory will be supported by visual processing regions located upstream from the MTL (Bussey & Saksida, 2005; Cowell et al., 2010; Graham et al., 2010; Saksida & Bussey, 2010).

The design of the current experiment mirrored the previous one; participants studied objects in one of two encoding tasks (is this object common/uncommon or does this object contain more edges or curves), which comprised the criterial contextual source information during the retrieval phase. In order to increase the engagement of the perirhinal cortex, the objects employed across the two encoding tasks were from overlapping semantic categories and contained many similar visual features. Participants had to rely, therefore, on processing visual object features at encoding in order to make their source judgements at retrieval. Furthermore, one of the encoding tasks asked participants to indicate whether the presented objects contained more edges or curves, which was used to focus their attention on processing the visual features of the presented objects.

It follows from the key features of representational accounts (Bussey & Saksida, 2010; Cowell et al., 2010; Graham et al., 2010), that by increasing the feature ambiguity between the stimulus materials (compared to Experiment 2), activity within the perirhinal cortex will reflect successful source memory encoding for objects. Although not directly predicted by representational accounts, it is also possible that, as the edges/curves task was likely to encourage participants to encode the visual features of the presented objects to a greater degree than the common/uncommon encoding task, perirhinal cortex contributions to source memory could be task-dependent.

Different predictions ensue from the key features of the dual-process and informational accounts previously described (see earlier and Sections 1.4, 1.5). In keeping with a dual-process account, source/recollection effects for objects should occur in the hippocampus and item/familiarity effects in the perirhinal cortex. Similarly, an informational account could also accommodate dissociable item and source memory effects within the perirhinal cortex and hippocampus (respectively), as well as the demonstration of source memory effects in the parahippocampal gyrus (BIC: Diana et al., 2007). Notably, as the source information comprises a contextual detail (the encoding task) as opposed to an item feature, the incidence of significant source memory effects in the perirhinal cortex would be extremely problematic for both dual-process and informational accounts. Furthermore, if the pattern of activity reflected greater activity for high confidence hit, relative to all other source responses, this would be inconsistent with the proposition from a strength-based account that a non-linear relationship between neural activity and memory strength should not occur within the perirhinal cortex.

4.2. *Materials and methods*

4.2.1. *Participants*

Thirty-seven volunteers (27 female) participated. According to self-report, all participants were right-handed native-English speakers with normal or corrected to normal vision and no neurological and/or psychiatric disorders. Three participants (2 female) were removed from the analyses due to poor source memory accuracy (<0.55), and a further 2 (female) participants were removed due to excessive movement in the scanner. The mean age of the remaining 32 participants was 21.8 years (range = 19-30). All participants gave written informed consent prior to the experiment and were paid £10/hr for their participation. The experiment received ethical approval from the Cardiff University School of Psychology Ethics Committee.

4.2.2. *Materials*

Stimuli comprised a set of 732 black and white images of everyday objects taken from the Hemera Photo Objects database (Volumes I, II and III), plus 2 grey scaled images of arrows, one pointing left and the other right, for the active-baseline task (as with Experiment 2; see Section 3.2.2). Twelve objects were used in a practice session, and

of the remaining 720 objects, 360 were presented to participants in the study and test phases, and the other 360 as new items in the test phase only.

4.2.3. Tasks and procedure

The experiment was run using the same programme (E-prime), laptop, General Electric 3-T HDx MRI system and MR compatible equipment as described previously (see Section 2.2.3).

Participants were scanned at encoding, with a surprise test phase following the scanning session (Fig. 4.1). In the scanned encoding phase there were 3 separate study runs, each of which contained 120 object and 30 active-baseline trials. Study items were re-presented in the test phase, alongside unstudied objects. No objects were presented in more than one study or test run, and the order of object and active-baseline trials at study, and object trials at test, was randomised.

Study items were presented in the centre of the screen against a black background for 3000ms, separated by a jittered inter-stimulus interval (ISI: 500ms-4000ms, mean = 2250ms), during which the screen remained black. For each study item participants either had to indicate if the displayed object was common or uncommon, or if it contained more edges or curves; with the prompt for the judgement appearing beneath each study item. Within a given run, half of the objects were presented in the common/uncommon (conceptual) task, and the other half in the edges/curves (perceptual) task in a random order. Throughout each of the study runs, a baseline task was intermixed with the object trials. For the baseline task, participants had to indicate whether the arrow presented to them pointed to the left or right (see Section 3.2.3). They responded using their right index and middle fingers to indicate right/common/edges and left/uncommon/curves, respectively. As with Experiment 2, the (a) old/new status of the objects, (b) encoding task objects were presented in, and (c) finger used to signal to signal common/edges and uncommon/curves was counterbalanced across participants.

Following the study phase, participants were presented with a surprise self-paced recognition memory test, which comprised studied and new objects split across three runs (120 old: 120 new per run). For each test item, participants were prompted to

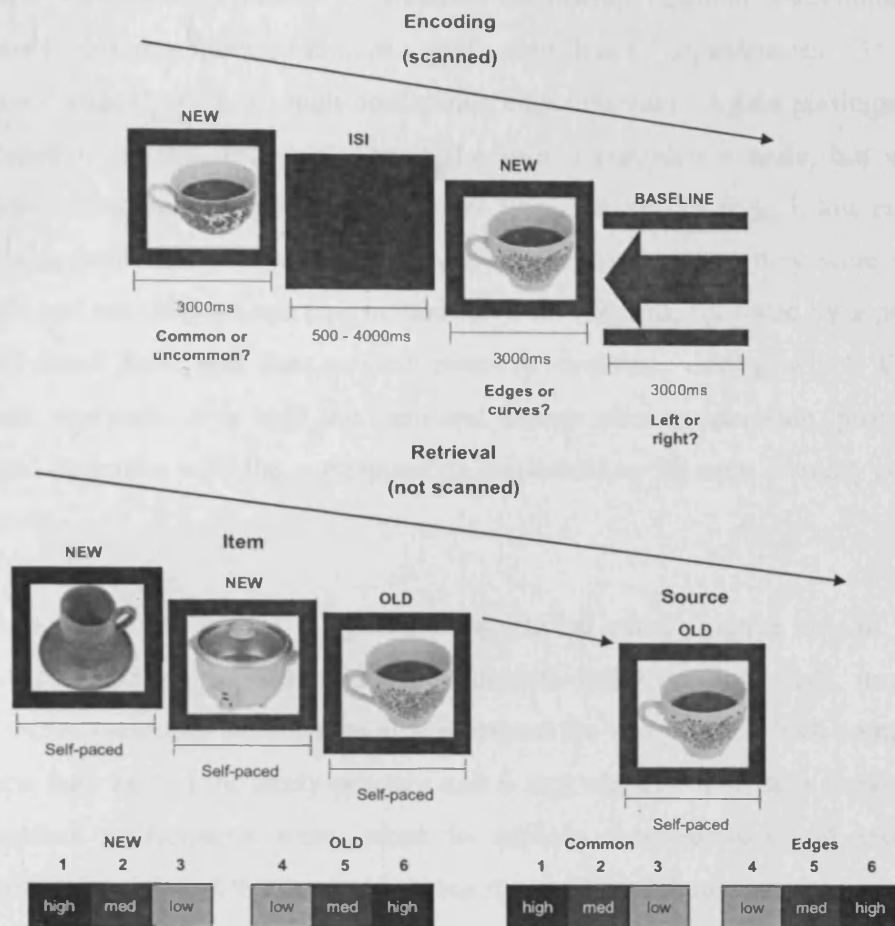


Figure 4.1: Stimuli and procedure. At encoding participants made common/uncommon or edges/curves judgements about novel objects. At retrieval participants were presented with previously studied and new objects and made old/new judgements to stimuli using a 6-point scale. For old judgements participants also had to indicate, using a 6-point confidence scale, which of the two tasks the item was originally presented in (1 = high confidence common, 2 = medium confidence common, 3 = low confidence common, 4 = low confidence edges, 5 = medium confidence edges, and 6 = high confidence edges).

indicate, using a 6-point scale, their confidence that the object was studied or new (1: high confidence new, 2: medium confidence new, 3: low confidence new, 4: low confidence old, 5: medium confidence old, 6: high confidence old). Participants were encouraged to make use of the entire scale (Yonelinas et al., 2005). Following this, if the participant responded new, the experiment automatically continued onto the next test trial. If the response was old, participants were prompted to make a source memory judgement, indicating if the item initially appeared in the common/uncommon or edges/curves task across a 6-point confidence scale (1: high

confidence common/uncommon, 2: medium confidence common/uncommon, 3: low confidence common/uncommon, 4: low confidence edges/curves, 5: medium confidence edges/curves, 6: high confidence edges/curves). Again participants were encouraged to spread responses across the source confidence scale, but were also specifically instructed to use low confidence response options (e.g. 3: low confidence common/uncommon or 4: low confidence edges/curves) when they were guessing. For each test trial objects were presented for a set 2500ms, followed by a prompt for the self-paced item and then source memory decision, during which the object remained onscreen. For both the item and source memory decision, prompts were presented on screen with the corresponding response key for each memory confidence judgement.

Prior to entering the MRI suite participants carried out a practice task of the study phase, where they were presented with 6 objects and 4 baseline trials, in a random order. After scanning, participants also practiced the test phase, which comprised the 6 objects they saw in the study practice and 6 new objects. For each response in the test practice participants were asked to explain their decision, to ensure they understood the task and the item and source memory confidence scales.

4.2.4. Functional localiser task and procedure

To create unbiased fROIs, the scanning protocol also included a functional localiser run, which was identical to the one used in Experiment 2 (see Section 3.2.4).

4.2.5. Scanning parameters

Experiment 2 scanning parameters were used in the current experiment (see Section 3.2.5 and 2.2.4).

4.2.6. fMRI data pre-processing

The same data pre-processing was used in all 3 experiments reported in this thesis (see Section 2.2.5 and 3.2.6).

4.3. *Data analysis*

4.3.1. *Whole-brain fMRI data analysis*

After pre-processing the three object encoding runs for each fMRI time series for each participant, the data were submitted to a (random effects) general linear model, with one predictor that was convolved with a standard model of the haemodynamic response function (HRF) for each event-type. The encoding trials were analysed both as a function of subsequent recognition memory confidence (item memory) and as a function of source memory performance (source memory). Separate regressors were, therefore, modelled for each event-type in the item and source memory analysis. For the item memory analysis, there were 6 regressors, one for each subsequent recognition memory confidence response: (a) subsequent high confidence hit (s6), (b) subsequent medium confidence hit (s5), (c) subsequent low confidence hit (s4), (d) subsequent low confidence miss (s3), (e) subsequent medium confidence miss (s2) and (f) subsequent high confidence miss (s1).

The formation of regressors in the source memory analysis was guided by factors of encoding task (conceptual/perceptual), subsequent source memory accuracy and source confidence (for hit-hit only¹¹). This resulted in 4 regressors for each encoding task (conceptual and perceptual). These were: (a) subsequent miss (sMM) - items labelled as new, (b) subsequent hit-miss (sHM) - items identified as old, but for which the source judgement was incorrect, (c) subsequent low confidence hit-hit (sLCHH) - items identified as old, which also received a correct low confidence source judgement, and (d) subsequent high confidence hit-hit (sHCHH) - items identified as old, which also received a correct high and medium confidence source judgement.

Parameter estimates relating the height of the HRF response to each regressor were calculated on a voxel by voxel basis, via a multiple linear regression of the response time-course, to create one beta image for each regressor per run, per participant. Individual runs were then concatenated for each participant in a fixed effects analysis using FEAT. The subsequent parameter estimate images were then combined in a higher-level (group) FLAME analysis (FMRIB's Local Analysis of Mixed Effects;

¹¹ There were not sufficient trial numbers to look at different levels of source confidence for hit-miss.

Beckmann et al., 2003; Woolrich et al., 2004). The whole-brain analysis for the current experiment is similar to that from Experiment 2 (see Section 3.3.2). To examine the relationship between encoding activity and graded increases in subsequent item familiarity for objects, a linear contrast was performed using the recognition memory confidence regressors ('s5' = +2, 's4' = +1, 's3' = 0, 's2' = -1, 's1' = -2: Ranganath et al., 2004). Brain regions sensitive to subsequent recollection were investigated by performing a contrast between high confidence hit and medium confidence hit ($s_6 > s_5$). To identify regions that were sensitive to subsequent source memory accuracy, separate source memory contrasts were performed between high confidence source hit-hit (sHCHH) and hit-miss (sHM) for the two encoding tasks (conceptual sHCHH > conceptual HM; perceptual sHCHH > perceptual HM). For the above contrasts, FEAT group (gaussianised) t-statistics were then converted to z-statistics and thresholded using a voxel significance level of $p < 0.001$, uncorrected for multiple comparisons. Only significant activations involving contiguous clusters of at least 9 voxels are reported, unless stated otherwise. These probability and extent thresholds are equivalent to a mapwise false-positive rate for the MTL (encompassing the hippocampus, parahippocampal gyrus and perirhinal cortex) of $p < 0.05$ (estimated using the Monte Carlo procedure implemented in the AlphaSim program in AFNI). Co-ordinates (x, y, z) of significant effects are reported in MNI space.

4.3.2. Functional region of interest (fROI) fMRI analysis

The fROIs were created using the object and scene trials from the functional localiser (see Section 3.3.3). To ensure consistency across the three experiments reported in this thesis, scene-sensitive fROIs were created and memory effects for objects were investigated within these. Voxels that showed greater activation for objects over scenes (Fig 4.2) were identified in the perirhinal cortex only (left peak: -32, -2, -40, $z = 3.32$, 71 voxels; right peak: 32, -8, -36, $z = 3.36$, 52 voxels). When compared with objects, scene-sensitive functional ROIs (Fig. 4.2) were identified in the hippocampus (left peak: -22, -12, -24, $z = 3.86$, 83 voxels; right peak: 24, -18, -18, $z = 4.57$, 174 voxels) and parahippocampal gyrus (left peak: -18, -36, -12, $z = 6.06$, 477 voxels; right peak: 20, -36, -12, $z = 7.36$, 594 voxels).

As with Experiment 2, separate fROI analyses were conducted to identify significant item confidence and source memory effects. Parameter estimate values were

extracted (using Featquery) for the 6 item confidence (s1 to s6) and 8 source memory regressors (sHCHH, sLCHH, sHM and sMM for conceptual and perceptual) contrasted to active-baseline trials, within each of the object and scene-sensitive MTL fROIs. Parameter estimate values were converted to percent signal change (see Section 3.3.3).

In order to identify linear increases in brain activity according to subsequent recognition memory confidence, the individual percent signal change values from the 6 item memory confidence regressors were entered into a 2*6 ANOVA with factors of 'hemisphere' (right vs. left) and 'memory' (high, medium, and low confidence hit and miss). If there was no significant hemisphere*memory interaction, effects were collapsed across hemisphere in subsequent analyses.

For the source memory analysis, percent signal change values for each source memory regressor (8) were entered in to a 2*2*4 ANOVA, with factors of 'hemisphere' (right vs. left), 'task' (conceptual vs. perceptual) and 'memory' (sHCHH, sLCHH, sHM and sMM). As with the item memory analyses, in the absence of an interaction involving hemisphere, effects were collapsed across this factor for subsequent analyses.

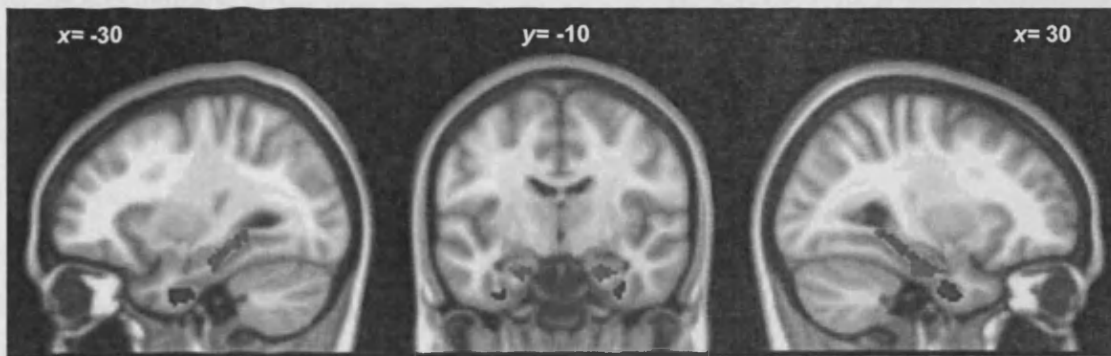


Figure 4.2: Left sagittal (left), coronal (middle) and right sagittal (right) views of functional ROIs located within the hippocampus (green), parahippocampal gyrus (pink) and perirhinal cortex (blue) derived from the object > scene (perirhinal cortex) and scene > object (hippocampus and parahippocampal gyrus) contrasts from the functional localiser.

4.4. Behavioural results

Overall old/new discrimination, as measured by $p(\text{hit})-p(\text{false alarm})$, was significantly above chance (0.49, SE = 0.26; $t(31) = 19.21$, $p < 0.01$). The hit rate was greater for the conceptual task than the perceptual task (conceptual: 0.71, SE = 0.02; perceptual: 0.59, SE = 0.02; $t(31) = 11.84$, $p < 0.01$). The mean response proportions and reaction times for each type of memory confidence judgement, for old (separated by task) and new items, are displayed in Table 4.1. As with Experiments 1 and 2, the distribution of responses, for old and new items, increased monotonically with confidence from correct to incorrect judgments and responses were faster for high confidence judgements (1 or 6), compared to low confidence judgements (3 or 4). Reaction times for item memory judgements, collapsed across confidence, did not differ according to task (conceptual: 1280, SE = 116; perceptual: 1229, SE = 98; $t(31) = 0.55$). During the encoding phase, however, the mean reaction time to items in the perceptual task was significantly faster (conceptual: 1780ms, SE = 55ms; perceptual: 1700ms, SE = 51ms; $t(31) = 2.33$, $p < 0.05$).

Source memory accuracy ($p(\text{hit-hit})/p(\text{hit})$) was above chance for both encoding tasks (conceptual: 0.73, SE = 0.02, $t(31) = 13.94$, $p < 0.01$; perceptual: 0.79, SE = 0.02, $t(31) = 15.05$, $p < 0.01$), and was higher for the perceptual task ($t(31) = 2.44$, $p < 0.05$). Source responses for the false alarms indicated a trend ($t(31) = 1.96$, $p = 0.06$) towards a bias to guess edges/curves (0.54, where no bias would be 0.50). Source memory accuracy at each level of source confidence for the two encoding tasks (Table 4.2) was significantly above chance (all $t(31) > 2.30$, $p < 0.05$). These data were entered into a 2*3 ANOVA with factors of 'task' (conceptual vs. perceptual) and 'confidence' (high, medium vs. low), revealing a significant task*confidence interaction ($F(2,62) = 3.61$, $p < 0.05$). For the conceptual task, pairwise comparisons revealed greater accuracy for high confidence vs. medium confidence ($t(31) = 6.71$, $p < 0.01$), high confidence vs. low confidence ($t(31) = 7.84$, $p < 0.01$) and medium confidence vs. low confidence responses ($t(31) = 3.68$, $p < 0.01$). For the perceptual task, response accuracy was greater for high confidence vs. medium confidence ($t(31) = 5.35$, $p < 0.01$), high confidence vs. low confidence ($t(31) = 7.32$, $p < 0.01$) and medium confidence vs. low confidence ($t(31) = 2.76$, $p = 0.01$). For pairwise comparisons

Table 4.1: Mean proportion of responses and reaction times across the confidence scale for old and new objects, separated by encoding task¹²

	Recognition judgements					
	1	2	3	4	5	6
<i>Proportion of responses</i>						
Conceptual old	0.08 (0.02)	0.10 (0.01)	0.11 (0.01)	0.14 (0.01)	0.22 (0.02)	0.35 (0.03)
Perceptual old	0.12 (0.02)	0.14 (0.01)	0.15 (0.01)	0.16 (0.01)	0.18 (0.02)	0.25 (0.03)
New	0.36 (0.04)	0.29 (0.02)	0.19 (0.02)	0.08 (0.01)	0.05 (0.01)	0.03 (0.01)
<i>Mean reaction time (ms)</i>						
Conceptual old	1074 (290)*	987 (98)	1302 (167)	2100 (408)	1315 (95)	965 (68)
Perceptual old	811 (136) ⁺	861 (71)	1191 (120)	1990 (265)	1456 (140)	1091 (97)
New	669 (45)	1042 (106)	1448 (194)	1826 (184)	1539 (138)	1453 (415)*

¹² The values shown are across-participant means with standard error in brackets. As some participants did not make all types of response to old, as well as new items, mean reaction times for * and ⁺ are based on 30 and 31 participants, respectively. Abbreviations: (1) high confidence new, (2) medium confidence new, (3) low confidence new, (4) low confidence old, (5) medium confidence old, (6) high confidence old.

made across the conceptual and perceptual tasks, source accuracy reliably differed for low confidence responses only ($t(31) = 3.63, p < 0.01$).

Table 4.2: Mean proportions and reaction times of correct source responses for objects that attracted a correct old judgment, separated by confidence and encoding task¹³

	Source confidence		
	High confidence	Med confidence	Low confidence
<i>Accuracy</i>			
Conceptual	0.90 (0.02)	0.70 (0.02)	0.56 (0.03)
Perceptual	0.90 (0.02)	0.77 (0.03)	0.70 (0.03)
<i>Mean reaction time (ms)</i>			
Conceptual	1568 (116)	2073 (127)	2352 (174)
Perceptual	1347 (121)	1885 (141)	2106 (161)

Reaction times for high, medium and low confidence hit-hit (HH), as well as hit-miss (HM conceptual: 1919, SE = 107; HM perceptual: 2020, SE = 144) for the two encoding tasks were entered into a 2*4 ANOVA with factors of 'task' (conceptual vs. perceptual) and 'source response' (high HH, medium HH, low HH vs. HM). Overall reaction times were significantly faster for items from the perceptual task, as indicated by a main effect of task (conceptual: 1978ms; perceptual: 1840ms; $F(1,31) = 4.93, p < 0.05$). There was also a main effect of source response ($F(3,93) = 20.90, p < 0.01$). Pairwise comparisons revealed reliable differences between reaction times for high confidence HH compared to medium confidence HH ($t(31) = 5.44, p < 0.01$), low confidence HH ($t(31) = 6.27, p < 0.01$) and HM ($t(31) = 5.15, p < 0.01$), medium confidence HH and low confidence HH ($t(31) = 2.22, p = 0.04$), and low confidence HH compared to HM ($t(31) = 3.24, p < 0.01$).

¹³ The values shown are across-participant means with standard error in brackets.

4.5. Functional imaging results

4.5.1. Whole-brain analysis

This experiment was designed to observe the brain regions associated with subsequent source memory encoding for objects. As with Experiment 2, for the whole-brain analysis there were contrasts between item confidence response regressors ($s_5 = +2$, $s_4 = +1$, $s_3 = 0$, $s_2 = -1$, $s_1 = -2$ and $s_6 > s_5$), and high confidence correct and incorrect source judgements (separately for the two encoding tasks; conceptual sHCHH > conceptual HM; perceptual sHCHH > perceptual HM).

Results from the whole-brain analyses are summarised in Fig. 4.3 and 4.4 and Tables 4.3-4.6. There was significant memory-related activity in the superior frontal gyrus, inferior frontal gyrus, precentral gyrus, lingual gyrus, fusiform gyrus, inferior temporal gyrus, and precuneus (as there was in Experiment 2, and in Ranganath et al., 2004). Replicating findings from Experiment 2, object memory encoding activated regions throughout the occipitotemporal and extrastriate cortices, known to make up the visual processing streams (fusiform cortex and occipital fusiform cortex, Haxby et al., 1991). There was also activity in the LOC, which is a region that is highly specialised for visual object processing (Kanwisher et al., 1996; Kanwisher, Woods et al., 1997; Malach et al., 1995). Notably, for the linear contrast across item memory regressors, effects were detected in the parahippocampal place area (PPA: using reported coordinates from Peelen & Downing, 2005; see Sections 2.6.1 and 3.5.1), which has been previously linked to spatial processing and was associated with memory only for scenes in Experiments 1 and 2. Due to the specific predictions of the current experiment, only significant effects in the MTL are discussed.

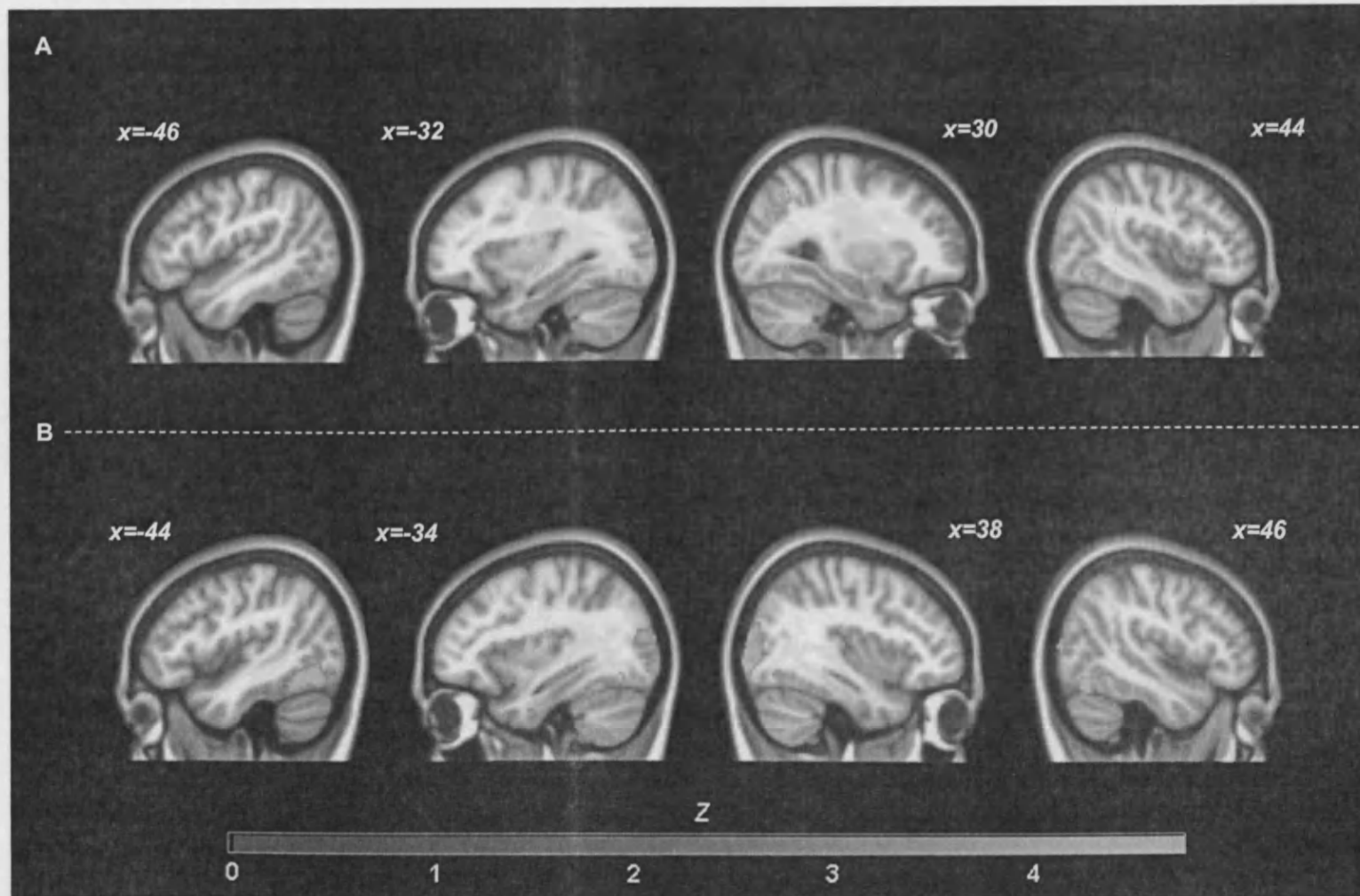


Figure 4.3: Significant memory encoding activity from the (A) linear contrast across recognition memory confidence regressors and (B) high confidence hit > medium confidence hit contrast. Images are overlaid onto a MNI-152 T1 2mm standard brain.

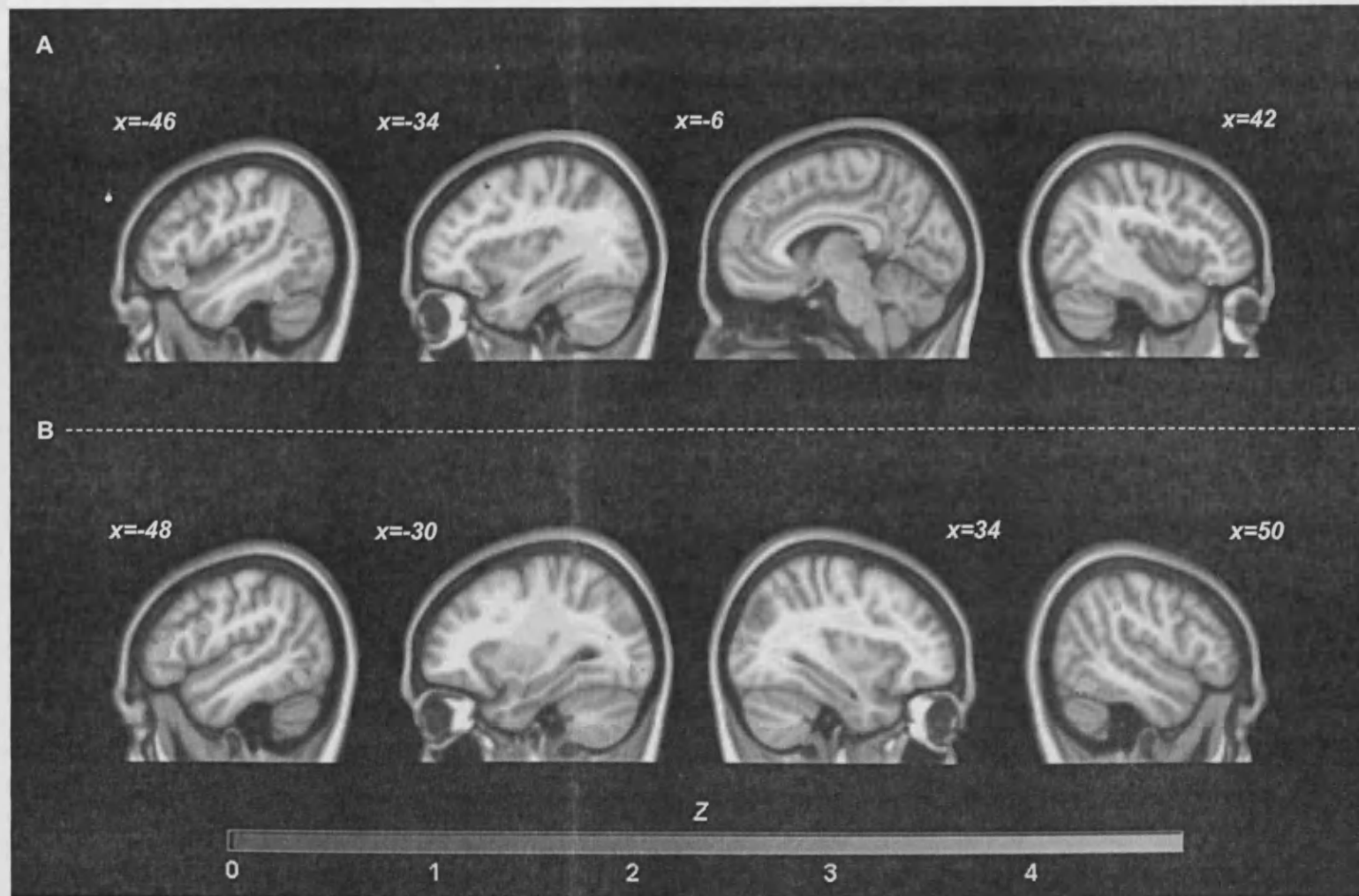


Figure 4.4: Significant memory encoding activity from the (A) conceptual high confidence hit-hit > conceptual hit-miss contrast and (B) perceptual high confidence hit-hit > perceptual hit-miss contrast. Images are overlaid onto a MNI-152 T1 2mm standard brain.

Table 4.3: Local maxima with regions according to the Harvard-Oxford sub-cortical structural atlas observed for the linear contrast across subsequent memory confidence ($p < 0.001$, cluster > 9 voxels).

Region				
	Z	x	y	z
<i>Left occipital pole</i>	3.57	-30	-96	10
<i>Right occipital pole</i>	3.74	38	-92	10
<i>Left lateral occipital cortex, inferior division</i>	3.84	-50	-70	-12
<i>Right lateral occipital cortex, inferior division</i>	3.34	40	-72	-14
<i>Left lateral occipital cortex, superior division</i>	3.60	-34	-88	14
<i>Right lateral occipital cortex, superior division</i>	3.88	28	-66	34
<i>Right occipital fusiform gyrus</i>	3.56	40	-68	-12
<i>Left temporal occipital fusiform cortex (PPA)</i>	4.04	-32	-46	-18
<i>Right temporal occipital fusiform cortex</i>	3.77	32	-60	-12
<i>Left inferior temporal gyrus, temporooccipital part</i>	3.21	-46	-58	-14
<i>Right inferior temporal gyrus, temporooccipital part</i>	4.57	48	-60	-10

Table 4.4: Local maxima with regions according to the Harvard-Oxford sub-cortical structural atlas observed for the subsequent high confidence $>$ medium confidence hit contrast ($p < 0.001$, cluster > 9 voxels).

Region				
	Z	x	y	z
<i>Left occipital pole</i>	3.77	-28	-96	-10
<i>Left lateral occipital cortex, superior division</i>	4.04	-34	-86	16
<i>Right lateral occipital cortex, superior division</i>	4.61	40	-88	12
<i>Left lateral occipital cortex, inferior division</i>	4.96	-46	-68	-12
<i>Right lateral occipital cortex, inferior division</i>	4.89	46	-66	-16
<i>Left temporal occipital fusiform cortex</i>	4.89	-44	-58	-14
<i>Left occipital fusiform gyrus</i>	3.55	-36	-72	-12
<i>Right occipital fusiform gyrus</i>	3.67	38	-70	-10
<i>Left temporal fusiform cortex, posterior division</i>	3.66	-30	-38	-20
<i>Left perirhinal cortex</i> ¹⁴	3.55	-32	-4	-36

¹⁴ Effects with a probability threshold of $p < 0.001$, cluster size > 6 voxels are equivalent to a mapwise false-positive rate for the perirhinal cortex mask of $p < 0.04$ (estimated using the Monte Carlo procedure implemented in the AlphaSim program in AFNI).

Table 4.5: Local maxima with regions according to the Harvard-Oxford sub-cortical structural atlas observed for the subsequent conceptual high confidence hit-hit > conceptual hit-miss contrast ($p < 0.001$, cluster > 9 voxels).

Region				
	Z	x	y	z
<i>Left frontal pole</i>	4.76	-8	58	20
<i>Left superior frontal gyrus</i>	4.87	-12	34	46
<i>Left middle frontal gyrus</i>	3.92	-44	6	46
<i>Left inferior frontal gyrus, pars opercularis</i>	3.62	-56	18	8
<i>Left frontal orbital cortex</i>	4.69	-46	24	-12
<i>Right frontal orbital cortex</i>	3.71	42	30	-18
<i>Left paracingulate gyrus</i>	3.94	-2	46	26
<i>Left precuneus cortex</i>	3.92	-4	-60	14
<i>Left cingulate gyrus, posterior division</i>	4.02	-2	-40	36
<i>Left lateral occipital cortex, superior division</i>	4.90	-48	-64	24
<i>Right lateral occipital cortex, inferior division</i>	3.28	44	-80	-10
<i>Right occipital fusiform gyrus</i>	3.78	42	-66	-22
<i>Left temporal occipital fusiform cortex</i>	3.28	-42	-56	-24
<i>Right temporal occipital fusiform cortex</i>	3.52	40	-48	-24
<i>Left temporal fusiform cortex, posterior division</i>	3.95	-44	-44	-26
<i>Right temporal fusiform cortex, posterior division</i>	3.71	32	-38	-20
<i>Left middle temporal gyrus, temporooccipital part</i>	4.54	-64	-46	-4
<i>Left middle temporal gyrus, posterior division</i>	4.69	-56	-42	-8
<i>Left middle temporal gyrus, anterior division</i>	3.90	-56	-8	-26
<i>Left inferior temporal gyrus, temporooccipital part</i>	3.86	-46	-48	-22
<i>Left inferior temporal gyrus, posterior division</i>	3.17	-52	-14	-24
<i>Left lingual gyrus</i>	3.88	-12	-52	-2
<i>Left parahippocampal gyrus, posterior division</i>	3.39	-24	-36	-18
<i>Left anterior temporal pole</i>	3.89	-32	16	-40

Table 4.6: Local maxima with regions according to the Harvard-Oxford sub-cortical structural atlas observed for the subsequent perceptual high confidence hit-hit > perceptual hit-miss contrast ($p < 0.001$, cluster > 9 voxels).

Region				
	Z	x	y	z
<i>Left frontal pole</i>	4.26	-50	42	0
<i>Right frontal pole</i>	3.70	46	38	10
<i>Left inferior frontal gyrus, pars opercularis</i>	3.19	-44	6	14
<i>Left inferior frontal gyrus, pars triangularis</i>	4.33	-50	34	8
<i>Left precentral gyrus</i>	4.67	-38	6	26
<i>Right precentral gyrus</i>	3.35	42	4	28
<i>Right supramarginal gyrus, posterior division</i>	3.69	48	-36	40
<i>Left occipital pole</i>	3.96	-36	-92	-6
<i>Right occipital pole</i>	3.51	32	-92	-6
<i>Left lateral occipital cortex, superior division</i>	3.54	-24	-72	38
<i>Right lateral occipital cortex, superior division</i>	3.94	36	-86	20
<i>Left lateral occipital cortex, inferior division</i>	3.50	-30	-86	-8
<i>Right lateral occipital cortex, inferior division</i>	3.75	46	-62	-10
<i>Left inferior temporal gyrus, temporooccipital part</i>	4.39	-50	-62	-10
<i>Right inferior temporal gyrus, temporooccipital part</i>	4.50	52	-56	-16

4.5.1.1. MTL effects

In the left perirhinal cortex there was a group of voxels that showed greater activity for subsequent high confidence hit relative to subsequent medium confidence hit ($s_6 > s_5$; see Fig. 4.3 and Table 4.4). This cluster comprised 6 voxels ($p < 0.001$), which falls below the 9 voxel cluster size threshold that is equivalent to a mapwise false-positive rate of $p < 0.05$ for the combined hippocampal, parahippocampal gyrus and perirhinal cortex MTL mask (estimated using the Monte Carlo procedure implemented in the AlphaSim program in AFNI). If the Monte Carlo correction is restricted to just the perirhinal cortex mask (defined using the probabilistic map derived from Devlin & Price, 2007; see Sections 2.3.3 and Fig. 2.3), however, a cluster-extent of 6 voxels is equivalent to a mapwise false-positive rate of $p < 0.04$ (also estimated using the AFNI Monte Carlo procedure). To investigate the pattern of memory-related activity within this group of significant perirhinal cortex voxels, parameter estimate values were extracted for each level of subsequent recognition confidence (Fig. 4.5A). Values were entered into a repeated measures ANOVA with

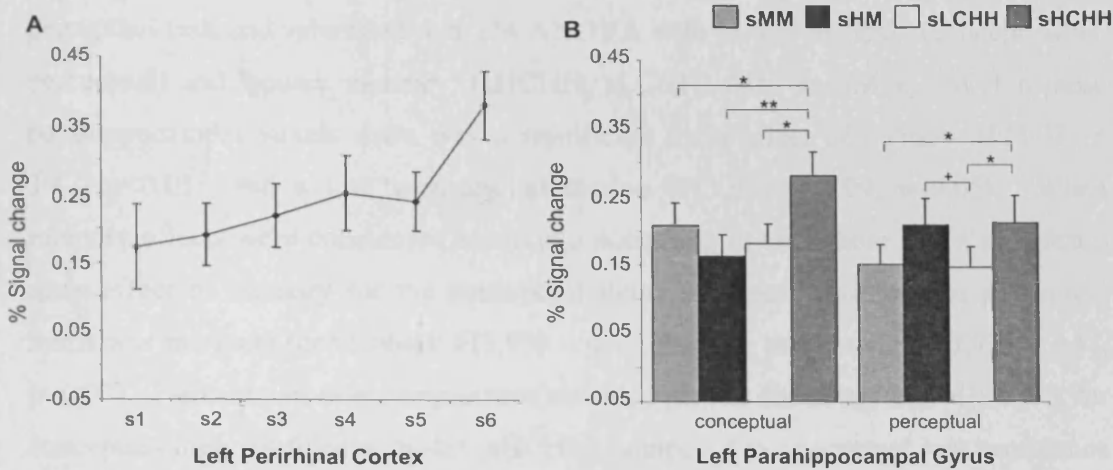


Figure 4.5: Patterns of memory encoding activity for (A) recognition confidence for objects revealed by the high confidence hit > medium confidence hit contrast in the left perirhinal cortex, and (B) source memory accuracy for objects revealed by the high confidence hit-hit > hit-miss contrast in the left posterior parahippocampal gyrus. Abbreviations: (s1) subsequent high confidence miss, (s2) subsequent medium confidence miss, (s3) subsequent low confidence miss, (s4) subsequent low confidence hit, (s5) subsequent medium confidence hit, and (s6) subsequent high confidence hit; (sMM) subsequent miss (light grey), (sHM) subsequent hit-miss (black), (sLCHH) subsequent low confidence hit-hit (white) and (sHCHH) subsequent high confidence hit-hit (dark grey). + $p \leq 0.07$; * $p < 0.05$; ** $p < 0.01$.

6 levels of memory (s1 to s6), revealing a significant main effect of memory ($F(5,155) = 4.74, p < 0.01$) and a linear trend ($F(1,31) = 15.14, p < 0.01$). Although the quadratic trend was not reliable ($F(1,31) = 1.85$), pairwise comparisons revealed that activity within these perirhinal cortex voxels showed the following pattern; $s6 > s5 = s4 = s3 = s2 = s1$ (see Fig 4.5A). Encoding activation for high confidence hit (s6) was greater than all other levels of memory response ($s6 > s5: t(31) = 5.86, p < 0.01$; $s6 > s4: t(31) = 3.61, p < 0.01$; $s6 > s3: t(31) = 3.51, p < 0.01$; $s6 > s2: t(31) = 4.16, p < 0.01$; $s6 > s1: t(31) = 4.08, p < 0.01$). No other pairwise comparisons between subsequent item confidence regressors were significant within these perirhinal cortex voxels.

Within the left posterior parahippocampal gyrus there was a reliable effect of source memory encoding for the conceptual task (conceptual sHCHH > conceptual sHM: see Fig 4.4 and Table 4.5). As with effects in the perirhinal cortex, subsequent analyses were conducted to investigate the specific pattern of source memory-related activity for the conceptual and perceptual tasks within these significant voxels (Fig. 4.5B). Values for each source memory regressor were extracted for the conceptual and

perceptual task and submitted to a 2*4 ANOVA with factors of ‘task’ (conceptual vs. perceptual) and ‘source memory’ (sHCHH, sLCHH, sHM vs. sMM). Within these parahippocampal voxels there was a significant main effect of memory ($F(3,93) = 3.47, p < 0.05$), and a task*memory interaction ($F(3,93) = 3.09, p < 0.05$). When memory effects were considered separately according to task, there was a significant main effect of memory for the conceptual items, whereas the effect for perceptual items was marginal (conceptual: $F(3,93) = 4.40, p < 0.01$; perceptual: $F(3,93) = 2.42, p = 0.07$). Planned pairwise comparisons revealed greater encoding-related activity for conceptual high confidence hit-hit (sHCHH) compared to conceptual low confidence hit-hit (sLCHH), hit-miss and miss (sHCHH > sLCHH: $t(31) = 2.65, p < 0.05$; sHCHH > sHM: $t(31) = 4.45, p < 0.01$; sHCHH > sMM: $t(31) = 2.11, p < 0.05$). For the perceptual task, there were differences between sHCHH and sLCHH, sHCHH and sMM, and a marginal difference between sLCHH and sHM (sHCHH > sLCHH: $t(31) = 2.07, p < 0.05$; sHCHH > sMM: $t(31) = 2.21, p < 0.05$; sHM > sLCHH: $t(31) = 1.89, p = 0.07$).

4.5.2. Functional region of interest analysis

4.5.2.1. Subsequent item memory effects

As with Experiment 2, item memory effects according to subsequent recognition confidence were investigated within MTL functional ROIs that showed a greater response to scenes compared to objects (hippocampus and parahippocampal gyrus), and objects compared to scenes (perirhinal cortex), the results of which are summarised in Fig. 4.6. Within each of the scene-sensitive fROIs (Fig. 4.6A and B), there were no significant patterns of activity that related to subsequent item memory ($F(5,155) < 0.73$).

Within the object-sensitive perirhinal cortex voxels (Fig. 4.6C), there was a main effect of memory ($F(5,155) = 3.38, p < 0.01$), which demonstrated a reliable linear trend ($F(1,31) = 11.71, p < 0.01$). Planned pairwise comparisons revealed greater encoding-related activity for: (a) high confidence hit (s6) relative to low (s3), medium (s2) and high confidence (s1) miss (s6 > s3: $t(31) = 3.49, p < 0.01$; s6 > s2: $t(31) = 3.24, p < 0.01$; s6 > s1: $t(31) = 2.54, p < 0.05$), (b) medium confidence hit (s5) relative to low and high confidence miss (s5 > s3: $t(31) = 2.27, p < 0.05$; s5 > s1: $t(31) = 2.14, p < 0.05$ and (c) low confidence hit (s4) relative to low confidence miss (s4 > s3: $t(31) = 2.26, p < 0.05$; as well as a trend for s4 > s1: $t(31) = 1.79, p = 0.08$).

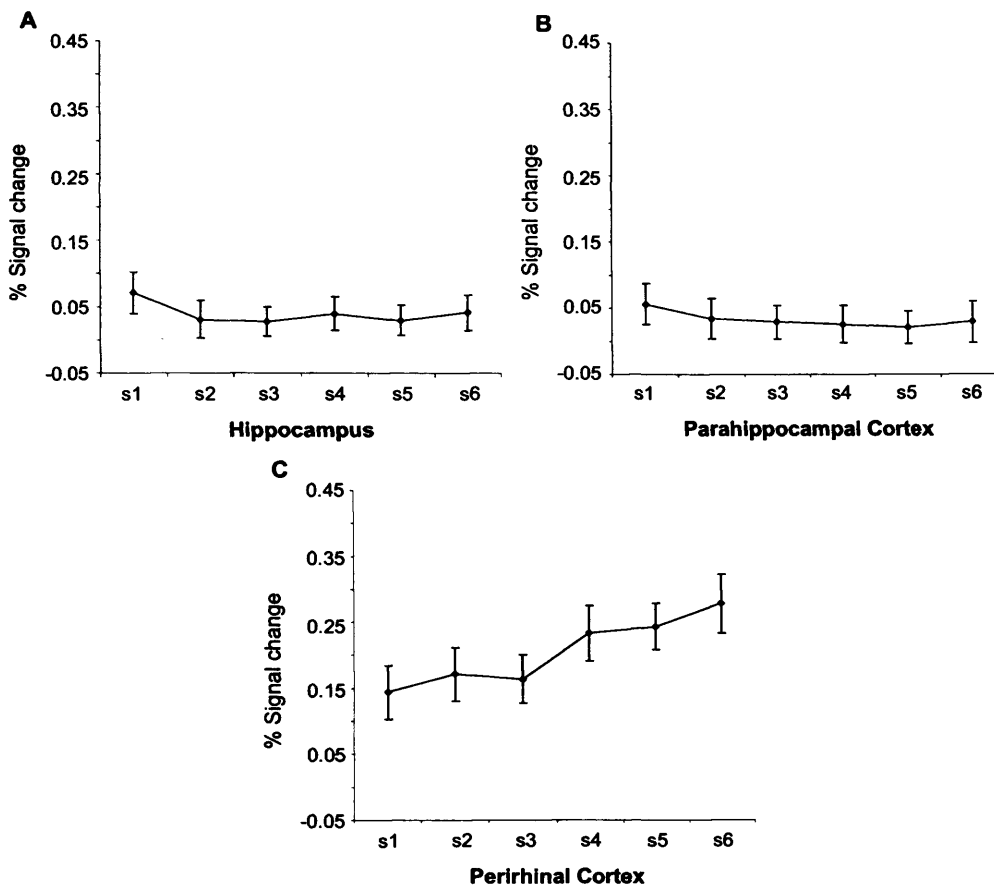


Figure 4.6: Patterns of memory encoding activity relating to recognition confidence for objects and scenes in functionally defined MTL regions of interest from (A, B) scenes > objects and (C) objects > scenes. Percent signal change (arbitrary units) in the (A) hippocampus, (B) parahippocampal gyrus, and (C) perirhinal cortex. Abbreviations: (s1) subsequent high confidence miss, (s2) subsequent medium confidence miss, (s3) subsequent low confidence miss, (s4) subsequent low confidence hit, (s5) subsequent medium confidence hit, and (s6) subsequent high confidence hit.

4.5.2.2. Subsequent source memory effects

The second stage of the fROI analyses was to investigate patterns of subsequent source memory within the parahippocampal and hippocampal scene-sensitive voxels, and the perirhinal cortex object-sensitive voxels (Fig. 4.7). In the scene-sensitive hippocampal fROIs (Fig. 4.7A and B) there was a significant hemisphere*task*memory interaction ($F(3,93) = 2.78, p < 0.05$). To follow up this interaction, memory effects were considered separately according to encoding task

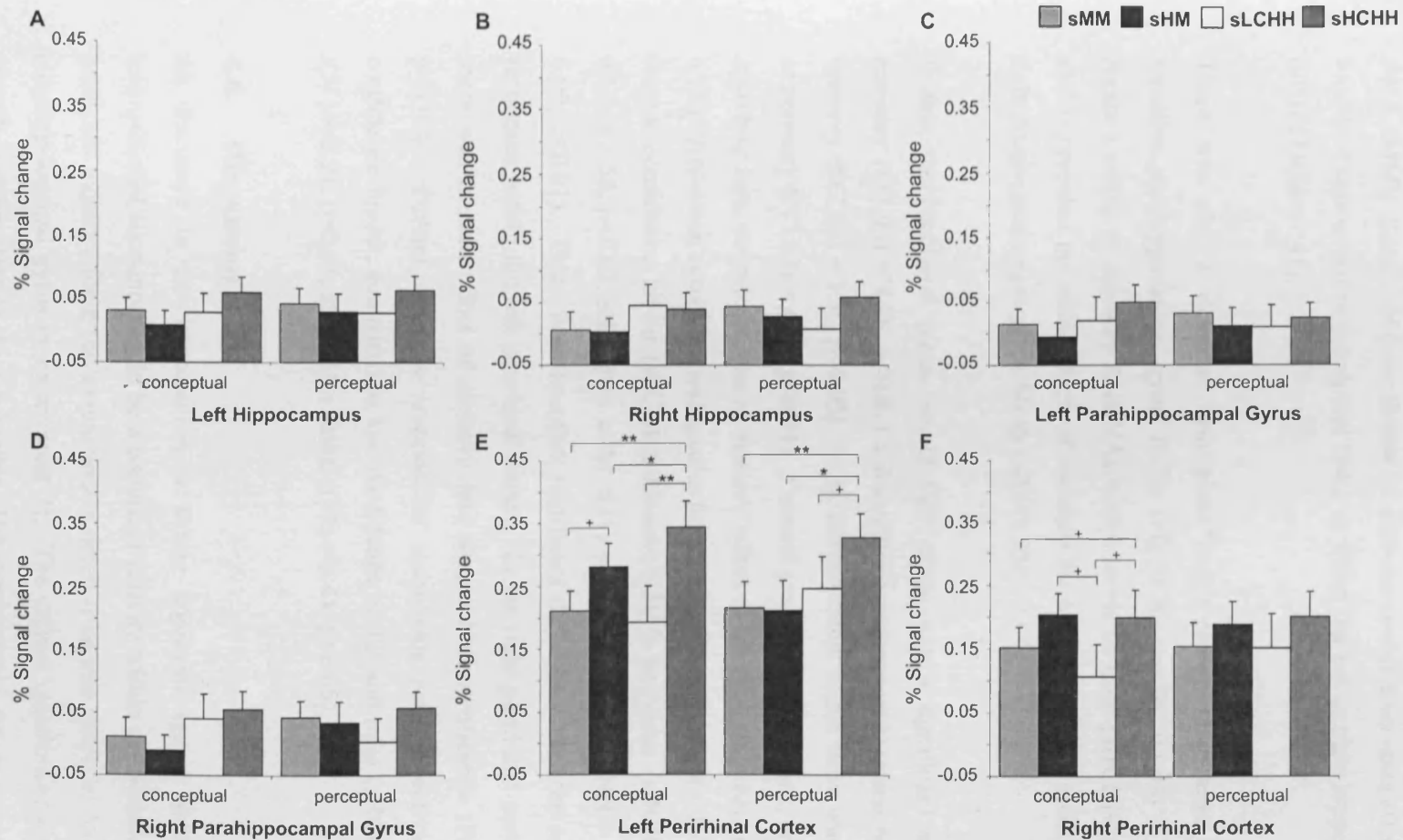


Figure 4.7: Patterns of memory encoding activity separated according to source memory accuracy for objects in functionally defined MTL regions of interest from (A, B, C, D) scenes > objects and (E, F) objects > scenes. Percent signal change (arbitrary units) in the (A) left hippocampus, (B) right hippocampus, (C) left parahippocampal gyrus, (D) right parahippocampal gyrus, (E) left perirhinal cortex and (F) right perirhinal cortex. Abbreviations: (sMM) subsequent miss (light grey), (sHM) subsequent hit-miss (black), (sLCHH) subsequent low confidence hit-hit (white) and (sHCHH) subsequent high confidence hit-hit (dark grey). + $p \leq 0.09$; * $p < 0.05$; ** $p < 0.01$.

(conceptual and perceptual), within the left and right hippocampal fROIs by conducting a series of one-way ANOVAs with 4 levels on each (sHCHH, sLCHH, sHM, sMM). Results of these follow up analyses revealed no main effects of memory for either conceptual or perceptual tasks, in either the left or right hippocampal fROIs (all $F(3,93) < 1.41$).

There was also a marginal hemisphere*task*memory interaction in the scene-sensitive parahippocampal gyrus fROIs (Fig. 4.7C and D; $F(3,93) = 2.42, p=0.07$). Again a series of one-way ANOVAs with 4 levels on each (sHCHH, sLCHH, sHM, sMM) revealed no main effects of memory for either encoding tasks, in the left or right parahippocampal gyrus fROIs (all $F(3,93) < 1.94$).

Within the perirhinal cortex object fROI there was a significant main effect of memory ($F(3,93) = 4.76, p<0.01$) and a reliable interaction between hemisphere and memory ($F(3,93) = 3.30, p<0.05$). In the left perirhinal cortex there was a main effect of memory ($F(3,93) = 6.30, p<0.01$). Planned pairwise comparisons, collapsed across encoding task, revealed a source memory effect in the left perirhinal cortex (see Fig. 4.7E). Encoding activation was greater for high confidence hit-hit (sHCHH), relative to low confidence hit-hit (sLCHH), hit-miss (sHM) and miss (sHCHH > sLCHH: $t(31) = 3.59, p<0.01$; sHCHH > sHM: $t(31) = 2.91, p<0.01$; sHCHH > sMM: $t(31) = 6.09, p<0.01$). There were no other significant differences between source memory responses within the left perirhinal cortex. In the right perirhinal cortex (Fig. 4.7F) there was a main effect of memory that approached significance ($F(3,93) = 2.47, p=0.07$). Further analyses revealed an ambiguous pattern; activation for high confidence hit-hit, compared to low confidence hit-hit and miss (sHCHH > sLCHH: $t(31) = 2.21, p<0.05$; sHCHH > sMM: $t(31) = 2.41, p<0.05$).

4.6. Discussion

As discussed in the Introduction, a strong argument against dual-process and informational accounts would be a pattern of activity within the perirhinal cortex that predicted memory for a contextual source detail (like that observed for scenes in the parahippocampal gyrus in Experiment 2). The current experiment was designed to provide a strong test of these accounts. The experimental design, which was largely

based on Experiment 2 (and on Ranganath et al., 2004), required participants to make item and source memory judgements to previously studied, and new, objects. As with Experiment 2, the design used in the current experiment permitted the measurement and comparison of changes in activity according to the accuracy of contextual source memory judgements, as well as item response confidence. The current experiment differed from previous studies, however, as (a) source judgements were also made on a 6-point confidence scale (to reduce the contamination of source guesses to the analyses), (b) the stimulus materials (objects) contained more overlapping visual features than the objects from the previous experiment (they were more featurally ambiguous: Bussey & Saksida, 2005; Cowell et al., 2010; Graham et al., 2010; Saksida & Bussey, 2010) and (c) one of the encoding tasks (which served as the criterial source information at retrieval) was included to directly encourage participants to process the visual features of the presented objects.

Under these experimental manipulations, encoding activity within the perirhinal cortex showed a pattern across subsequent recognition confidence responses that has been previously linked to recollection (Cohn et al., 2009; Daselaar et al., 2006; Yonelinas et al., 2005), and that also reflected success for the contextual source memory judgement (Davachi et al., 2003; Ranganath et al., 2004). In the following sections I have (a) summarised these memory effects, (b) discussed the data points in light of the specific predictions laid out in the Introduction and (c) evaluated how the current findings can be accommodated by different models of MTL function.

4.6.1. Summary of findings

4.6.1.1. Source confidence

In contrast to Experiment 2, participants made their source judgements on a 6-point confidence scale, which was implemented to allow the removal of low confidence source judgements from the analyses. Behaviourally, for false alarms there was a marginal bias to indicate that items were presented in the perceptual rather than the conceptual task ($p=0.06$), and the source accuracy advantage for perceptual compared to conceptual items was driven primarily by differences between the levels of accuracy for low confidence responses (see Section 4.4 and Table 4.2).

For both encoding tasks, accuracy for low confidence source judgements was significantly above chance (perceptual: 0.70 and conceptual: 0.56), making it unlikely that all low confidence responses were guesses. In combination, these data indicate a graded relationship between confidence and source accuracy, which is consistent with the view that recollection, like familiarity, is a continuous process (Mickes, Wais & Wixted, 2009; Slotnick, 2010; Wixted, 2007; Wixted & Stretch, 2004). These behavioural data are not consistent with the classic dual-process signal detection view which models recollection as a threshold/categorical process (see Section 1.4.1.3; Yonelinas, 1994; 2002; Yonelinas & Parks, 2007). One possibility is that above chance accuracy for low confidence source responses in this task reflects the contribution of familiarity to source discriminations (Diana et al., 2008; Diana et al., 2010; Haskins et al., 2008; Quamme et al., 2007; Yonelinas et al., 1999), although as already noted current dual-process accounts have not incorporated familiarity-based contributions to memory for novel item-context associations (see later Section 4.6.3).

Irrespective of the validity of the considerations given above, however, it remains reasonable to assume that the removal of low confidence source hits from the fMRI analyses will permit a stronger contrast when the intention is to identify brain regions that contribute to accurate source judgments of the kind required in this experiment. Notably, for the source memory effects detailed below (left posterior parahippocampal gyrus: Section 4.6.1.2; and left perirhinal cortex: Section 4.6.1.3), activity associated with subsequent low confidence hit-hit (sLCHH) was significantly lower than subsequent high confidence hit-hit (sHCHH) and, in fact, looked more similar to activity relating to subsequent miss (sMM). These observations are important as the inclusion of low confidence source responses in an overall hit-hit response category could have occluded source memory effects (e.g. an average of high confidence hit-hit > low confidence hit-hit = hit-miss could look like hit-hit = hit-miss).

4.6.1.2. Whole-brain analysis

In keeping with Experiment 2, for the whole-brain analysis, regions associated with familiarity were investigated via linear contrasts across recognition confidence regressors ($s_5 = +2$, $s_4 = +1$, $s_3 = 0$, $s_2 = -1$, $s_1 = -2$). A contrast between items later remembered with high confidence or medium confidence was performed to identify

regions relating to recollection ($s_6 > s_5$). In the current experiment, to elucidate regions associated with contextual source memory encoding, there were also separate contrasts according to subsequent source memory accuracy for items encoded in the conceptual (common/uncommon) and perceptual (edges/curves) encoding tasks. These contrasts comprised a comparison between items that elicited a correct source judgement with high confidence (sHCHH) and those for which the source judgement was incorrect (conceptual sHCHH > conceptual sHM and perceptual sHCHH > perceptual sHM).

Within the MTL, there was a significant effect for high confidence compared to medium confidence hit ($s_6 > s_5$) in the left perirhinal cortex. Further investigation of memory effects within the perirhinal voxels yielded by this contrast revealed greater encoding activity for high confidence hit, compared to medium and low confidence hit, and high, medium and low confidence miss ($s_6 > s_5 = s_4 = s_3 = s_2 = s_1$). According to a dual-process signal detection (DPSD) account, recollection is a threshold process that is commonly endorsed by high confidence memory judgments (Yonelinas, 1994; Yonelinas, 2001b; Yonelinas et al., 2005). As such, a non-linear fMRI signal that exhibits a steep increase in activity for high confidence judgements relative to all other levels of recognition confidence, like that observed in the perirhinal cortex in the current experiment, has been linked to recollection (Cohn et al., 2009; Daselaar et al., 2006; Yonelinas et al., 2005).

Results from the whole-brain analyses also revealed significant activation for the conceptual high confidence hit-hit > conceptual hit-miss contrast in the left posterior parahippocampal gyrus. Follow up analyses of source memory effects within these parahippocampal voxels revealed a significant task*memory interaction; there was a significant main effect of memory for items encoded in the conceptual task, whereas the effect memory for items from the perceptual task was marginal. For the conceptual task, encoding activity for high confidence hit-hit (sHCHH) was greater than low confidence hit-hit (sLCHH), hit-miss and miss (sHCHH > sLCHH = sHM = sMM), thus reflecting contextual source memory encoding for the conceptual task (Davachi et al., 2003; Ranganath et al., 2004; Staresina & Davachi, 2006; 2008). When the pattern of memory effects was considered for the perceptual task, however, activity was greater for sHCHH compared to sLCHH and sMM, sHM compared to

sLCHH, and there was no difference between sHCHH and sHM, and sHM and sMM (sHCHH > sLCHH < sHM = sMM). The pattern of memory-related activity for the perceptual task, therefore, was ambiguous and cannot be confidently labelled as reflecting contextual source or item memory processing.

4.6.1.3. *Functional region of interest analysis*

As the current experiment was designed to investigate patterns of memory-related activity for objects within the MTL, directed analyses were conducted within object-sensitive MTL functional regions of interest (fROI), which were created using trials from an orthogonal functional localiser task (see Sections 3.2.4 and 3.3.3). Object-sensitive fROIs were identified in the perirhinal cortex only. To remain consistent with Experiments 1 and 2, however, memory effects for objects were also investigated within scene-sensitive fROIs identified in the hippocampus and parahippocampal gyrus. Separate analyses were conducted within these object- and scene-sensitive fROIs to isolate changes in activity according to subsequent item response confidence (item memory analysis), as well as subsequent contextual source memory accuracy (source memory analysis). In both of these analyses, significant effects of memory were evident only in the perirhinal cortex object fROIs.

Within the perirhinal cortex, there was an interaction between hemisphere and source memory effects. In the left perirhinal fROI there was a main effect of memory, which showed greater activity for high confidence hit-hit compared to all other levels of source memory response (sHCHH > sLCHH = sHM = sMM). Effects in the left perirhinal cortex, therefore, followed a pattern that has been previously linked to successful contextual source memory encoding (Davachi et al., 2003; Ranganath et al., 2004; Staresina & Davachi, 2006; 2008). In the right perirhinal fROI, the main effect of memory was marginal and the pattern of response was ambiguous; there was only a significant difference between high and low confidence hit-hit, and high confidence hit-hit and miss (sHCHH > sLCHH; sHCHH > sMM; sHCHH = sHM). As a result, effects in the right perirhinal cortex will not be discussed further. Notably, there were no significant task*memory interactions within the left or right perirhinal cortex, like those seen in the posterior parahippocampal gyrus in the whole-brain analyses.

The general pattern from the item memory analysis within the perirhinal cortex was an overall hit versus miss effect ($s_6 = s_5 = s_4 > s_3 = s_2 = s_1$), which increased linearly with recognition confidence (as evidenced by a significant linear trend). This item memory effect was similar to that identified in the perirhinal cortex for objects in the previous experiment, and has been previously associated with familiarity (Davachi, 2003; Kensinger & Schacter, 2006). In sum, the patterns of results from the item and source memory analyses were inconsistent, and could lead to alternative conclusions regarding memory processing within the perirhinal cortex. Additional analyses detailed below (see Appendix A), however, offer one straight-forward explanation that can accommodate these discrepancies.

Given that there were hemisphere differences between source memory effects in the perirhinal cortex, a potentially useful way of understanding the inconsistent source and item results is to also separate item memory effects according to hemisphere. Appendix A shows the analyses of item memory effects in the perirhinal cortex fROI. These additional analyses confirmed that, despite there being no interaction between hemisphere and item memory in the perirhinal cortex, significant item memory effects were only evident in the left hemisphere (see Appendix A). In addition to showing a trend towards an overall hit versus miss effect, encoding activity in the left perirhinal cortex was also greater for high confidence hit relative to low and medium confidence hit, whereas activity for medium and low confidence hit did not differ ($s_6 > s_5 = s_4 >$

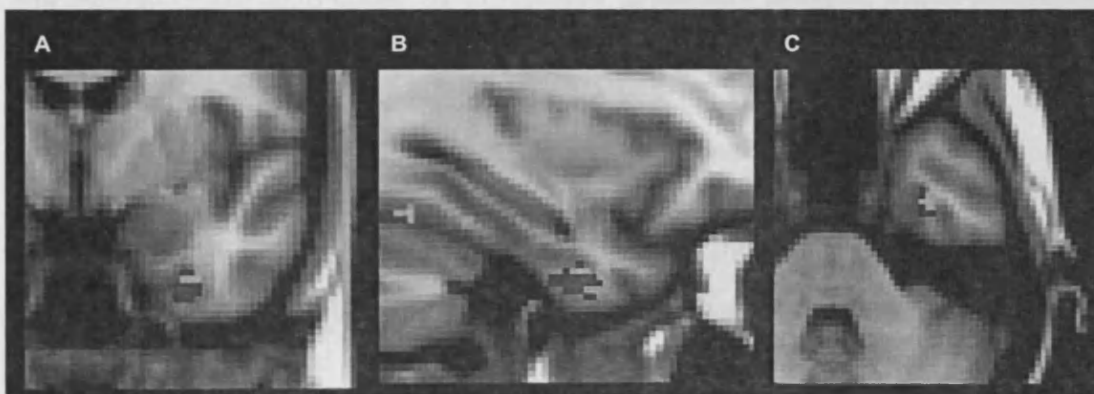


Figure 4.8: Magnified (A) coronal (left), (B) sagittal (middle) and (C) axial (right) slices of a standard MNI-152 T1 2mm brain with significant activation from the high confidence hit > medium confidence hit contrast (yellow) overlaid on the left perirhinal cortex object-sensitive fROI (blue). This indicates the degree of overlap between significant voxels for the $s_6 > s_5$ contrast and the perirhinal cortex fROI.

$s_3 = s_2 = s_1$). Furthermore, in the whole-brain analysis there was a pattern that reflected recollection in the left perirhinal cortex ($s_6 > s_5 = s_4 = s_3 = s_2 = s_1$; see Fig 4.3B and 4.5A), which comprised a subset of the functional ROI voxels derived from the orthogonal functional localiser (see Fig. 4.8). These additional analyses showed similarities between significant item and source memory effects within the left perirhinal cortex fROI, which were consistent with findings that have been previously linked to recollection; activity was greater for high confidence hit, relative to all other confidence responses (Cohn et al., 2009; Daselaar et al., 2006; Yonelinas et al., 2005) and high confidence source hit, relative to all other source responses (Davachi et al., 2003; Kensinger & Schacter, 2006; Ranganath et al., 2004; Staresina & Davachi, 2006; 2008).

4.6.2. Implications for a strength account

There is a substantial body of neuropsychological and fMRI research that supports a dual-process neuro-anatomical model of MTL function; the hippocampus has been consistently linked to recollection-based judgements and memory for novel associations, and the perirhinal cortex to familiarity-based recognition and item memory (e.g. Aggleton et al., 2005; Cohn et al., 2009; Davachi et al., 2003; Henson et al., 1999; Johnson & Rugg, 2007; Montaldi et al., 2006; Yonelinas et al., 1998; Yonelinas et al., 2002; Yonelinas et al., 2005). According to Squire et al. (2007), however, behavioural techniques used to correlate neural activity with recollection and familiarity are confounded by differences in memory strength, which ultimately leads to the incorrect characterisation of strong and weak memories as recollection and familiarity, respectively (see Sections 1.4.1 and 1.4.4, as well as Kirwan et al., 2008; Wais et al., 2010; although see Cohn et al., 2009). An additional proposition of a strength-based account is that dissociations between neural activity in the hippocampus and perirhinal cortex could reflect regional differences in the relationship between the fMRI signal and memory strength, as opposed to qualitative distinctions in mnemonic processing. As discussed in the Introduction of this chapter (see also Section 3.6.4 and Fig. 3.11), patterns of activity in the hippocampus associated with recollection could result from a non-linear relationship between BOLD and memory strength. In contrast, familiarity-like monotonic changes in brain activity commonly observed in the perirhinal cortex (that increase at encoding and decrease at retrieval), could arise due to a linear relationship between BOLD and

memory strength, which plateaus for strong memories (high confidence or correct source judgements).

A non-linear recollection-like pattern of neural activity in the perirhinal cortex that relates to the accuracy of contextual source memory judgements, and item response confidence, is not in keeping with this strength view. Furthermore, a strength account would assume that low confidence source hits will have a higher level of memory strength associated with them than hit-misses or misses. Where a strength account would predict a linear increase in activity from miss to high confidence hit-hit in the perirhinal cortex ($sHCHH > sLCHH > sHM > sMM$), here, however, activity for low confidence hit-hit was lower than high confidence hit-hit, and did not differ from hit-miss or miss ($sHCHH > sLCHH = sHM = sMM$). The data in the current experiment, therefore, bolsters arguments for the inadequacy of the strength-based/unitary account (see also Diana et al., 2010), at least in reference to assumptions about different patterns of BOLD across MTL regions.

4.6.3. Implications for dual-process and informational accounts

Based on certain aspects of dual-process accounts there are recent suggestions for how the perirhinal cortex can support memory for novel associations via a familiarity signal (e.g. unitisation: Diana et al., 2008; Quamme et al., 2007; Yonelinas et al., 1999 or Domain Dichotomy: Mayes et al., 2004; Mayes et al., 2007). Moreover, informational accounts also postulate that the perirhinal cortex can support recollection for item-related mnemonic details (Davachi, 2006; Diana et al., 2007; Diana et al., 2010; Staresina & Davachi, 2006; 2008). These ideas were covered in the Introduction of this Chapter (see also Section 1.5) and are recapitulated briefly below.

It has been proposed that the perirhinal cortex can support associative memory for configurally bound item-item feature representations by means of unitisation (see Section 4.1; Diana et al., 2008; Haskins et al., 2008, Quamme et al., 2007; Yonelinas et al., 1999). Unitisation is the integration of separate features into a single unit, and as a result, it is assumed that memory for configurally bound item-item feature representations can be supported by familiarity. Perirhinal cortex contributions to associative memory via familiarity are supported by observations that (a) unitisation

can ameliorate associative memory deficits in individuals with focal hippocampal damage (Quamme et al., 2007), (b) encoding activity in the perirhinal cortex for unitised word pairs is greater than for non-unitised word pairs (Haskins et al., 2008), and (c) associative memory ROCs for unitised word pairs are curvilinear (Diana et al., 2008; Haskins et al., 2008; Sauvage et al., 2008). It is notable, however, that most examples of associative memory effects within the perirhinal cortex have been for item-item feature representations (e.g. word-word and word-colour); it is currently unclear, therefore, whether item-context relations can or cannot be unitised. Also under-specified are the circumstances under which unitisation between item-based and contextual information is likely to occur.

There is another model of MTL function (DD: Mayes et al., 2007) which, in addition to mapping recollection and familiarity on to hippocampal and perirhinal cortex function (respectively) suggests that the formation of associative representations is contingent upon the amount of information that can be bound together within a given MTL structure. According to this account, the perirhinal cortex can form links between proximal representations of items from the same processing domain (also known as within-domain associations). Consequently, perirhinal cortex can support memory for *non-unitised* (as well as unitised) within-domain associations, which comprise two separate, but highly related, mnemonic representations (see Fig. 1.20). Perirhinal cortex cannot, however, support memory for associations (via familiarity), for which the representations are relatively distal. Between-domain (or item and context) associations are the principle example of this type, and thus ‘converge mainly, if not solely within the hippocampus’ (Mayes et al., 2007, pp. 127) and rely on recollection. Support for DD comes from observations that patients with focal lesions to the hippocampus show a relative sparing for within-, compared to between-domain item-item associative memory (Mayes et al., 2004; Vargha-Khadem et al., 1997); convergent evidence from functional neuroimaging is yet to be investigated (Mayes et al., 2007).

It follows from unitisation and DD that, in the current experiment, memory for item-context/between-domain object-encoding task associations would have required recollection, and therefore the hippocampus. To reiterate, however, encoding activity that related to subsequent memory for the object-encoding task association was

observed in the perirhinal cortex only. Furthermore, this source memory effect was indexed by a non-linear pattern of activity that has been previously linked with recollection (e.g. $sHCHH > sLCHH = sHM = sMM$, whereas a familiarity-based source memory effect may look more like $sHCHH > sLCHH > sHM > sMM$). There are previous demonstrations of a recollection signal in the perirhinal cortex for item-based source information (Awipi & Davachi, 2008; Diana et al., 2010; Staresina & Davachi, 2008), but not for contextual source information. According to informational accounts, however, perirhinal cortex cannot support associative recollection when the source information comprises a contextual detail. Consequently, the findings in the current study are extremely problematic for dual-process, as well as informational models.

4.6.4. Implications for representational accounts

As previously mentioned, there is a growing body of neuropsychological and fMRI research that has implicated the hippocampus in memory and higher-level perception for scenes and spatially demanding tasks, whereas the perirhinal cortex is generally associated with processing visual features of objects (Barens et al., 2005; Barens et al., 2007; Barens, Henson et al., 2010; Lee, Buckley et al., 2005; Lee, Bussey et al., 2005; Lee et al., 2008; Meunier et al., 1993; Pihlajamaki et al., 2004). Given these observations it has been proposed that MTL regions may form stimulus-specific representations of complex visual information that can be utilised across all cognitive domains (EMA: Graham et al., 2010; see also Bussey & Saksida, 2005; Saksida & Bussey, 2010). According to EMA, profiles of activity within, and the consequences of damage to, the MTL will be determined by the stimuli employed, rather than the specific mnemonic/perceptual operations that underpin task performance. A unique prediction of EMA, therefore, is that patterns of activity reflecting recollection and familiarity will not be limited to any one MTL region. As this is the main point of divergence between a representational and informational/dual-process view, EMA is the only account that can accommodate a profile of activity that predicts contextual source memory encoding for objects within the perirhinal cortex.

An additional feature of representational accounts is that stimulus-specific representations are organised hierarchically, from simple to complex, along the visual processing streams, which eventually converge in the MTL (Bussey & Saksida, 2005;

Cowell et al. 2010; Graham et al., 2010; Saksida & Bussey, 2010). As such, object information is represented down the ventral processing stream with the emergence of increasingly complex conjunctions of features. Representational accounts, therefore, predict that memory and perception of objects with simple, non-overlapping features will not require the perirhinal cortex. When objects contain many overlapping features, or are high in 'feature ambiguity' (Bussey & Saksida, 2005; Cowell et al., 2010; Saksida & Bussey, 2010), the perirhinal cortex is required to integrate multiple object features and successfully distinguish between items. For Experiment 2, the pattern of neural activity within the perirhinal cortex predicted overall item memory for objects but did not additionally increase according to the subsequent recovery of contextual source information. The stimulus materials in the current experiment were selected to contain more overlapping semantic information and visual features across the two encoding tasks. In accordance with the theoretical underpinnings of representational accounts, the increase in feature ambiguity for objects across the two encoding tasks could explain the presence of a significant source memory effect in the perirhinal cortex in the current study.

4.6.5. Task-dependent subsequent memory

Another difference between the current experiment and Experiment 2 was the adoption of an encoding task that encouraged participants to process the visual features of the objects. Although there was no task*memory interaction within the perirhinal cortex separate analyses of task-dependent memory effects within the left perirhinal cortex (see Fig. 4.7E and Appendix B) indicated that, while the patterns of memory-related activity for the perceptual and conceptual tasks both reflected significant source memory processing, activity for the latter was also greater for hit-miss compared to miss. This graded effect can be viewed as an index of subsequent memory strength (Squire et al., 2007). Effects for the perceptual task, however, are in keeping with a non-linear recollection-like signal as characterised by dual-process models. This difference across tasks suggests that the inclusion of the perceptual encoding task could have contributed to the significant effects identified in the perirhinal cortex in the current study, and highlights a potential avenue for further investigation.

In the current data set there was a significant task-dependent source memory effect in the posterior parahippocampal gyrus (or parahippocampal cortex); activity for the conceptual task followed a pattern that related to subsequent contextual source memory accuracy. For the perceptual task, however, the pattern was ambiguous. This is in keeping with the suggestion that subsequent memory effects can vary according to the task employed at study (Otten & Rugg, 2001; Otten et al., 2002; Park et al., 2008). While dual-process and representational accounts do not make explicit predictions about the role of the parahippocampal gyrus, informational accounts claim that it is important for processing spatial (item and context: Davachi, 2006) and non-spatial (BIC: Diana et al., 2007) contextual information, which is then passed to the hippocampus to form domain-general item-context associations. In light of informational accounts, the implications of a task specific contextual source memory effect in the parahippocampal gyrus are unclear for two main reasons. First, the contextual source information in the current study was not spatial, and so cannot be easily accommodated by the item and context model (Davachi, 2006). Second, Diana and colleagues (2007) are yet to define what denotes contextual information in their BIC model, and the circumstances under which the parahippocampal cortex will be recruited to process this.

Although Diana et al. (2007) are yet to make a definitive claim about exactly what information the parahippocampal cortex supports, there is a suggestion from Bar and colleagues (Aminoff et al., 2007; Bar, 2004; Bar & Aminoff, 2003; Bar, Aminoff, & Ishai, 2008; Bar, Aminoff, & Schacter, 2008) that parahippocampal contextual processing involves the formation of associations between a study item and information relating to its (conceptual) identity and spatial location. This account is supported by observations that the parahippocampal gyrus shows greater activity for (a) objects that are strongly conceptually related to a specific spatial context (such as a roulette wheel or a boxing glove: Bar & Aminoff, 2003; Aminoff et al., 2007), (b) famous, compared to non-famous faces (Bar, Aminoff, & Ishai, 2008), (c) pictures of scenes which contain a strongly conceptually related object (such as an airport with a luggage trolley: Bar, Aminoff, & Schacter, 2008), as well as (d) interactions based on the spatial congruency and semantic relatedness of re-presentations of object pairs (Gronau, Neta, & Bar, 2008). If the parahippocampal cortex is indeed important for the integration of spatial and conceptually related information, it is unsurprising that

subsequent memory effects were present for a source task that required participants to make conceptual judgements about objects. The pattern for the perceptual task may be less clear because participants were not directly asked to consider associated conceptual information. Working within Bar's definition of context, and the assumptions that underlie these interpretations, these data points support the role of the parahippocampal cortex in the formation of conceptually related contextual associations necessary for episodic encoding (Bar et al., 2004; Bar & Aminoff, 2003; Bar, Aminoff, & Ishai, 2008).

4.7. Conclusions

In the current experiment, there was activity relating to contextual source recollection in the left perirhinal cortex and the left posterior parahippocampal gyrus (which was task-dependent). Contextual source memory effects in the perirhinal cortex are inconsistent with strength-based, dual-process and informational views of MTL function, even in light of unitisation (Diana et al., 2008; Haskins et al., 2008, Quamme et al., 2007; Yonelinas et al., 1999) and Domain Dichotomy explanations (Mayes et al., 2007). Only representational accounts (Bussey & Saksida, 2005; Graham et al., 2010; Saksida & Bussey, 2010), which suggest the perirhinal cortex processes and stores representations of objects that can support mnemonic and perceptual operations, predict this finding. It is notable that, while effects in the posterior parahippocampal gyrus can be accommodated by accounts that have implicated its role in the formation of contextual associations (Bar et al., 2004; Bar & Aminoff, 2003; Aminoff & Bar, 2007; Bar, Aminoff, & Ishai, 2008), these are also not problematic for a representational account. The current study, albeit via a single process estimation method, provides some evidence for a representational account, and demonstrates theoretical shortcomings of the alternatives.

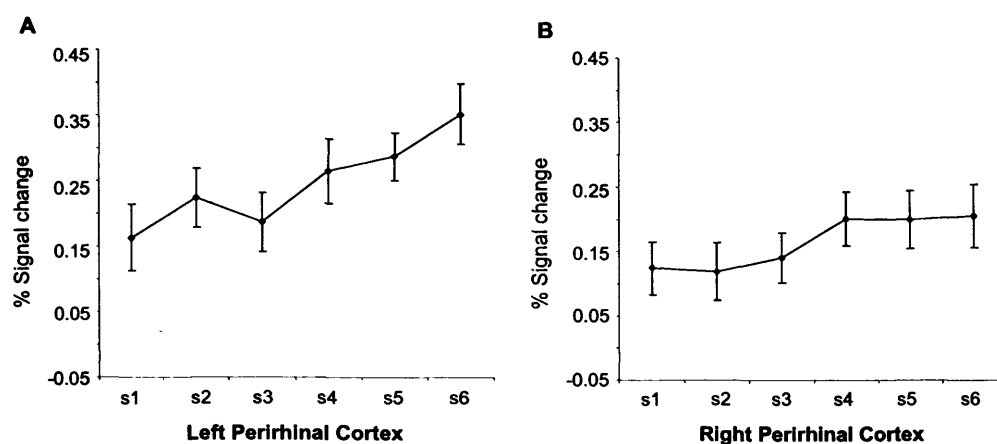
Appendix A: Additional item memory analyses in the perirhinal cortex

Figure A.1: Patterns of memory encoding activity relating to recognition confidence for objects and scenes in functionally defined MTL regions of interest from objects > scenes. Percent signal change (arbitrary units) in the (A) left perirhinal cortex and (B) right perirhinal cortex. Abbreviations: (s1) subsequent high confidence miss, (s2) subsequent medium confidence miss, (s3) subsequent low confidence miss, (s4) subsequent low confidence hit, (s5) subsequent medium confidence hit, and (s6) subsequent high confidence hit.

In the left perirhinal cortex there was a significant main effect of memory ($F(5,155) = 4.51, p < 0.01$), that was not evident in the right ($F(5,155) = 1.55$). Pairwise comparisons for the left revealed greater activity for (a) medium confidence hit compared to low and high confidence miss ($s5 > s3: t(31) = 2.75, p < 0.01$; $s5 > s1: t(31) = 2.66, p < 0.05$), (b) low confidence hit compared to high confidence miss that was marginal ($s4 > s1: t(31) = 1.79, p = 0.08$) and (c) high confidence hit, relative to all other levels of confidence ($s6 > s5: t(31) = 2.68, p < 0.05$; $s6 > s4: t(31) = 2.15, p < 0.05$; $s6 > s3: t(31) = 4.01, p < 0.01$; $s6 > s2: t(31) = 3.35, p < 0.01$; $s6 > s1: t(31) = 3.56, p < 0.01$).

Appendix B: Analyses of memory effects according to encoding task in the perirhinal cortex

When memory effects in the perirhinal cortex (see Fig. 4.7E) were separated according to task there were significant and marginal main effects of memory for the conceptual and perceptual tasks in the left hemisphere (conceptual: $F(3,93) = 4.76$, $p < 0.01$; perceptual $F(3,93) = 2.42$, $p = 0.07$), and a marginal main effect of memory for the conceptual task in the right hemisphere ($F(3,93) = 2.50$, $p = 0.07$). Pairwise comparisons revealed: (a) greater activity for sHCHH compared to sLCHH, sHM and sMM, as well as a marginal increase for sHM compared to sMM for conceptual items in the left (sHCHH > sLCHH: $t(31) = 2.84$, $p < 0.01$; sHCHH > sHM: $t(31) = 2.18$, $p < 0.05$; sHCHH > sMM: $t(31) = 4.5$, $p < 0.01$; sHM > sMM: $t(31) = 2.01$, $p = 0.05$); (b) greater activity for sHCHH relative to sLCHH (marginal), sHM and sMM for perceptual items in the left (sHCHH > sLCHH: $t(31) = 1.78$, $p = 0.09$; sHCHH > sHM: $t(31) = 2.32$, $p < 0.05$; sHCHH > sMM: $t(31) = 4.17$, $p < 0.01$); and (c) for conceptual items in the right, marginal differences between sHCHH and sLCHH, sHCHH and sMM, and sHM and sLCHH (sHCHH > sLCHH: $t(31) = 1.91$, $p = 0.07$; sHCHH > sMM: $t(31) = 1.88$, $p = 0.07$; sHM > sLCHH: $t(31) = 1.88$, $p = 0.07$).

Chapter 5

General discussion

Guided by divergent findings from the animal, human lesion and functional imaging literature that has developed over the past 50 years, the central theme for the current thesis was to consider and compare the neural predictions of four accounts of MTL function, particularly in the context of human long-term memory. In the Introduction these accounts were categorised as (a) unitary/strength-based (Squire & Zola-Morgan, 1991; Squire et al., 2004; Squire, 2004; Squire et al., 2007), (b) dual-process (Aggleton & Brown, 1999; Brown & Aggleton, 2001; Mayes et al., 2007), (c) informational (Eichenbaum, 1994; Eichenbaum et al., 2007; Davachi et al., 2006; Diana et al., 2007), and (d) representational (Murray et al., 1999; Bussey & Saksida, 2005; Cowell et al., 2010; Graham et al., 2010; Saksida & Bussey, 2010).

According to (a), the unitary/strength-based account (Squire & Zola-Morgan, 1991; Squire et al., 2004; Squire, 2004; Squire et al., 2007), MTL subregions (the hippocampus, parahippocampal cortex and perirhinal cortex) act in concert to form a single declarative memory system. Notably, however, (b) dual-process, (c) informational and (d) representational accounts all agree that MTL subregions functionally fractionate. For dual-process accounts, MTL fractionation is guided by the contributions of two dissociable memory processes (recollection and familiarity: Aggleton & Brown, 1999; Brown & Aggleton, 2001; see also Mayes et al., 2007). Informational accounts emphasise a division of labour based upon different types of mnemonic information, which are related, but not necessarily restricted, to the processes of recollection and familiarity (e.g. items vs. contexts; Davachi, 2006; Diana et al., 2007). Finally, representational accounts (e.g. Graham et al., 2010; Saksida & Bussey, 2010) suggest that MTL subregions process and store representations of complex visual stimuli and, therefore, MTL function should reflect the properties of the stimulus materials employed by the task rather than the processes/information-types that support memory judgements. A representational view forms a broader class of account; it does not restrict the unique contribution of

the MTL to long-term memory, but extends to short-term memory, as well as, higher-level perception.

The experiments in this thesis were designed to investigate, using functional magnetic resonance imaging (fMRI), some predictions stemming from these four models, by observing the MTL correlates of successful memory encoding (Experiments 1-3) and retrieval (Experiment 1) for different types of complex visual stimuli, such as faces (Experiment 1), objects (Experiment 2 and 3) and scenes (Experiment 1 and 2). The majority of the published literature has focused on verbal stimuli (e.g. words: Davachi et al., 2003; Daselaar et al., 2006; Henson et al., 1999; Ranganath et al., 2004; Yonelinas et al., 1998; Yonelinas et al., 2002; Yonelinas et al., 2005; although see Montaldi et al., 2006). As a result, it was unclear whether the assumptions inherent to most models, that MTL contributions to memory are domain-general, would be upheld for visual stimuli.

As dual-process accounts (Aggleton & Brown, 1999; Brown & Aggleton, 2001) postulate that MTL subregions differentially support the processes that underlie recognition memory judgements, in all experiments, participants made confidence judgements in their old/new decisions. According to one dual-process view, known as dual-process signal detection (DPSD: Yonelinas, 1994; 2002, in particular see Section 1.4.1.3) confidence judgements can be used to determine whether memory judgements are made on the basis of recollection or familiarity (Cohn et al., 2009; Daselaar et al., 2006; Montaldi et al., 2006; Ranganath et al., 2004; Yonelinas et al., 2005). In a similar vein, and in light of informational accounts (Davachi, 2006; Diana et al., 2007), there were also measurements in Experiments 2 and 3 that assessed whether patterns of neural activity related to the accuracy of contextual source judgements made at retrieval (Davachi et al., 2003; Ranganath et al., 2004). This allowed the opportunity to investigate whether significant memory effects reflected processing of item- and/ or contextual-based mnemonic information. The specific designs of these experiments are summarised in the section below, alongside the fMRI and behavioural findings from each study. This section is followed by a discussion about how these results relate to the four accounts of MTL function briefly described above, as well outstanding questions and suggestions for future research.

5.1. *Summary of findings*

In Experiment 1 participants were scanned during the study and test phases of a recognition memory task that comprised faces and scenes. During the test phase, they were presented with previously studied and novel faces and scenes and indicated, using a 6-point confidence scale (e.g. 1 = sure new to 6 = sure old), whether they thought the items were old or new. Whole-brain contrasts were performed on the fMRI data from the study (encoding) and test (retrieval) phases according to the accuracy of participants' memory judgements, separately for the faces and scenes. Memory encoding and retrieval effects were also investigated within face- and scene-specific regions of interest (fROI). These fROIs were identified within hippocampal, parahippocampal gyrus and perirhinal MTL subregions, and were created via contrasts between the novel faces and scenes from the retrieval phase. These analyses revealed some evidence for stimulus-specific memory-related activity for scenes and faces in the left posterior hippocampus and perirhinal cortex (respectively) during encoding, and for faces in the left anterior hippocampus, left anterior parahippocampal gyrus and perirhinal cortex at retrieval. At encoding there was a significant domain-general pattern in the posterior parahippocampal gyrus, as well as numerical trends towards domain-general memory processing in the right posterior hippocampus, anterior hippocampus and anterior parahippocampal gyrus. When recognition memory confidence was investigated, only the face-specific retrieval effect in the anterior hippocampus pointed conclusively to recollection; activity was greater for old items remembered with high confidence, compared to low confidence hits and misses (SO > PO = M: e.g. Yonelinas et al., 2005). There were no effects that reliably reflected familiarity as all other patterns were ambiguous; activity was greater for high confidence hits relative to missed items only (SO > M).

As trends towards stimulus-specific memory effects for scenes in the left posterior hippocampus (encoding), and for faces in the left anterior hippocampus (retrieval), anterior parahippocampal gyrus (retrieval) and perirhinal cortex (encoding and retrieval) could reduce to differences between the memorability of the stimuli (Yonelinas et al., 1999), these were considered in conjunction with aspects of the behavioural data. First, overall memory accuracy between the faces and scenes was matched. Second, behavioural estimates derived from ROC analyses indicated higher

recollection for the scenes, but matched familiarity. As such, the tentative evidence for scene-specific processing in the left posterior hippocampus could reflect scene memory relying to a greater extent on recollection. This explanation does not hold for face-specific effects in the anterior hippocampus at retrieval, nor in the perirhinal cortex at encoding and retrieval, because recollection estimates were lower for faces than scenes, while familiarity estimates did not differ.

For Experiment 1, only the face-specific memory retrieval effect within the anterior hippocampus could be reliably attributed to recollection (via recognition confidence: Yonelinas et al., 2005). All other encoding and retrieval effects followed an ambiguous pattern in relation to recollection and familiarity. It was hypothesised in the discussion of Experiment 1 that ambiguous patterns may have occurred due to the concatenation of medium and low confidence hits into a single 'probably old' regressor. In Experiment 2, trial numbers were increased (Experiment 1: 120 old, 90 new; Experiment 2: 258 old, 129 new) so that high, medium and low confidence hits could remain separate in the fMRI analyses. Moreover, in terms of informational accounts, in Experiment 1 it could not be ascertained whether any of the patterns of memory encoding and retrieval activity reflected the processing/recovery of item-based versus contextual mnemonic information. In order to elucidate whether patterns of neural activity for different stimulus types would reflect memory for items compared to contextual encoding, a source memory procedure was employed in Experiment 2. This source memory procedure was based on the design from Ranganath et al., 2004 (see Section 3.1), who, using words, observed dissociable hippocampal and perirhinal cortex activity based upon item recognition confidence and the accuracy of contextual source memory judgements made at retrieval. Supporting both dual-process and informational accounts, the perirhinal cortex showed a linear increase in activity based on subsequent recognition confidence, but was insensitive to the subsequent recovery of an associated contextual source detail (e.g. hit-hit = hit-miss > miss). In the hippocampus, however, the pattern reflected successful encoding of contextual source information; activity was greater for correct versus incorrect source judgements (e.g. hit-hit > hit-miss = miss; see also Davachi et al., 2003).

In Experiment 2, participants were scanned while they studied objects and scenes presented in one of two encoding contexts (is this object/scene common/uncommon or pleasant/unpleasant). In the unscanned test phase, as with Experiment 1, old/new judgements to objects and scenes were made on a 6-point confidence scale; for old judgements, however, participants also identified the encoding context in which the objects and scenes were originally presented. As with the Ranganath et al. (2004) study, encoding activity for objects and scenes was analysed both as a function of subsequent recognition confidence and the accuracy of source judgements. Memory encoding effects for objects and scenes were investigated (a) at the whole-brain level, by performing contrasts between item confidence and source memory regressors, and (b) within object- and scene-sensitive fROIs identified using an orthogonal functional localiser task.

There was encoding activity within the hippocampus and parahippocampal gyrus that reflected scene-specific recollection, whereas encoding activity within the perirhinal cortex was associated with object-specific familiarity (all of which were inferred from the behavioural data separated by recognition confidence and contextual source memory accuracy: Davachi et al., 2003; Ranganath et al., 2004; Yonelinas et al., 2005). Behaviourally, item memory accuracy was greater for the objects than the scenes, and ROC estimates indicated that this advantage was largely driven by an increased contribution of recollection to object memory; familiarity estimates did not differ. Object-specific activity in the perirhinal cortex could, therefore, reflect an increased reliance for object memory on item-based mnemonic information. As familiarity estimates for the objects and scenes did not differ reliably, however, object-specific effects in the perirhinal cortex were unlikely to reflect an increased reliance for object memory on familiarity-based recognition. Moreover, scene-specific effects in the parahippocampal gyrus and hippocampus cannot be easily explained via the behavioural data; source memory accuracy was matched and recollection estimates were higher for objects.

It is also notable that, no significant patterns of neural activity were detected in the MTL that related to successful encoding of contextual source memory for objects. It was hypothesised that this absence may have occurred because the design for Experiment 2 was not sufficiently sensitive to source memory processing within the

perirhinal cortex. In light of this, the final experiment in this thesis was designed to re-examine perirhinal cortex contributions to contextual source memory for objects. The design for Experiment 3 was similar to Experiment 2; participants were scanned while they studied objects in one of two encoding conditions (does this object contain more edges or curves; is this object common/uncommon), and at test made item confidence and contextual source memory judgements. Participants also made confidence judgements for the source memory response; this comprised a 6-point scale that ranged from sure common/uncommon to sure edges/curves. Confidence ratings were collected for the source memory judgement because activity associated with accurate source guesses (or low confidence hit-hits) could reduce average levels of activity for hit-hit responses overall, making the comparison between hit-hits and hit-misses more ambiguous. By removing low confidence source hits from this contrast it should be possible to obtain a cleaner measure of successful source memory.

Based upon predictions from the representational models, the stimuli in Experiment 3 were selected from overlapping semantic categories, and contained more similar visual features than those used in Experiment 2. In addition to this, one of the encoding tasks was changed to encourage participants to encode the visual properties of the objects (does this object contain more edges or curves). The analysis strategy was identical to that from Experiment 2; encoding activity for item confidence and source memory accuracy was investigated via whole-brain contrasts and within object- and scene-sensitive fROIs. These analyses revealed significant memory effects for objects in the perirhinal cortex and posterior parahippocampal gyrus. In the left perirhinal cortex activity reflected recollection according to subsequent recognition confidence (Yonelinas et al., 2005) and the accuracy of the contextual source memory judgements (Davachi et al., 2003; Ranganath et al., 2004). In the left posterior parahippocampal gyrus, memory effects were task-dependent; activity for the items encoded in the common/uncommon task was greater for accurate, compared to inaccurate source memory judgements, whereas activity for the perceptual (edges/curves) could not be attributed to a specific memory process/operation.

5.2. *Relation to accounts of MTL function*

5.2.1. *Unitary/strength-based account*

As discussed previously, according to Squire's (& Zola-Morgan, 1991; Squire et al., 2004; Squire et al., 2007) unitary/strength-based account (in particular see Section 1.3), subregions within the MTL act in concert to form a single declarative memory system. This account is based on observations that damage to the hippocampus is both critical and necessary for impairments to declarative memory, and when additional structures proximal to the hippocampus become damaged, memory impairments increase in a quantitative fashion (Press et al., 1989; Zhu et al., 1995; Zola-Morgan et al., 1994). Notably, despite a pervasive loss of long-term memory, other cognitive abilities including short-term memory, perceptual, intellectual and lexical abilities remain intact following damage to the MTL (Corkin, 1984; Drachman & Arbit, 1966; Kensinger et al., 2001; Milner et al., 1968; Milner et al., 1998). A key feature of this account is that MTL structures make equivalent contributions to long-term memory (Squire et al., 2007).

In the first instance, this view is inconsistent with research that has demonstrated qualitative differences in memory impairments following varying amounts of damage to individual MTL structures (e.g. Aggleton & Shaw, 1996; Aggleton et al., 2005; Bowles et al., 2007; Fortin et al., 2004; Holdstock et al., 2005; Yonelinas et al., 1998) and/or dissociable patterns of neural activity within the MTL that reflect recollection and familiarity (Davachi et al., 2003; Henson et al., 1999; Johnson & Rugg, 2007; Ranganath et al., 2004). According to Squire and colleagues (Squire et al., 2007), however, the measurements generally used to investigate recollection and familiarity-based memory judgements are actually parsing strong from weak memories (which could comprise a combination of recollection and familiarity, Wixted, 2007), respectively (Kirwan et al., 2008; Wais et al., 2006; Wais et al., 2010; Wixted et al., 2010). Wixted notes that these assumptions are confirmed by observations that memory accuracy for 'strong' recollection based responses is almost always greater than accuracy for 'weaker' familiarity based responses (Wixted et al., 2010, although see Montaldi et al., 2006). As such, for this specific strength/unitary view dissociable patterns of memory-related activity within the MTL reflect regional differences in the relationship between the MRI signal and increases in memory strength (see Section

1.5 and 3.6.4, and Fig. 3.9), which arise when fMRI contrasts between behavioural correlates of recollection and familiarity are confounded by differences in memory strength.

The strength-based account offered by Wixted, in combination with the work of Squire, has come to prominence relatively recently, and has been considered as a realistic alternative to dual-process formulations. The concept of strength in Wixted's account however, is problematic. First, these post-hoc concepts are left relatively vague and implicit, and are generally considered implausible (Ranganath, 2010). And second, inferences about the strengths of stored memories are made on the basis of variables measured at the time of retrieval, and it is not straightforward to envisage how strength of storage might be measured directly and accurately. Currently these remain serious challenges for the strength account.

Importantly for the findings in this thesis, Squire's view does not make explicit reference to whether there is a stimulus-specific division of labour within the MTL. As such, the stimulus-specific patterns of memory-related activity in Experiments 1 and 2, and lack of memory effects in the hippocampus for objects in Experiment 3, present a challenge for this strength-based/unitary view. The most problematic data point in the current thesis for this account, however, is the non-linear recollection-like signal in the perirhinal cortex that predicted contextual source memory for objects in Experiment 3.

5.2.2. Dual-process account and informational accounts

Unlike a unitary view, there are accounts which state that MTL subregions make qualitatively different contributions to long-term memory (Aggleton & Brown, 1999; Davachi, 2006; Diana et al., 2007; Graham et al., 2010; Mayes et al., 2007). As covered throughout this thesis, dual-process accounts state that the hippocampus and perirhinal cortex support recollection- and familiarity-based memory (Aggleton & Brown, 1999; Brown & Aggleton, 2001; see also Mayes et al., 2007). In Experiments 1 and 2, although significant patterns of recollection and familiarity related activity in the MTL were restricted to the hippocampus and perirhinal cortex (respectively), the suggestion that these effects were stimulus-specific is problematic for dual-process accounts.

One way that stimulus-specific memory effects could be accommodated by dual-process accounts, however, is if different stimuli rely to varying degrees on the processes of recollection and familiarity. Notably, across the experiments in this thesis behavioural estimates of recollection and familiarity for face, object and scene memory do not conform with this explanation, because: (a) despite there being trends towards perirhinal cortex face- and object-specific effects in Experiments 1 and 2, there were no reliable differences in familiarity estimates between faces and scenes, or objects and scenes, and (b) face-specific and scene-specific hippocampal recollection effects were observed in Experiments 1 and 2 (respectively), despite these being the stimuli for which behavioural estimates of recollection were reliably lower. Crucially, the convergent data in the current thesis suggest that differences between MTL contributions to recognition memory for different stimulus types cannot be easily attributed to a differing dependence, across visual categories, on recollection and familiarity.

For the binding item and context informational account (BIC: Diana et al., 2007), the perirhinal cortex processes item-based mnemonic information, the parahippocampal cortex processes spatial and non-spatial contextual information and the hippocampus forms domain-general representations of items and contexts. It follows from the BIC model that, as recollection is associated with the storage and recovery of contextual information, and familiarity can be supported by item information, patterns of memory-related activity should generally honour a dual-process distinction. According to another (similar) informational view, the perirhinal cortex processes item-based information, the parahippocampal cortex processes *spatial*-contextual information and the hippocampus binds items with their spatial-contextual information (item-context: Davachi, 2006). As discussed throughout this thesis, for both the BIC and item-context models, the perirhinal cortex can support source recollection when the source detail comprises item-based information. An informational view therefore, provides a more flexible account of MTL function than dual-process; recollection-based memory judgements are not restricted to the hippocampus, but can operate via the parahippocampal and perirhinal cortices under certain circumstances (Diana et al., 2010; Staresina & Davachi, 2006; 2008; Diana et al., 2010).

It is possible that memory for objects, faces and scenes may disproportionately rely on item-based and contextual mnemonic information, thereby explaining the stimulus-specific effects observed in this thesis. In Experiment 2, item and context memory for objects and scenes was directly measured using of a source memory paradigm (Ranganath et al. 2004; reiterated in Section 5.1). The object-specific effect in the perirhinal cortex was coupled with greater overall item memory accuracy for the objects than the scenes. As stated earlier, the mnemonic advantage for objects was driven by recollection (in ROC analyses), while overall contextual source memory for objects and scenes was matched. In light of informational accounts, therefore, the object-specific effect in perirhinal cortex could reflect an increased reliance of object memory on item-based mnemonic information, predominately driven by ‘non-criterial’ recollection of item features (Yonelinas & Jacoby, 1996).

As the item-context model (Davachi, 2006) predicts that the parahippocampal cortex processes spatial-contextual information, scene-specific effects within the parahippocampal gyrus (like that in Experiment 2) are not inconsistent with this account. Scene-specific effects in the hippocampus, however, provide a challenge for both the item-context and BIC accounts, as hippocampal contributions should be domain-general. Furthermore, as the recollection estimate was higher for objects, and contextual source memory was matched, the behavioural data cannot explain the scene-specific effects in the hippocampus. The overall conclusion from the above considerations is that neither differential contributions of memory *process*, nor mnemonic *information*, can easily explain all of the memory effects for stimulus types, in all of the functional regions of interest, in Experiments 1 and 2.

In sum, the pattern of stimulus-specific activity observed in Experiments 1 and 2 of this thesis provides tentative evidence against dual-process and informational theories of MTL function. Notably, the main finding from Experiment 3 directly disagrees with these models, as memory-related activity within the perirhinal cortex reflected successful encoding of contextual source details (or item-context associations). To reiterate, according to a unitisation account, the perirhinal cortex can support familiarity for configurally bound, or unitised, associative item-item feature representations (e.g. Yonelinas et al., 1999; Quamme et al., 2007; Diana et al., 2008).

It is currently unclear, however, whether the concept of unitisation can be applied to binding of item-context associations. In fact, according to the Domain-Dichotomy view, between-domain/item-context associations are predominantly, if not exclusively, supported by the hippocampus (Mayes et al., 2007). As such, it is unlikely that the perirhinal cortex source memory effect in Experiment 3 reflected *familiarity* for configurally bound representations between objects and the encoding task. Notably, informational accounts state that the perirhinal cortex can support *recollection* of item-features/item-related information. This explanation is also inadequate, however, as the source detail in Experiment 3 comprised contextual information (the encoding task objects had been encountered in: Diana et al., 2010; Staresina & Davachi, 2006; 2008).

In Experiment 3, there was also evidence for a task-specific source memory effect in the posterior parahippocampal gyrus; activity reflected subsequent source memory accuracy for items encoded in the common/uncommon task, and an ambiguous pattern for the edges/curves task that could not be attributed to a specific type of mnemonic process/information. As this contextual source memory effect had little relevance to spatial processing it is inconsistent with the item-context account (Davachi, 2006). Proponents of BIC (Diana et al., 2007) are yet to state what denotes contextual information, and consequently, the implications of task-dependent contextual processing in the posterior parahippocampal gyrus for this model are unclear. There is a recent view of contextual processing, however, which suggests that the parahippocampal cortex is responsible for forming contextual associations between item location and conceptually relevant information (see Section 4.6.5; Aminoff & Bar, 2003; Bar et al., 2004; Bar, Aminoff, & Ishai, 2008; Gronau et al., 2008). In light of this view, it is unsurprising that source memory processing occurred within the posterior parahippocampal gyrus for an encoding task that directly asked participants to make a conceptual (common/uncommon) judgement about objects. As discussed later, the role of the parahippocampal gyrus in memory and perception requires further investigation.

5.2.3. Representational accounts

There is an increasing body of research which suggests that subregions within the MTL perform stimulus-specific functions (e.g. Awipi & Davachi, 2008; Barense,

Henson et al., 2010; Lee et al., 2008; Litman et al., 2008; Taylor et al., 2007; Winters et al., 2004); a proposal that draws support from the extent of connections between MTL structures and lower level visual processing regions. For example, as the perirhinal cortex receives a variety of information that projects from unimodal cortical areas within the ventral visual, or ‘what’, processing stream, it is ideally suited for forming complex multi-sensory representations of objects (Ungerleider & Haxby, 1994; Burwell, 2000). Cells in the perirhinal cortex are sensitive to the presentation of novel objects (Zhu et al., 1995), and a selective lesion to this region impairs memory for objects (Meunier et al., 1993). The hippocampus, however, has been shown to be insensitive to object-based information (Zhu et al., 1995), but is responsive to changes in the spatial environment, changes in the spatial arrays of items, and associations between items and their locations (O’Keefe & Nadal, 1978; O’Keefe, 1976; O’Keefe & Dostrovsky, 1971; O’Keefe et al., 1998; Eichenbaum et al., 1994; Eichenbaum, 2004).

Recent findings from lesion research and functional imaging indicating that the object vs. scene stimulus-specific distinction described above also applies to short-term memory and perceptual tasks (Barens et al., 2005; Barens et al., 2007; Bartko et al., 2007; 2007; Bussey et al., 2002; 2003; Lee, Buckley et al., 2005; Lee, Bussey et al., 2005; Lee et al., 2006; Litman et al., 2008; Pihlajamaki et al., 2004; Rudebeck & Lee, 2010). These data have formed the basis for representational accounts, in which stimulus-specific representations are processed and stored within MTL subregions, which do not just support long-term memory, but also short-term memory and perceptual discrimination (e.g. Bussey & Saksida, 2005; Graham et al., 2010; Saksida & Bussey, 2010). In the first instance, the loci of significant memory effects in this thesis are generally consistent with representational accounts (faces and objects: perirhinal cortex; scenes: hippocampus). Furthermore, Experiment 2 provides evidence that stimulus-specific memory effects for objects and scenes can occur within the same paradigm and participants (Awipi & Davachi, 2008; for similar effects in rats see also Winters et al., 2004).

In Experiment 1, there was evidence of domain-general encoding effects for faces and scenes within the hippocampus (and parahippocampal gyrus). These domain-general effects mirror the findings from previous studies that have also directly compared

memory for faces and scenes within the hippocampus (Preston et al., 2010; Prince et al., 2009), and are consistent with experiments that have observed effects for faces within the hippocampus using memory (Gonsalves et al., 2005) and perceptual tasks (Barens, Henson et al., 2010; Lee, Bandelow et al., 2006). It is possible, therefore, that recognition memory for faces, although sufficiently object-like to be supported by the perirhinal cortex, involves a variety of additional MTL brain regions, such as the hippocampus and parahippocampal gyrus. It has been observed, however, that memory and perception for faces is intact in patients with focal hippocampal lesions, but is significantly impaired when (a) lesions also encompass the perirhinal cortex and (b) in individuals with semantic dementia, which is characterised by disproportionate cell loss in the perirhinal cortex (Barens, Rogers et al., 2010; Davies et al., 2004; Lee et al., 2007). These data imply that, although the parahippocampal gyrus and hippocampus contribute towards recognition memory for faces, their roles may not be *necessary* for long-term memory for faces.

Based upon the postulations above, the domain-general findings at encoding in Experiment 1 are not necessarily challenging for representational accounts, such as EMA (Graham et al., 2010). Furthermore, when the stimuli comprised objects and scenes (Experiment 2), rather than faces and scenes, stimulus-specific distinctions honoured a representational account; namely, no memory effects for objects were detected within the hippocampus (see also Experiment 3). Due to the focus on representations, rather than cognitive operations, EMA also predicts that effects at encoding and retrieval should be equivalent. In Experiment 1, memory-related activity within the hippocampus and parahippocampal gyrus was domain-general at encoding, and face-specific at retrieval. The latter effects could have occurred due to a failure to detect significant memory effects for scenes, however, further experiments are required to resolve this discrepancy.

As noted in previous sections, the findings from Experiment 3 provide the strongest evidence against unitary/strength-based, dual-process and informational accounts of MTL function. In contrast, there are two features of representational accounts that can accommodate the observed pattern of neural activity within the perirhinal cortex in Experiment 3. First, as representational accounts denote stimuli, rather than process, as the overruling factor in MTL contributions to long-term memory, EMA predicts

that the phenomenologically and functionally distinct processes of recollection and familiarity can emerge from the same representation (Graham et al., 2010). As a result, EMA can explain activity that related to contextual source memory processing for objects within the perirhinal cortex. This is not in keeping with dual trace theories of recognition (Norman & O'Reilly, 2003; Norman, 2010; see also Henson & Gagnepain, 2010), which suggest that as recollection and familiarity are functionally distinct, information supporting these memory judgements should be encoded, stored, and reinstated separately. Notably, not all computational models of memory agree that recollection and familiarity necessarily require the presence of two memory traces (Greve, Donaldson, & van Rossum, 2010; see also Berry, Shanks, & Henson, 2008).

Second, a key feature of representational accounts is that object representations are organised hierarchically, from simple to complex, along the ventral visual processing stream. Specifically, the prediction is that perirhinal cortex will be recruited to discriminate between stimuli that contain overlapping visual features (Bussey & Saksida, 2005; Graham et al., 2010; Saksida & Bussey, 2010). When stimuli contain features that do not sufficiently overlap, regions upstream of the perirhinal cortex (e.g. inferior temporal cortex) can solve the discrimination (Cowell et al., 2010). Compared to the stimuli in Experiment 2, the stimuli across the two encoding tasks in Experiment 3 were from overlapping semantic categories (e.g. cups, balls and pagers) and contained more visually similar features. At retrieval, therefore, participants had to discriminate between old and new objects, as well as old objects from the two encoding tasks, that were semantically and visually similar (e.g. an old cup vs. a new cup; an old edges/curves cup vs. an old common/uncommon cup). As such, accuracy for source memory judgements was contingent upon the formation of robust complex visual representations of the study items, which, according to representational accounts, is perirhinally dependent.

In the current thesis, support for representational accounts was obtained using an unconventional fROI analysis approach. This fROI approach was driven by the predictions of representational accounts, which state that MTL regions process and store representations of different types of complex visual stimuli (such as objects and scenes) that will support memory and perception in a stimulus-specific manner. It is

somewhat unsurprising, therefore, that some stimulus-specific memory effects were identified within these fROIs. It is also possible that assuming some degree of functional homogeneity across groups of sampled voxels within individual fROIs could have increased the likelihood of making of type I errors, and that this functional ROI approach led to heavily biased results (Friston et al., 2006). It is notable that, in reference to these latter points (a) voxel-wise whole brain analysis is likely to suffer from a similar fate as even single voxels comprise thousands of individual neurons, and that (b) the a priori selection of functionally defined voxels can crucially maximise statistical power, thus avoiding type II errors that may otherwise occur using an overly conservative analysis approach (Saxe et al., 2006). To remain consistent with previous fMRI experiments and complementary to the fROIs, however, unbiased whole-brain analyses were also performed¹⁵. For the most part, results from the whole-brain contrasts mirrored the findings from the directed fROI analyses. As such, the conclusions of this thesis were unaffected by the adoption of a more conventional whole-brain analysis strategy, often used in experiments that have provided support for dual-process and informational accounts.

5.3. Outstanding questions and future directions

5.3.1. Problems associated with fMRI

While fMRI is a valuable research tool, it is not without its problems. First and most importantly, a lack of fMRI signal does not necessarily mean that the brain is not responding. Likewise, how and why quantitative changes in fMRI activity occur across different areas of the brain must be approached with caution. These points not only relate to considerations of signal to noise, but also to assumptions about what processes we are measuring within and across brain regions. Of significant concern is that the BOLD signal associated with a specific cognitive task is unlikely to reflect identical processing entities from different cortical structures (Logethesis, 2008). As such, it currently cannot be ascertained whether regional dissociations always relate to differences in functionality. Ambiguities between processing occurring within different regions clearly has important implications for making comparisons across

¹⁵ Note, due to the statistical constraints associated with fROI and whole-brain analyses, a combined approach is recommended (Saxe et al., 2006).

structures within the MTL, which is integral for confirming or rejecting the models discussed here.

Second, fMRI cannot indicate the necessity of a given brain region for a particular cognitive function. As discussed in the Introductory chapter (see Section 1.4.4), however, the relative merits of fMRI can often be strengthened by complementary findings from human lesion research. As such, many of the conclusions from this thesis are bolstered, and/or clarified, by consideration of stimulus-specific memory and perceptual impairments in individuals with different profiles of MTL damage (e.g. Cipolotti et al., 2006; Lee, Bussey et al., 2005; Taylor et al., 2007). For example, one interpretation of the effects in Experiment 1 is that, although there can be patterns of memory-related activity in a variety of MTL regions, recognition memory for faces only requires the perirhinal cortex (see Section 5.2.3). In light of the predictions made by different accounts of MTL function, the findings from previous neuropsychological investigations and the data in the current thesis, there are a number of outstanding questions/opportunities for future research, some of which are discussed below.

As outlined in Section 1.6 of the Introduction, there are several neuropsychological investigations of recognition memory for faces and scenes in individuals with MTL damage, the majority of which adopted ROCs to observe the contributions of recollection and familiarity (Bird et al., 2007; Bird et al., 2008; Cipolotti et al., 2006; Taylor et al., 2007). These data indicate that hippocampal damage selectively impairs memory for scenes, but leaves memory for faces intact. Moreover, MTL amnesics with an intact perirhinal cortex also show normal levels of familiarity and recollection for faces (Bird et al., 2007; Bird et al., 2008; Cipolotti et al., 2006). These patient ROC data therefore support the notion that the perirhinal cortex can support recollection and familiarity for faces. Although these data are compelling, they are not sufficient to discount informational accounts of MTL function; equivalent recollection estimates from ROC analyses for patients and their controls could reflect the recovery of item features in the former (Bird et al., 2007; Bird et al., 2008; Cipolotti et al., 2006). For example, mirroring the findings from several imaging experiments (Diana et al., 2010; Staresina & Davachi, 2006; 2008), Diana et al. (2010) observed that source memory impairments in individuals with hippocampal

damage were less pronounced when the patients encoded colour source information as an item feature, compared to when colour information comprised a contextual feature.

In addition to the ambiguities associated with mnemonic deficits for item-based versus contextual information outlined above, and despite there being a number of neuropsychological studies of face and scene recognition memory in amnesia, no study has also looked at memory for objects. It follows from these observations that it makes sense to assess item and context memory for objects, faces and scenes in individuals with different profiles of MTL damage. This could be achieved using a source memory paradigm similar to those in Experiments 2 and 3. Based on the predictions of representational accounts, previous neuropsychological investigations (e.g. Cipolotti et al., 2006; Bird et al., 2007; Bird et al., 2008; Taylor et al., 2007) and the findings from Experiments 2 and 3, individuals with lesions to the hippocampus should show both item and contextual source memory impairments for scenes, but less impaired performance on both of these measures for objects and faces. In contrast, patients with MTL lesions that include the hippocampus and the perirhinal cortex should show impairments in item and contextual source memory for all three stimulus types.

It is notable that Experiment 3 was also the only fMRI experiment to not directly compare memory for two stimulus types. As claims about stimulus-specificity are central to the predictions made by EMA, another logical future direction for this thesis would be to conduct Experiment 3 again using objects and scenes. This could determine whether it is possible to obtain dissociable contextual source memory effects for objects and scenes in the perirhinal cortex and hippocampus (respectively) within the same subjects and scanning session. This experiment would also complement the findings from the proposed item and context patient experiment described above.

5.3.2. Task-dependent memory effects

In Experiment 3, one of the encoding tasks was employed to encourage participants to process the visual features of the study items (does this object contain more edges/curves). Results revealed that, although not supported by a task*memory interaction, the subsequent source memory effect within the perirhinal cortex for the

conceptual task was graded (sHCHH > sLCHH = sHM > sMM), whereas the pattern for the perceptual task was non-linear, and therefore, more indicative of successful contextual source memory encoding. As a result, in addition to increases in visual feature overlap across the stimulus materials, there may have been some impact of the use of an encoding task that encouraged participants to process these overlapping object features. A follow up study needs to be conducted to investigate the use of different encoding tasks, in a manner that is orthogonal to feature ambiguity manipulations.

In such an experiment there would be 2 study-test phases, possibly scanned in separate sessions. In phase 1, stimulus materials high in semantic and visual feature ambiguity (like those in Experiment 3) would be presented in two different encoding blocks; for block 1 the encoding tasks would comprise common/uncommon and pleasant/unpleasant judgements (conceptual block), whereas for block 2 the tasks would be common/uncommon and edges/curves judgements (conceptual/perceptual block). Following this, participants would conduct a test phase outside the scanner comprising items previously studied in blocks 1 and 2, and similar new items. As with Experiment 3, participants would make old/new, as well as source memory judgements to the test items on a 6-point confidence scale. Notably, there would also be conceptual and conceptual/perceptual blocks for study-test phase 2, however the stimuli here would be low in semantic and visual feature ambiguity. By analysing perirhinal cortex subsequent memory effects separately for each task, within each block, and each phase, this 2x2 design could investigate whether (a) the inclusion of a perceptual encoding task, (b) the increase in feature ambiguity, or (c) both manipulations drove the source memory effect in Experiment 3.

5.3.3. The role of the parahippocampal gyrus

Across the three experiments there were different findings relevant to the role of the parahippocampal gyrus in memory for complex visual stimuli; in Experiment 1 memory effects were evident for both faces and scenes, in Experiment 2 recollection effects were scene-specific, and in Experiment 3 there was significant contextual processing for objects for the conceptual source task. It was proposed in the discussion of Experiment 2 that the posterior parahippocampal gyrus (i.e. parahippocampal cortex) contributes to the formation of spatial representations, which

has been demonstrated in previous fMRI investigations (Awipi & Davachi, 2008; Lee et al., 2008; Litman et al., 2009; Preston et al., 2010). The evidence from Experiment 3, however, indicates that the posterior parahippocampal cortex can also contribute to non-spatial conceptually related contextual processing (Bar & Aminoff, 2003; Bar et al., 2004; see also Diana et al., 2007). In Section 5.3.1, it was suggested that another fMRI experiment could be run to compare source memory for objects *and* scenes using the design from Experiment 3. The data from this experiment could also be used to systematically investigate the role of the parahippocampal cortex in memory for spatial and non-spatial contextual processing. In light of the findings in this thesis there are two main predictions for this experiment. First, supporting a contextual view of parahippocampal cortex function (and mirroring the findings from Experiment 3), there should be significant contextual source memory effects for scenes and objects from the uncommon/common conceptual source task but not the edges/curves perceptual task. Second, in support of a stimulus-specific view (and the findings from Experiment 2) contextual source memory effects should be present for scenes, for both encoding tasks, and not present at all for the objects.

5.3.4. Stimulus-specific memory and perception

A central component of representational accounts is that stimulus-specific representations, processed and stored within MTL subregions, support long-term memory and perceptual discriminations (e.g. Graham et al., 2010; Saksida & Bussey, 2010). Providing support for the latter, there are behavioural neuroscience (Bartko et al., 2007a; 2007b; Buckley et al., 2001; Bussey et al., 2002; 2003;), neuropsychological (Barens et al., 2005; Barens et al., 2007; Lee, Buckley et al., 2005; Lee, Bussey et al., 2005; Lee & Rudebeck., 2010) and functional imaging (Devlin et al., 2007; Lee et al., 2008; Barens, Henson et al., 2010) experiments that have documented stimulus-specific MTL contributions to concurrent perceptual discrimination, as well as recognition memory (e.g. Awipi & Davachi, 2008; Cipolotti et al., 2006; Meunier et al., 1993). Furthermore, O'Neil et al. (2009; see Section 1.6.3 and Fig. 1.25) demonstrated that activity relating to accurate oddity and long-term memory retrieval judgements for faces significantly overlapped within the perirhinal cortex. The data from O'Neil et al. (2009) indicates, therefore, that perception and long-term memory retrieval for faces may be supported by the same representations within the perirhinal cortex (O'Neil et al., 2009).

Based on the design from O'Neil et al. (2009; see Section 1.6.3 and Fig. 1.25), it could be possible to concurrently measure encoding, retrieval and oddity perception for different types of complex visual stimuli. In this experiment participants would encode objects, faces and scenes in an unscanned study phase. Following this, participants would then undertake a task in the scanner that comprises object, face and scene mini blocks of 3-choice oddity trials using novel stimuli, intermixed with 3 item forced-choice recognition trials. Subsequent memory encoding effects for the novel objects, faces and scenes in the oddity trials will also be assessed in a second yes/no recognition test following the scanning session (adapted from Stark & Okado, 2003). Using this design, patterns of neural activity within functionally defined MTL regions of interest could be considered in terms of correct versus incorrect oddity and long-term memory encoding and retrieval responses. At issue is whether demonstrating that object, face and scene-specific representations code perceptual and mnemonic success in the same subjects in the same scanning session. Moreover, the outcomes of this experiment could also help to explain the reasons for the divergent encoding and retrieval effects for faces and scenes in Experiment 1.

5.3.5. Recognition memory for words

The vast majority of neuropsychological and neuroimaging experiments that have been interpreted as support for dual-process and informational accounts have used verbal stimuli (predominantly visually presented words). Although the findings in the current thesis provide some support for representational accounts, discrepant findings using verbal stimuli are not in keeping with the specific predictions made by EMA (Graham et al., 2010). It is possible that, if stimulus-specific memory effects for objects/faces and scenes arise due to disproportionate dependence on familiarity and recollection, respectively, the reverse could also be true; dissociable hippocampal and perirhinal cortex correlates of familiarity and recollection (or items and contexts) for words may differentially reflect relative fluctuations in the level of object and spatial processing associated with these memory judgements.

Although there is little spatial information associated with single presentations of words (like that in standard yes/no recognition tasks), for items that are subsequently 'recollected', as indicated by correct source, remember (using R/K; see Section

1.4.1.2) and high confidence old judgements, participants may base their responses on some non-criterial spatial-contextual information. For example participants could consciously (and unconsciously) adopt certain spatially relevant encoding strategies to improve memory performance; such as noting the location of the study word on-screen, or imaging the presented study words in a particular spatial environment (e.g. when presented with the word 'bucket' a participant may imagine a beach to enhance memory encoding). In fact, there are previous experiments that have used location on screen at encoding as the criterial source information at retrieval, thus directly encouraging spatial contributions to behavioural estimates of recollection (Cansino et al., 2002; Uncapher et al., 2006; Uncapher & Rugg, 2009). Furthermore, it has been shown that activity in the perirhinal cortex correlates with successful source memory encoding and retrieval under circumstances where participants are directly encouraged to imagine the referent of presented nouns in a particular colour (Diana et al., 2010; Staresina & Davachi, 2006; 2008). When participants do not base retrieval judgements on imagined object representations, however, source memory effects were not detected in the perirhinal cortex (Diana et al., 2010).

These issues raise three main suggestions/opportunities for future research. First, if not directly controlled, experiments designed to investigate memory for words should endeavour to reduce, or at least make equivalent, contributions of confounding visuo-spatial and object-based information to recollection and familiarity-based recognition judgements. Second, as discrepancies are based upon comparisons made across experiments that have used different stimulus types, a necessary step would be to compare neural activity that relates to memory encoding and retrieval for visually presented objects, scenes and words in a manner that is similar to the experiments reported in this thesis. Third, as most experiments have used nouns, it could be interesting to observe the relative hippocampal contributions (using fMRI and lesion research) to memory for nouns that refer to everyday objects (e.g. table, pen, cup) compared to memory for spatially relevant words (e.g. up, down, near). According to representational accounts, memory for object nouns versus spatial words may differentially rely on object and spatial representations, and therefore, dissociable memory effects should occur between MTL subregions.

5.3.6. *Representations in the extrastriate cortex*

A key feature of representational accounts is that stimulus guided representations are organised hierarchically, starting with very simple representations in primary visual regions with the emergence of increasingly complex representations moving rostrally along the visual processing streams towards the MTL (Cowell et al., 2010; Graham et al., 2010). In line with this, Cowell et al. (2010) predict that ‘a lesion at any point of the ventral visual stream will cause impairments in visual discrimination learning, if the to-be-discriminated stimuli possess a level of complexity best represented by the neurons in the lesioned area’ (pp.13). As noted throughout this thesis, recent neuropsychological data indicate that amnesics with MTL lesions, which include the perirhinal cortex, are only impaired on discrimination tasks that contain objects and faces that contain many overlapping features (e.g. Barense et al., 2005; Barense et al., 2007, Lee, Bussey et al., 2005; for similar effects in animals see Bartko et al., 2007a; 2007b; Buckley et al., 2001; Bussey et al., 2002; 2003). Based on this notion, therefore, EMA (Graham et al., 2010) explicitly denotes functional differences between regions of the extrastriate cortex and the MTL based upon levels of feature overlap between the stimulus materials (also known as feature ambiguity: Bussey & Saksida, 2005; Cowell et al., 2010; Saksida & Bussey, 2010). It should be possible, therefore, to observe significant memory effects for different stimulus types within their respective areas of the extrastriate cortex (e.g. scenes: PPA; objects: LOC; faces: FFA), and when feature ambiguity is sufficiently low, memory effects will be exclusive to the extrastriate cortex. In contrast, when feature ambiguity is high, memory effects should also be detected in MTL regions.

In this thesis there were examples of significant memory effects within stimulus-specific areas of the extrastriate cortex; for scenes within the parahippocampal place area (PPA; Peelan & Downing, 2005; Epstein et al., 1998; Epstein et al., 2006) in Experiments 1 and 2, for faces in the fusiform face area (FFA: Kanwisher et al., 1996; Kanwisher, McDermott et al., 1997; Peelen & Downing, 2005) in Experiment 1, and for objects, faces and scenes in the lateral occipital cortex (LOC: Kanwisher et al., 1996; Kanwisher, Woods et al., 1997; Malach et al., 1995) in all three experiments. Notably, previous neuroimaging investigations have provided conflicting support for long-term memory effects within extrastriate cortex; for example, while it has been demonstrated that FFA contributes to retrieval of faces (Prince et al., 2009), others

have not replicated these findings (O'Neil et al., 2009). In light of the points discussed above, however, it is possible that these discrepancies have occurred due to differences in the level of feature ambiguity of the stimulus materials employed.

In response to the issues outlined in this section, there is a recent fMRI experiment where differences between the contributions of the MTL and extrastriate regions to learning of scene and face discriminations have been demonstrated. Mundy et al. (submitted) observed that, while perirhinal cortex and FFA were both activated during discrimination learning of visually similar face pairs, but not scene pairs, only perirhinal cortex activity changed according to accuracy (correct > incorrect). Critically, an identical pattern, but now for featurally ambiguous scene and not face stimuli, was seen in posterior hippocampus and PPA; while activity in posterior hippocampus was greater for correct compared to incorrect scene discriminations, no such difference was present in PPA. This pattern reveals that, at least in the domain of visual discrimination learning, stimulus by memory interactions can occur in stimulus-specific regions within the MTL, particularly when highly visually similar items are presented. Furthermore, the roles of these stimulus-specific regions in the MTL seem to differ from those of FFA and PPA. An important next step is an extension of this paradigm into recognition memory and the incorporation of a manipulation of feature ambiguity during both visual discrimination learning (replicating Mundy et al., submitted) and long-term memory (extending the task described here). It may also be fruitful to investigate the effects of feature ambiguity manipulations on extrastriate and MTL activity during the concurrent oddity, retrieval and encoding task described earlier (see Section 5.3.4).

5.3.7. Representations in frontal and parietal cortices

In this thesis there was evidence of significant memory-related activity for objects, faces and scenes in the prefrontal and parietal cortices. These patterns of activity reflect the findings from other experiments that have measured memory-related activity for words (Daselaar et al., Ranganath et al., 2004; Yonelinas et al., 2005; Uncapher et al., 2006) and scenes (Montaldi et al., 2006) using recognition confidence and source memory accuracy to index recollection and familiarity. Notably, however, the four accounts reviewed in this thesis only make explicit reference to the contributions of MTL regions to long-term memory. Below there are two sections

which briefly outline accounts of prefrontal and parietal contributions to memory, including suggestions of how these regions may (or may not) also perform stimulus-specific functions.

5.3.7.1. Prefrontal cortex

The general consensus is that the prefrontal cortex is involved in a vast range of higher level cognitive abilities including planning, problem solving, language comprehension, attention and decision-making. There is a large body of animal and human research (e.g. Curtis & D'Esposito, 2003; Funahashi, Bruce, & Goldman-Rakic, 1989; Fuster & Alexander, 1971; Goldman-Rakic, 1995; Kubota & Niki, 1971) that also indicates a specialised role for the prefrontal cortex during the active and temporary maintenance and manipulation of information, also known as working memory (Baddley, 1986). Although the general role of the prefrontal cortex in working memory is generally undisputed, the specific roles of subregions are yet to be agreed. In fact, in his early postulations, Baddeley (1986) suggested that working memory may comprise several distinct functional units that could fractionate according to stimulus-specificity. According to proponents of this view, it is possible that there are separate systems that differentially serve verbal and visuospatial information. As such, subregions within the prefrontal cortex may subdivide in line with these different verbal and visuospatial working memory systems (Smith & Jonides, 1997; although see Cohen et al., 1994).

In addition to a verbal/spatial fractionation, it has been proposed that there is a division of labour within the prefrontal cortex for spatial versus non-spatial (object) working memory. This dichotomy is suggested by differential projections to ventrolateral and dorsolateral prefrontal cortices from the ventral and dorsal processing streams. Ventral and dorsal processing streams are thought to be specialised for representing object (what) compared to spatial (where) information, respectively (Ungerleider & Haxby, 1994; see also Sections 1.2.1; 1.5 and 1.6). Honouring this distinction, early primate lesion experiments indicated that damage to the ventrolateral frontal cortex can impair performance on single-object working memory tasks, whereas lesions to the dorsolateral prefrontal cortex interrupt object-location working memory (Fuster, 1997; Petrides, 1994). Currently, however, there is little conclusive evidence from the functional imaging literature that an object versus

scene division of labour within the ventrolateral versus dorsolateral prefrontal cortex applies to humans (D'Esposito et al., 1998; Nystrom et al., 2000; Owen, 1997). Furthermore, there is recent data from animal research that the *ventrolateral* prefrontal cortex is involved in learning object-location associations via projections from inferior temporal regions (Baxter, Browning, & Mitchell, 2008; Parker & Gaffan, 1998; Wilson, Gaffan, Mitchell, & Baxter, 2007). From the evidence briefly reviewed here, therefore, it is unclear whether and/or which subregions within the prefrontal cortex perform stimulus-specific functions.

5.3.7.2. *Parietal cortex*

Despite the consistency with which activity is observed in the parietal cortex in memory experiments (for a reviews see Cabeza, Ciaramelli, Olson, & Moscovitch, 2008; Hutchinson, Uncapher, & Wagner, 2009; Simons & Mayes, 2008; Uncapher & Wagner, 2009; Wagner, Shannon, & Buckner, 2005), human lesion evidence regarding the necessity of the parietal cortex for long-term memory remains inconclusive (Berryhill, Phuong, Picasso, Cabeza, & Olson, 2007; Davidson et al., 2008; Mesulam, 1999; Simons & Mayes, 2008; Simons et al., 2008). It has been recently proposed that activity within the parietal cortex reflects the engagement of attention mechanisms associated with remembering across a broad range of memory tasks and a wide variety of stimuli (Cabeza et al., 2008; Uncapher & Wagner, 2009; although see Hutchinson et al., 2009). There is, however, some indication that areas of the parietal cortex perform specialised roles in spatial attention (for a review see Corbetta, Patel, & Shulman, 2008). For example, in a recent fMRI experiment, Uncapher & Rugg (2009) demonstrated greater activity within the superior parietal cortex when participants attended to the location of presented objects, compared to background colour. Furthermore, in this experiment, activity within the superior parietal cortex predicted subsequent memory for the object-location associations, but not object-colour.

Converging evidence from the animal literature also suggests that the parietal cortex is involved in memory and perception of spatial information (Kesner, 2009; Rogers & Kesner, 2007; Save & Poucet, 2009), indicating a functional relationship between the hippocampus and parietal cortex in the acquisition and retention of spatial information (see also Bird & Burgess, 2008). The specific temporal relationship between the

hippocampus and parietal cortex is unknown, however, and currently there are two propositions: (a) the initial acquisition of spatial information operates via the hippocampus, whereas the parietal cortex comprises the long-term store for spatial information (Cho & Kesner, 1996; Cho, Kesner, & Brodale, 1995), (b) different types of spatial information are processed in parallel in the parietal cortex and hippocampus, then converges within the parietal cortex for storage (Rogers & Kesner, 2006).

5.3.8. *Functional connectivity between representations*

Functional connectivity refers to the functional relationship, often, but not necessarily informed by the anatomical connectivity between brain regions for a particular cognitive task, and has become one of the most influential concepts in modern cognitive neuroscience (Fingelkurts, Fingelkurts, & Kahkonen, 2005). Based upon the observations in the previous sections, it could be interesting to run functional and effective connectivity analyses on the current data sets to observe neural networks that operate between visual processing and MTL regions supporting memory encoding and retrieval for scenes, objects and faces. One form of functional connectivity entails a seed partial least squares (PLS) analysis, which examines the relationship between activity in a given brain region (or seed voxel) and activity across the brain as a function of time (McIntosh & Lobaugh, 2004). These analyses identify brain regions that are temporally related, thus delineating the functional similarity between certain regions for a given stimulus type during a given mnemonic operation.

Once these networks have been identified one can then use structural equation modelling (SEM) to investigate the effective connectivity between certain brain regions. Specifically, SEM uses inter-regional correlations between selected brain regions to compute path co-efficients, which provide information about the strength and directionality of effects. As such, these analyses could reveal projections from stimulus-specific areas of the extrastriate cortex to MTL subregions; a relationship that may be altered when the level of feature ambiguity between stimulus materials is manipulated. Using functional connectivity, it would also be possible to investigate whether stimulus-specific information projects from the MTL and remains separate within neocortical regions, such as the prefrontal and parietal cortices, or if neural networks converge within these regions reflecting more domain-general contributions

to long-term memory encoding and retrieval, as well as working memory and perception. These analyses could also indicate the direction of informational projections between extrastriate, medial temporal, parietal and prefrontal regions for different types of complex visual stimuli.

Functional and effective connectivity could be used to investigate the relationship between spatial and non-spatial contextual processing within the parahippocampal cortex. Specifically, to observe whether parahippocampal contributions to context memory are supported by inputs for object- and spatially-related information from dorsal and ventral processing streams, or back projections from the perirhinal cortex and hippocampus. Using the object versus scene context memory experiment described earlier (see Section 5.3.3), if the parahippocampal cortex does support contextual source memory for scenes and objects, it is possible that these effects are supported by the contribution of spatial information from the dorsal processing stream, whereas object information enters via projections from the perirhinal cortex, rather than the ventral processing stream. This pattern, therefore, would indicate that, although the parahippocampal cortex supports memory for spatial and non-spatial contextual information, the former aids the construction of scene-based representations in the hippocampus, whereas the latter is guided by object based representations from the perirhinal cortex.

5.4. Conclusions

When interpreted together, the three fMRI experiments described in thesis provide compelling evidence for stimulus-specific contributions to long-term memory encoding and retrieval. These data, therefore, provide a challenge for all accounts that do not highlight differences in MTL function based upon the nature of the to-be-remembered stimuli. Above all else, the findings in this thesis, and the findings motivating representational accounts in general, highlight the requirement to consider confounding effects of stimulus-related processing when investigating MTL contributions to memory and perception. While representational accounts provide the most adequate explanation for the findings in this thesis, the number of discrepant findings in the literature emphasise that further experiments are required (e.g. Aggleton & Shaw, 1996; Awipi & Davachi, 2008; Barense et al., 2005; Barense et al.,

2007; Cipolotti et al., 2006; Cohn et al., 2009; Davachi et al., 2003; Diana et al., 2010; Holdstock et al., 2005; Kirwan et al., 2008; Kopelman et al., 2007; Lee, Buckley et al., 2005; Lee, Bussey et al., 2005; Lee et al., 2008; Mayes et al., 2002; Montaldi et al., 2006; Preston et al., 2010; Scoville & Milner, 1957; Taylor et al., 2007; Wais et al., 2010; Wais et al., 2006; Yonelinas et al., 1998). Furthermore the findings in this thesis offer little insight into whether stimulus-specific processing within the MTL is restricted to long-term mnemonic function.

It seems reasonable to claim that there is currently not a single account of MTL function that accommodates all existing findings. The novel findings described here do argue, however, that focusing on content or stimuli, rather than processes or operations, is a step in the right direction. Most importantly, experiments that are designed to adjudicate between dual-process, informational and representational accounts of MTL function will ultimately lead to more flexible and interactive models of human memory, and hence a better understanding of the diagnosis and treatment of memory disorders such as organic amnesia, Alzheimer's disease and semantic dementia, all of which are associated with damage to the MTL.

References

- Adolphs, R., Tranel, D., Damasio, H., & Damasio, A. (1994). Impaired recognition of emotion in facial expressions following bilateral damage to the human amygdala. *Nature*, *372*, 669-672.
- Aggleton, J. P., & Brown, M. W. (1999). Episodic memory, amnesia and the hippocampal-anterior thalamic axis. *Behavioral and Brain Sciences*, *22*, 425-489.
- Aggleton, J. P., & Brown, M. W. (2005). Contrasting hippocampal and perirhinal cortex function using immediate early gene imaging. *Quarterly Journal of Experimental Psychology*, *58B*, 218-233.
- Aggleton, J. P., Hunt, P. R., & Rawlins, J. N. P. (1986). The effects of hippocampal lesions upon spatial and non-spatial tests of working memory. *Behavioural Brain Research*, *19*, 133-146.
- Aggleton, J. P., Kyda, R. J., & Bilkey, D. K. (2004). When is the perirhinal cortex necessary for the performance of spatial memory tasks? *Neuroscience and Biobehavioral Reviews*, *28*, 611-624.
- Aggleton, J. P., McMakin, D., Carpenter, K., Hornok, J., Kapur, N., & Halpin, S. (2000). Differential cognitive effects of colloid cysts in the third ventricle that spare or compromise the fornix. *Brain*, *123*, 800-815.
- Aggleton, J. P., & Shaw, C. (1996). Amnesia and recognition memory: a re-analysis of psychometric data. *Neuropsychologia*, *34*, 51-62.
- Aggleton, J. P., Vann, S. D., Denby, C., Dix, S., Mayes, A. R., & Roberts, N. (2005). Sparing the familiarity component of recognition memory in a patient with hippocampal pathology. *Neuropsychologia*, *43*, 1810-1823.
- Alvarez-Royo, P., Zola-Morgan, S., & Squire, L. R. (1995). Damage limited to the hippocampal region produces long-lasting memory impairment in monkeys. *Journal of Neuroscience*, *15*, 3796-3807.
- Aminoff, E., Grounau, N., & Bar, M. (2007). The parahippocampal cortex mediates spatial and non-spatial associations. *Cerebral Cortex*, *17*, 1493-1503.
- Atkinson, R. C., & Shiffrin, R. M. (1968). Human memory: A proposed system and its control processes. In K. W. Spence & J. T. Spence (Eds.), *The Psychology of Learning and Motivation* (pp. 89-195). London: Academic Press.

- Awipi, T., & Davachi, L. (2008). Content-specific source encoding in the human medial temporal lobe. *Journal of Experimental Psychology: Learning, Memory and Cognition*, *34*, 769-779.
- Baddeley, A. (1986). *Working Memory*. New York: Oxford University Press.
- Baddeley, A. (2010). Working memory. *Current Biology*, *20*, 136-140.
- Baddeley, A., Emslie, H., & Nimmo-Smith, I. (1994) *Doors and People: A Test of Visual and Verbal Recall and Recognition*. Thames Valley Test Co. Bury St. Edmunds, UK.
- Baddeley, A., & Hitch, G. J. (1974). Working memory. In G. A. Bower (Ed.), *Recent Advances in Learning and Motivation* (Vol. 8, pp. 47-89). New York: Academic Press.
- Baddeley, A., Vargha-Khadem, F., & Mishkin, M. (2001). Preserved recognition in a case of developmental amnesia: Implications for the acquisition of semantic memory? *Journal of Cognitive Neuroscience*, *13*, 357-369.
- Bar, M. (2004). Visual objects in context. *Nature Reviews Neuroscience*, *5*, 617-629.
- Bar, M., & Aminoff, E. (2003). Cortical analysis of visual context. *Neuron*, *38*, 347-358.
- Bar, M., Aminoff, E., & Ishai, A. (2008). Famous faces activate contextual associations in the parahippocampal cortex. *Cerebral Cortex*, *18*, 1233-1238.
- Bar, M., Aminoff, E., & Schacter, D. L. (2008). Scenes Unseen: The parahippocampal cortex intrinsically subserves contextual associations, not scenes or places per se. *Journal of Neuroscience*, *28*, 8539-8544.
- Barbeau, E. J., Felician, O., Joubert, S., Sonthiener, A., Ceccaldi, M., & Poncet, M. (2005). Preserved visual recognition memory in an amnesic patient with hippocampal lesions. *Hippocampus*, *15*, 587-596.
- Barense, M. D., Bussey, T. J., Lee, A. C., Rogers, T. T., Rhys Davies, R., Saksida, L. M., . . . Graham, K. S. (2005). Functional specialization in the human medial temporal lobe. *Journal of Neuroscience*, *25*, 10239-10246.
- Barense, M. D., Gaffan, D., & Graham, K. S. (2007). The human medial temporal lobe process online representations of complex objects. *Neuropsychologia*, *45*, 2963-2974.
- Barense, M. D., Henson, R. N., Lee, A. C., & Graham, K. S. (2010). Medial temporal lobe activity during complex discriminations of faces, objects and scenes: Effects of viewpoint. *Hippocampus*, *20*, 389-401.

- Barense, M. D., Rogers, T. T., Bussey, T. J., Saksida, L. M., & Graham, K. S. (2010). Influence of conceptual knowledge on visual object discrimination: Insights from semantic dementia and MTL amnesia. *Cerebral Cortex*, [EPub Feb 11].
- Bartko, S. J., Winters, B. D., Cowell, R. A., Saksida, L. M., & Bussey, T. J. (2007a). Perceptual functions of perirhinal cortex in rats: Zero-delay object recognition and simultaneous oddity discriminations *Journal of Neuroscience*, *27*, 2548 - 2549.
- Bartko, S. J., Winters, B. D., Cowell, R. A., Saksida, L. M., & Bussey, T. J. (2007b). Perirhinal cortex resolves feature ambiguity in configural object recognition and perceptual oddity tasks *Learning and Memory*, *14*(821–832).
- Bastin, C., Van der Linden, M., Charnallet, A., Denby, C., Montaldi, D., Roberts, N., & Mayes, A. (2004). Dissociation between recall and recognition memory performance in an amnesic patient following carbon monoxide poisoning. *Neurocase*, *10*, 330-344.
- Baxter, M. G., Browning, P. G., & Mitchell, A. S. (2008). Perseverative interference with object-in-place scene learning in rhesus monkeys with bilateral ablation of ventrolateral prefrontal cortex. *Learning and Memory*, *15*, 126-132.
- Beckmann, C. F., Jenkinson, M., & Smith, S. M. (2003). General multilevel linear modeling for group analysis in FMRI. *NeuroImage*, *20*, 1052-1063.
- Berntsen, D., & Thomsen, D. K. (2005). Personal memories for historical events: Accuracy and clarity of flashbulb memories related to World War II. *Journal of Experimental Psychology: General*, *134*, 242-257.
- Berry, C. J., Shanks, D. R., & Henson, R. N. (2008). A unitary signal-detection model of implicit and explicit memory. *Trends in Cognitive Sciences*, *12*, 367-373.
- Berryhill, M. E., Phuong, L., Picasso, L., Cabeza, R., & Olson, I. R. (2007). Parietal lobe and episodic memory: Bilateral damage causes impaired free recall of autobiographical memory. *Journal of Neuroscience*, *27*, 14415-14423.
- Bird, C. M., & Burgess, N. (2008). The hippocampus and memory: insights from spatial processing. *Nature*, *9*, 182-194.
- Bird, C. M., Shallice, T., & Cipolotti, L. (2007). Fractionation of memory in medial temporal amnesia. *Neuropsychologia*, *45*, 1160-1171.
- Bird, C. M., Vargha-Khadem, F., & Burgess, N. (2008). Impaired memory for scenes but not faces in developmental hippocampal amnesia: A case study. *Neuropsychologia*, *46*, 1050-1059.

- Bowles, B., Crupi, C., Mirsattari, S. M., Pigott, S. E., Parrent, A. G., & Pruessner, J. C. (2007). Impaired familiarity with preserved recollection after anterior temporal-lobe resection that spares the hippocampus. *PNAS*, *104*, 16382-16387.
- Bowles, B., Crupi, C., Pigott, S. E., Parrent, A. G., Wiebe, S., Janzen, L., & Kohler, S. (2010). Double dissociation of selective recollection and familiarity impairments following two different surgical treatments for temporal-lobe epilepsy. *Neuropsychologia*, *48*, 2640-2647.
- Brewer, J. B., Zhao, Z., Desmond, J. E., Glover, G. H., & Gabrieli, J. D. (1998). Making memories: Brain activity that predicts how well visual experience will be remembered. *Science*, *281*, 1185-1187.
- Brown, M. W., & Aggleton, J. P. (2001). Recognition memory: What are the roles of the perirhinal cortex and hippocampus? . *Nature Neuroscience*, *2*, 51-61.
- Brown, M. W., & Xiang, J. Z. (1998). Recognition memory: Neuronal substrates of the judgement prior occurrence. *Progress in Neurobiology*, *55*, 149-189.
- Buckley, M. J. (2005). The role of the perirhinal cortex and hippocampus in learning, memory, and perception. *Quarterly Journal of Experimental Psychology*, *58B*, 246-268.
- Buckley, M. J., Booth, M. C. A., Rolls, E. T., & Gaffan, D. (2001). Selective perceptual impairments after perirhinal cortex ablation. *Journal of Neuroscience*, *21*, 9824-9836.
- Buckley, M. J., Charles, D. P., Browning, P. G., & Gaffan, D. (2004). Learning and retrieval of concurrently presented spatial discrimination tasks: Role of the fornix. *Behavioral Neuroscience*, *118*, 138-149.
- Buckley, M. J., & Gaffan, D. (1997). Impairment of visual object-discrimination learning after perirhinal cortex ablation. *Behavioral Neuroscience*, *111*, 467-475.
- Buckley, M. J., & Gaffan, D. (1998). Perirhinal cortex ablation impairs visual object identification. *Journal of Neuroscience*, *18*, 2268-2275.
- Buffalo, E. A., Bellgowan, P. S. F., & Martin, A. (2009). Distinct roles for medial temporal lobe structures in memory for objects and their locations. *Learning and Memory*, *13*, 638-643.

- Buffalo, E. A., Ramus, S. J., Clark, R. E., Teng, E., Squire, L. R., & Zola, S. M. (1999). Dissociation between the effects of damage to perirhinal cortex and area TE. *Learning and Memory*, *6*, 572-599.
- Buffalo, E. A., Ramus, S. J., Squire, L. R., & Zola, S. M. (2000). Perception and recognition memory in monkeys following lesions of area TE and perirhinal cortex. *Learning and Memory*, *7*, 375-382.
- Buffalo, E. A., Reber, P. J., & Squire, L. R. (1998). The human perirhinal cortex and recognition memory. *Hippocampus*, *8*, 330-339.
- Buffalo, E. A., Stefanacci, L., Squire, L. R., & Zola, S. M. (1998). A reexamination of the concurrent discrimination learning task: The importance of anterior inferotemporal cortex, area TE. *Behavioral Neuroscience*, *112*, 3-14.
- Burwell, R. D. (2000). The parahippocampal region: corticocortical connectivity. *Annals of New York Academy of Sciences* *911*, 25-42.
- Burwell, R. D. (2001). Borders and cytoarchitecture of the perirhinal and postrhinal cortices in the rat. *Journal of Comparative Neurology*, *437*, 17-41.
- Burwell, R. D., & Amaral, D. G. (1998). Cortical afferents of the perirhinal, postrhinal, and entorhinal cortices of the rat. *Journal of Comparative Neurology* *398*, 179-205.
- Bussey, T. J., & Saksida, L. M. (2002). The organization of visual object representations: A connectionist model of effects of lesions in perirhinal cortex. *European Journal of Neuroscience*, *15*, 355-364.
- Bussey, T. J., & Saksida, L. M. (2005). Object memory and perception in the medial temporal lobe: an alternative approach. *Current Opinion in Neurobiology*, *15*, 730-737.
- Bussey, T. J., Saksida, L. M., & Murray, E. A. (2002). Perirhinal cortex resolves feature ambiguity in complex visual discriminations. *European Journal of Neuroscience*, *15*, 365-374.
- Bussey, T. J., Saksida, L. M., & Murray, E. A. (2003). Impairments in visual discrimination after perirhinal cortex lesions: Testing 'declarative' vs. 'perceptual-mnemonic' views of perirhinal cortex function. *European Journal of Neuroscience*, *17*, 649-660.
- Bussey, T. J., Saksida, L. M., & Murray, E. A. (2005). The perceptual-mnemonic/feature conjunction model of perirhinal cortex function. *Quarterly Journal of Experimental Psychology*, *58B*, 269-282.

- Buzsaki, G. (2002). Large-scale recording of neuronal ensembles. *Nature Neuroscience*, 7, 446-451.
- Cabeza, R., Ciaramelli, E., Olson, I. R., & Moscovitch, M. (2008). The parietal cortex and episodic memory: An attentional account. *Nature Reviews Neuroscience*, 9, 613-625.
- Cansino, S., Maquet, P., Dolan, R. J., & Rugg, M. D. (2002). Brain activity underlying encoding and retrieval of source memory. *Cerebral Cortex*, 12, 1048-1056.
- Carlesimo, G. A., Fadda, L., Turriziani, P., Tomaiuolo, F., & Caltagirone, C. (2001). Selective sparing of face learning in a global amnesic patient. *Journal of Neurology, Neurosurgery and Psychiatry*, 71, 340-346.
- Cho, Y. H., & Kesner, R. (1996). Involvement of entorhinal cortex or parietal cortex in long-term spatial discrimination memory in rats: Retrograde amnesia. *Behavioural Neuroscience*, 110, 436-442.
- Cho, Y. H., Kesner, R., & Brodale, S. (1995). Retrograde and anterograde amnesia for spatial discrimination in rats: Role of hippocampus, entorhinal cortex and parietal cortex. *Psychobiology*, 23, 185-194.
- Cipolotti, L., Bird, C. M., Good, T., Macmanus, D., Rudge, P., & Shallice, T. (2006). Recollection and familiarity in dense hippocampal amnesia: A case study. *Neuropsychologia*, 44, 489-506.
- Cipolotti, L., & Maguire, E. A. (2003). A combined neuropsychological and neuroimaging study of topographical and non-verbal memory in semantic dementia. *Neuropsychologia*, 41, 1148-1159.
- Clark, R. E., West, A. N., Zola, S. M., & Squire, L. R. (2001). Rats with lesions of the hippocampus are impaired on the delayed nonmatching-to-sample task. *Hippocampus*, 11, 176-186.
- Clark, R. E., Zola, S. M., & Squire, L. R. (2000). Impaired recognition memory in rats after damage to the hippocampus. *Journal of Neuroscience*, 20, 8853-8860.
- Clayton, N. S., Bussey, T. J., & Dickinson, A. (2003). Can animals recall the past and plan for the future? *Nature Reviews Neuroscience*, 4, 685-691.
- Cohen, J. D., Forman, S. D., Braver, T. S., Casey, B. J., Servan-Schreiber, D., & Noll, D. C. (1994). Activation of prefrontal cortex in a non-spatial working memory task with functional MRI. *Human Brain Mapping*, 1, 293-304.

- Cohen, N. J., Poldrack, R. A., & Eichenbaum, H. (1997). Memory for items and memory for relations in the procedural/declarative memory framework. *Memory, 5*, 131-178.
- Cohn, M., Moscovitch, M., Lahatb, A., & McAndrews, M. P. (2009). Recollection versus strength as the primary determinant of hippocampal engagement at retrieval *PNAS, 52*, 22451-22455.
- Conway, M. A., Singer, J. A., & Tagini, A. (2004). The self and autobiographical memory: Correspondence and coherence. *Social Cognition, 22*, 491-529.
- Corbetta, M., Patel, G., & Shulman, G. L. (2008). The reorienting system of the human brain: from environment to theory of mind. *Neuron, 56*, 306-324.
- Corkin, S. (1965). Tactually-guided maze learning in man: effects of unilateral cortical excisions and bilateral hippocampal lesions. *Neuropsychologia, 3*, 339-351.
- Corkin, S. (1968). Acquisition of motor skill after bilateral medial temporal-lobe excision. *Neuropsychologia, 6*, 255-265.
- Corkin, S. (1984). Lasting consequences of bilateral medial temporal lobectomy: Clinical course and experimental findings in H.M. . *Seminars in Neurology, 4*, 252-262.
- Corkin, S. (2002). What's new with the amnesic patient H.M.? *Nature Reviews Neuroscience, 3*, 153-160.
- Corkin, S., Amaral, D. G., Johnson, K. A., & Hyman, B. T. (1997). H.M.'s medial temporal lobe lesion: findings from MRI. *Journal of Neuroscience, 17*, 3964-3979.
- Cowell, R. A., Bussey, T. J., & Saksida, L. M. (2010). Functional dissociations within the ventral object processing pathway: Cognitive modules or a hierarchical continuum? *Journal of Cognitive Neuroscience, 22*, 2460-2479.
- Curtis, C. E., & D'Esposito, M. (2003). Persistent activity in the prefrontal cortex during working memory. *Trends in Cognitive Sciences, 7*, 415-423.
- D'Esposito, M., Aguirre, G. K., Zarahn, E., Ballard, D., Shin, R. K., & Lease, J. (1998). Functional MRI studies of spatial and nonspatial working memory. *Cognitive Brain Research, 7*, 1-13.
- Daselaar, S. M., Fleck, M. S., & Cabeza, R. (2006). Triple dissociation in the medial temporal lobes: Recollection, familiarity and novelty. *Journal of Neurophysiology, 96*, 1902-1911.

- Daselaar, S. M., Rombouts, S. A. R. B., Veltman, D. J., Raaijmakers, J. G. W., Lazeron, R. H. C., & Jonker, C. (2001). Parahippocampal activation during successful recognition of words: A self-paced event-related fMRI study *NeuroImage*, *12*, 1113-1120.
- Davachi, L. (2006). Item, context and relational episodic encoding in human. *Current Opinion in Neurobiology*, *16*, 693-700.
- Davachi, L., Mitchell, J., & Wagner, A. D. (2003). Multiple routes to memory: Distinct medial temporal lobe processes build item and source memories. *PNAS*, *100*, 2157-2162.
- Davidson, P. S., Anaki, D., Ciaramelli, E., Cohn, M., Kim, A. S., Murphy, K. J., . . . Levine, B. (2008). Does lateral parietal cortex support episodic memory? Evidence from focal lesion patients. *Neuropsychologia*, *46*, 1743-1755.
- Davies, R. R., Graham, K. S., Xuereb, J. H., Williams, G. B., & Hodges, J. R. (2004). The human perirhinal cortex and semantic memory. *European Journal of Neuroscience*, *20*, 2441-2446.
- Devlin, J. T., & Price, C. P. (2007). Perirhinal contributions to human visual perception. *Current Biology*, *17*, 1484-1488.
- Diana, R. A., Yonelinas, A. P., & Ranganath, C. (2007). Imaging recollection and familiarity in the medial temporal lobe: A three-component model. *Trends in Cognitive Sciences*, *11*, 379-386.
- Diana, R. A., Yonelinas, A. P., & Ranganath, C. (2008). The effects of unitization on familiarity-based source memory: Testing a behavioural prediction derived from neuroimaging data. *Journal of Experimental Psychology: Learning, Memory and Cognition*, *34*, 730-740.
- Diana, R. A., Yonelinas, A. P., & Ranganath, C. (2010). Medial temporal lobe activity during source retrieval reflects information type, not memory strength. *Journal of Cognitive Neuroscience*, *22*, 1808-1818.
- Dobbins, I. G., Rice, H. J., Wagner, A. D., & Schacter, D. L. (2003). Memory orientation and success: Separable neurocognitive components underlying episodic recognition. *Neuropsychologia*, *41*, 318-333.
- Dolcos, F., LaBar, K. S., & Cabeza, R. (2005). Remembering one year later: Role of the amygdala and the medial temporal lobe memory system in retrieving emotional memories. *PNAS*, *102*, 2626-2631.

- Donaldson, D. I., Peterson, S. E., & Buckner, R. L. (2001). Dissociating memory retrieval processes using fMRI: Evidence that priming does not support recognition memory. *Neuron*, *31*, 1047-1059.
- Donaldson, W. (1996). The role of decision processes in remembering and knowing. *Memory & Cognition*, *24*, 523-533.
- Downing, P. E., Chan, A. W., Peelen, M. V., Dodds, C. M., & Kanwisher, N. (2006). Domain specificity in visual cortex. *Cerebral Cortex*, *16*, 1453-1461.
- Drachman, D. A., & Arbit, J. (1966). Memory and the hippocampal complex. II. Is memory a multiple process? *Archives of Neurology*, *15*, 52-61.
- Duncan, K. J., Pattamadilok, C., Knierim, I., & Devlin, J. T. (2009). Consistency and variability in functional localisers. *NeuroImage*, *46*, 1018-1026.
- Eacott, M. J., & Easton, A. (2010). Episodic memory in animals: Remembering which occasion. *Neuropsychologia*, *48*, 2273-2280.
- Eacott, M. J., Gaffan, D., & Murray, E. A. (1994). Preserved recognition memory for small sets, and impaired stimulus identification for large sets, following rhinal cortex ablations in monkeys. *European Journal of Neuroscience*, *6*, 1466-1478.
- Eacott, M. J., Machin, P. E., & Gaffan, D. (2001). Elemental and configural visual discrimination learning following lesions to perirhinal cortex in the rat. *Behavioural Brain Research*, *124*, 55-70.
- Eichenbaum, H. (2004). Hippocampus: cognitive processes and neural representations that underlie declarative memory. *Neuron*, *44*, 109-120.
- Eichenbaum, H., Otto, T., & Cohen, N. J. (1994). Two functional components of the hippocampal memory system. *Behavioral and Brain Sciences* *17*, 449-517.
- Eichenbaum, H., Yonelinas, A. P., & Ranganath, C. (2007). The medial temporal lobe and recognition memory. *Annual Review of Neuroscience*, *30*, 123-152.
- Eldridge, L. L., Knowlton, B. J., Furmanski, C. S., Bookheimer, S. Y., & Engel, S. A. (2000). Remembering episodes: a selective role for the hippocampus during retrieval. *Nature Neuroscience*, *3*, 1149-1152.
- Epstein, R. A., Higgins, J. S., Parker, W., Aguirre, G. K., & Coopermana, S. (2006). Cortical correlates of face and scene inversion: A comparison. *Neuropsychologia*, *44* 1145-1158.
- Epstein, R. A., & Kanwisher, N. (1998). A cortical representation of the local visual environment. *Nature*, *392*, 598-601.

- Epstein, R. A., & Ward, E. J. (2010). How reliable are visual context effects in the parahippocampal place area? *Cerebral Cortex*, *20*, 294-303.
- Fingelkurts, A. A., Fingelkurts, A. A., & Kahkonen, S. (2005). Functional connectivity in the brain-is it an elusive concept? *Neuroscience and Biobehavioral Reviews*, *28*, 827-836.
- Fitzgerald, J. M. (1988). Vivid memories and the reminiscence phenomenon: The role of a self narrative. *Human Development*, *31*, 261-273.
- Fortin, N. J., Wright, S. P., & Eichenbaum, H. (2004). Recollection-like memory retrieval in rats is dependant on the hippocampus. *Nature* *431*, 188-191.
- Forwood, S. E., Winters, B. D., & Bussey, T. J. (2005). Hippocampal lesions that abolish spatial maze performance spare object memory delays of up to 48 hours. *Hippocampus*, *15*, 347-355.
- Friston, K. J., Rotshtein, P., Geng, J. J., Sterzer, P., & Henson, R. N. (2006). A critique of functional localisers. *Neuroimage*, *30*, 1077-1087.
- Funahashi, S., Bruce, C. J., & Goldman-Rakic, P. (1989). Mnemonic coding of visual space in the monkey's dorsolateral prefrontal cortex. *Journal of Neurophysiology*, *61*, 331-349.
- Fuster, J. M. (1997). *The prefrontal cortex: Anatomy, physiology and neuropsychology of the frontal lobe* (3 ed.). New York: Lippincott-Raven.
- Fuster, J. M., & Alexander, G. E. (1971). Neuron activity related to short-term memory. *Science*, *173*, 652-654.
- Gabrieli, J. D., Corkin, S., Mickel, S. F., & Growdon, J. H. (1993). Intact acquisition and long-term retention of mirror-tracing skill in Alzheimer's disease and in global amnesia. *Behavioral Neuroscience*, *107*, 899-910.
- Gaffan, D. (1994). Scene-specific memory for objects: a model of episodic memory impairment in monkeys with fornix transection. *Journal of Cognitive Neuroscience*, *6*, 305-320.
- Gardiner, J. M. (1988). Functional aspects of recollective experience. *Memory & Cognition*, *16*, 309-313.
- Gardiner, J. M., Java, R. I., & Richardson-Klavehn, A. (1996). How level of processing really influences awareness in recognition memory. *Canadian Journal of Experimental Psychology*, *50*, 114-122.
- Gardiner, J. M., & Parkin, A. J. (1990). Attention and recollective experience in recognition memory. *Memory & Cognition*, *18*, 579-583.

- Gardiner, J. M., Richardson-Klavehn, A., & Ramponi, C. (1997). On reporting recollective experiences and "direct access to memory systems" *Psychological Science*, *8*, 391-394.
- Giovanello, K. S., Keane, M. M., & Verfaellie, M. (2006). The contribution of familiarity to associative memory in amnesia. *Neuropsychologia*, *44*, 1859-1865.
- Giovanello, K. S., Verfaellie, M., & Keane, M. M. (2003). Disproportionate deficit in associative recognition relative to item recognition in global amnesia. *Cognitive, Affective, and Behavioral Neuroscience*, *3*, 186-194.
- Glanzer, M., Kim, K., Hilford, A., & Adams, J. K. (1999). Slope of the receiver-operating characteristic in recognition memory. *Journal of Experimental Psychology: Learning, Memory and Cognition*, *25*, 500-513.
- Gold, J. J., Smith, C. N., Bayley, P. J., Shrager, Y., Brewer, J. B., Stark, C. E., . . . Squire, L. R. (2006). Item memory, source memory, and the medial temporal lobe: Concordant findings from fMRI and memory-impaired patients. *PNAS*, *103*, 9351-9356.
- Goldman-Rakic, P. (1995). Architecture of the prefrontal cortex and the central executive. *PNAS*, *769*, 71-83.
- Gonsalves, B. D., Kahn, I., Curran, T., Norman, K. A., & Wagner, A. D. (2005). Memory Strength and Repetition Suppression: Multimodal Imaging of Medial Temporal Cortical Contributions to Recognition. *Neuron*, *47*, 751-761.
- Graf, P., & Schacter, D. L. (1985). Implicit and explicit memory for new associations in normal subjects and amnesic patients. *Journal of Experimental Psychology: Learning, Memory and Cognition*, *11*, 501-518.
- Graham, K. S., Barense, M. D., & Lee, A. C. (2010). Going beyond LTM in the MTL: A synthesis of neuropsychological and neuroimaging findings on the role of the medial temporal lobe in memory and perception. *Neuropsychologia*, *48*, 831-853.
- Graham, K. S., Simons, J. S., Pratt, K. H., Patterson, K., & Hodges, J. R. (2000). Insights from semantic dementia on the relationship between episodic and semantic memory. *Neuropsychologia*, *38*, 313-324.
- Greenberg, D. L., Keane, M. M., Ryan, L., & Verfaellie, M. (2009). Impaired category fluency in the medial temporal lobe: The role of episodic memory. *Journal of Neuroscience*(29), 10900-10908.

- Gregg, V. H., & Gardiner, J. M. (1994). Recognition memory and awareness: A large effect of study-test modalities on “know” responses following a highly perceptual orienting task. *European Journal of Cognitive Psychology*, *6*, 131-147.
- Greve, A., Donaldson, D. I., & van Rossum, M. C. W. (2010). A single-trace dual-process model of episodic memory: A novel computational account of familiarity and recollection. *Hippocampus*, *20*, 235-251.
- Gronau, N., Neta, M., & Bar, M. (2008). Integrated contextual representation for objects' identities and their locations. *Journal of Cognitive Neuroscience*, *20*, 370-388.
- Guttentag, R. E., & Carroll, D. (1997). Recollection-based recognition: Word frequency effects. *Journal of Memory and Language*, *37*, 502-516.
- Hampton, R. R., Hampstead, B. M., & Murray, E. A. (2004). Selective hippocampal damage in rhesus monkeys impairs spatial memory in an open-field test. *Hippocampus*, *14*, 808-818.
- Haskins, A. L., Yonelinas, A. P., Quamme, J. R., & Ranganath, C. (2008). Perirhinal cortex supports encoding and familiarity-based recognition of novel associations. *Neuron*, *59*, 554-560.
- Haxby, J. V., Grady, C. L., Horwitz, B., Ungerleider, L. G., Mishkin, M., Carson, R. E., . . . Rapoport, S. I. (1991). Dissociation of object and spatial visual processing pathways in human extrastriate cortex. *PNAS*, *88*, 1621-1625.
- Haxby, J. V., Hoffman, E. A., & Gobbini, M. (2000). The distributed human neural system for face perception. *Trends in Cognitive Sciences*, *4*, 223-233.
- Heathcote, A. (2003). Item recognition memory and the ROC. *Journal of Experimental Psychology: Learning, Memory and Cognition*, *29*, 1210-1230.
- Henson, R. N. (2005). A mini-review of fMRI studies of human medial temporal lobe activity associated with recognition memory. *Quarterly Journal of Experimental Psychology*, *58B*, 340-360.
- Henson, R. N., Cansino, S., Herron, J. E., Robb, W. G. K., & Rugg, M. D. (2003). A familiarity signal in human anterior medial temporal cortex? . *Hippocampus*, *13*, 259-262.
- Henson, R. N., & Gagnepain, P. (2010). Predictive, interactive multiple memory systems. *Hippocampus*, *20*, 1315-1326.

- Henson, R. N., Rugg, M. D., Shallice, T., Josephs, O., & Dolan, R. J. (1999). Recollection and familiarity in recognition memory: an event-related functional magnetic resonance imaging study. *Journal of Neuroscience, 19*, 3962-3972.
- Holdstock, J. S., Mayes, A. R., Gong, Q. Y., Roberts, N., & Kapur, N. (2005). Item recognition is less impaired than recall and associative recognition in a patient with selective hippocampal damage. *Hippocampus, 15*, 203-215.
- Holdstock, J. S., Parslow, D. M., Morris, R. G., Fleminger, S., Abrahams, S., Denby, C., . . . Mayes, A. R. (2008). Two case studies illustrating how relatively selective hippocampal lesions in humans can have quite different effects on memory. *Hippocampus, 18*, 679-691.
- Hutchinson, B. J., Uncapher, M. R., & Wagner, A. D. (2009). Posterior parietal cortex and episodic retrieval: Convergent and divergent effects of attention and memory. *Learning and Memory, 16*, 343-356.
- Insausti, R., Juottonen, K., Soininen, H., Insausti, A. M., Partanen, K., Vainio, P., . . . Pitkanen, A. (1998). MR volumetric analysis of the human entorhinal, perirhinal, and temporopolar cortices. *American Journal of Neuroradiology, 19*, 659-671.
- Jacoby, L. L. (1984). Incidental versus intentional retrieval: Remembering and awareness as separate issues. In L. R. Squire & N. Butters (Eds.), *Neuropsychology of memory* (pp. 145-156). New York: Guilford Press.
- Jacoby, L. L. (1991). A process dissociation framework: Separating automatic from intentional uses of memory. *Journal of Memory and Language, 30* 513-541.
- James, W. (1890). *Principles of Psychology*. New York: Holt.
- Jenkins, T. A., Amin, E., Pearce, J. M., Brown, M. W., & Aggleton, J. P. (2004). Novel spatial arrangements of familiar stimuli promote activity in the rat hippocampal formation but not the parahippocampal cortices: A c-fos expression study. *Neuroscience, 124*, 43-52.
- Jenkinson, M. (2003). Fast, automated, N-dimensional phase-unwrapping algorithm. *Magnetic Resonance in Medicine, 49*, 193-197.
- Jenkinson, M., Bannister, P. R., Brady, M., & Smith, S. M. (2002). Improved optimization for the robust and accurate linear registration and motion correction of brain images. *NeuroImage, 17*, 825-841.

- Jenkinson, M., & Smith, S. M. (2001). A global optimisation method for robust affine registration of brain images. *Medical Image Analysis*, *5*, 143-156.
- Jezzard, P., & Balaban, R. S. (1995). Correction for geometric distortion in echo planar images from B0 field variations. *Magnetic Resonance in Medicine*, *34*, 65-73.
- Johnson, J. D., & Rugg, M. D. (2007). Recollection and the reinstatement of encoding-related cortical activity. *Cerebral Cortex*, *17*, 2507-2515.
- Kahn, I., Davachi, L., & Wagner, A. D. (2004). Functional-neuroanatomic correlates of recollection: Implications for models of recognition memory. *Journal of Neuroscience*, *24*, 4172-4180.
- Kanwisher, N., Chun, M. M., McDermott, J., & Ledden, P. J. (1996). Functional imaging of human visual recognition. *Cognitive Brain Research*, *5*, 55-67.
- Kanwisher, N., McDermott, J., & Chun, M. M. (1997). The fusiform face area: A module in human extrastriate cortex specialized for face perception. *Journal of Neuroscience*, *17*, 4302-4311.
- Kanwisher, N., Woods, R. P., Iacoboni, M., & Mazziota, J. C. (1997). A locus in human extrastriate cortex in visual shape analysis. *Journal of Cognitive Neuroscience*, *9*, 133-142.
- Kensinger, E., & Schacter, D. L. (2006). Amygdala activity is associated with the successful encoding of item, but not source, information for positive and negative stimuli. *Journal of Neuroscience*, *26*, 2564-2570.
- Kensinger, E., Ullman, M. T., & Corkin, S. (2001). Bilateral medial temporal lobe damage does not affect lexical or grammatical processing: evidence from amnesic patient H.M. *Hippocampus*, *11*, 347-360.
- Kesner, R. (2009). The posterior parietal cortex and long-term memory representation of spatial information. *Neurobiology of learning and memory*, *91*, 197-206.
- Kirwan, C. B., & Stark, C. E. (2004). Medial temporal lobe activation during encoding and retrieval of novel face-name pairs. *Hippocampus*, *14*, 919-930.
- Kirwan, C. B., Wixted, J. T., & Squire, L. R. (2008). Activity in the medial temporal lobe predicts memory strength, whereas activity in the prefrontal cortex predicts recollection. *Journal of Neuroscience*, *28*, 10541-10548.
- Knowlton, B. J., & Squire, L. R. (1995). Remembering and knowing: Two different expressions of declarative memory. *Journal of Experimental Psychology: Learning, Memory and Cognition*, *21*(3), 699-710.

- Kohler, S., Danckert, S., Gati, J. S., & Menon, R. S. (2005). Novelty responses to relational and non-relational information in the hippocampus and the parahippocampal region: a comparison based on event-related fMRI. *Hippocampus, 15*, 763-774.
- Kopelman, M. D., Bright, P., Buckman, J., Fradera, A., Yoshimasu, H., Jacobson, C., & Colchester, A. C. F. (2007). Recall and recognition memory in amnesia: patients with hippocampal, medial temporal lobe or frontal pathology. *Neuropsychologia, 45*, 1232-1246.
- Kubota, K., & Niki, H. (1971). Prefrontal cortical unit activity and delayed alternation performance in monkeys. *Journal of Neurophysiology, 34*, 337-347.
- LeCompte, D. C. (1995). Recollective experience in the revelation effect: Separating the contributions of recollection and familiarity. *Memory & Cognition, 23*, 324-334.
- Lee, A. C., Bandelow, S., Schwartzbauer, C., Henson, R. N., & Graham, K. S. (2006). Perirhinal cortex activity during visual object discrimination: An event-related fMRI study. *NeuroImage, 33*, 362-373.
- Lee, A. C., Barense, M. D., & Graham, K. S. (2005). The contribution of the human medial temporal lobe to perception: Bridging the gap between animal and human studies. *Quarterly Journal of Experimental Psychology, 58B*, 300-325.
- Lee, A. C., Buckley, M. J., Gaffan, D., Emery, T., Hodges, J. R., & Graham, K. S. (2006). Differentiating the roles of the hippocampus and perirhinal cortex in processes beyond long-term declarative memory: A double dissociation in dementia. *Journal of Neuroscience, 26*, 5198-5203.
- Lee, A. C., Buckley, M. J., Pegman, H. S., Scahill, V. L., Gaffan, D., Bussey, T. J., . . . Graham, K. S. (2005). Specialization in the medial temporal lobe for processing of objects and scenes. *Hippocampus, 15*, 782-797.
- Lee, A. C., Bussey, T. J., Murray, E. A., Saksida, L. M., Epstein, R. A., Kapur, N., . . . Graham, K. S. (2005). Perceptual deficits in amnesia: challenging the medial temporal lobe 'mnemonic' view. *Neuropsychologia, 43*, 1-11.
- Lee, A. C., Levi, N., Rhys Davies, R., Hodges, J. R., & Graham, K. S. (2007). Differing profiles of face and scene discrimination deficits in semantic dementia and Alzheimer's disease. *Neuropsychologia, 45*, 2135-2146.

- Lee, A. C., & Rudebeck, S. R. (2010). Human medial temporal lobe damage can disrupt the perception of single objects. *Journal of Neuroscience*, *30*, 6588-6594.
- Lee, A. C., Scahill, V. L., & Graham, K. S. (2008). Activating the medial temporal lobe during oddity judgement for faces and scenes. *Cerebral Cortex*, *13*(683-696).
- Leonard, B. W., Amaral, D. G., Squire, L. R., & Zola-Morgan, S. (1995). Transient memory impairment in monkeys with bilateral lesions of the entorhinal cortex. *Journal of Neuroscience*, *228*, 5637-5659.
- Lever, C., Wills, T., Cacucci, F., Burgess, N., & O'Keefe, J. (2002). Long-term plasticity in the hippocampal place cell representation of environmental geometry. *Nature*, *416*, 90-94.
- Levy, D. A., Shrager, Y., & Squire, L. R. (2005). Intact visual discrimination of complex and feature-ambiguous stimuli in the absence of perirhinal cortex. *Learning and Memory*, *12*, 61-66.
- Litman, L., Awipi, T., & Davachi, L. (2009). Category-specificity in the human medial temporal lobe cortex. *Hippocampus*, *19*, 308-319.
- Logothetis, N. K. (2008). What we can do and what we cannot do with fMRI. *Nature*, *453*, 869-878.
- Malach, R., Reppas, J. B., Benson, R. R., Kwong, K. K., Jiang, H., Kennedy, M., . . . Tootell, R. B. (1995). Object related activity revealed by functional magnetic resonance imaging in human occipital cortex. *PNAS*, *92*, 8135-8139.
- Mandler, G. (1980). Recognising: The judgement of previous occurrence. *Psychological Review*, *87*, 252-271.
- Mandler, G., & Boeck, W. (1974). Retrieval processes in recognition. *Memory & Cognition*, *2*, 613-615.
- Manns, J. R., Hopkins, R. O., Reed, J. M., Kitchener, E. G., & Squire, L. R. (2003). Recognition memory and the human hippocampus. *Neuron*, *37*, 171-180.
- Manns, J. R., & Squire, L. R. (1999). Impaired recognition memory on the Doors and People Test after damage limited to the hippocampal region. *Hippocampus*, *9*, 495-499.
- Mayes, A. R., Holdstock, J. S., Isaac, C. L., Hunkin, N. M., & Roberts, N. (2002). Relative sparing of item recognition memory in a patient with adult-onset damage limited to the hippocampus. *Hippocampus*, *12*, 325-340.

- Mayes, A. R., Holdstock, J. S., Issac, C. L., Montaldi, D., Grigor, J., Gummer, A., . . . Norman, K. A. (2004). Associative recognition in a patient with selective hippocampal lesions and relatively normal item recognition. *Hippocampus*, *14*, 763-784.
- Mayes, A. R., Issac, C. L., Holdstock, J. S., Hunkin, N. M., Montaldi, D., & Downes, J. J. (2001). Memory for single items, word pairs, and temporal order of different kinds in a patient with selective hippocampal lesions. *Cognitive Neuropsychology*, *18*, 97-123.
- Mayes, A. R., Montaldi, D., & Migo, E. (2007). Associative memory and the medial temporal lobes. *Trends in Cognitive Sciences*, *11*, 126-135.
- McIntosh, A. R., & Lobaugh, N. J. (2004). Partial least squares analysis of neuroimaging data: Applications and advances. *NeuroImage*, *23*, 250-263.
- Mesulam, M. M. (1999). Spatial attention and neglect: Parietal, frontal and cingulate contributions to the mental representation and attentional targeting of salient extrapersonal events. *Philosophical Transactions of the Royal Society London*, *354B*, 1325-1346.
- Meunier, M., Bachevalier, J., Mishkin, M., & Murray, E. A. (1993). Effects on visual recognition of combined and separate ablations of the entorhinal and perirhinal cortex in rhesus monkeys. *Journal of Neuroscience* *13*, 5418-5432.
- Mickes, L., Wais, P. E., & Wixted, J. T. (2009). Recollection is a continuous process: implications for dual-process theories of recognition memory. *Psychological Science*, *20*, 509-515.
- Milner, B. (1962). Les troubles de la me'moire accompagnant des le'sions hippocampiques bilate'rales. In P. Passouant (Ed.), *Physiologie de l'Hippocampe* (pp. 257-272). Paris: CNRS.
- Milner, B. (1972). Disorders of learning and memory after temporal lobe lesions in man. *Clinical Neurosurgery*, *19*, 421-446.
- Milner, B., Corkin, S., & Teuber, H. L. (1968). Further analysis of the hippocampal amnesic syndrome: 14-year follow-up study of H.M. *Neuropsychologia*, *6*, 215-234.
- Milner, B., Squire, L. R., & Kandel, E. R. (1998). Cognitive neuroscience and the study of memory. *Neuron*, *20*, 445-468.
- Mishkin, M. (1978). Memory in monkeys severely impaired by combined but not by separate removal of amygdala and hippocampus. *Nature*, *273*, 279-298.

- Montaldi, D., & Mayes, A. (2010). The role of recollection and familiarity in the functional differentiation of the medial temporal lobes. *Hippocampus*, *20*, 1291-1314.
- Montaldi, D., Spencer, T. J., Roberts, N., & Mayes, A. R. (2006). The neural system that mediates familiarity memory. *Hippocampus*, *16*, 504-520.
- Morris, R. G., Garrud, P., Rawlins, J. N. P., & O'Keefe, J. (1982). Place navigation impaired in rats with hippocampal lesions. *Nature* *297*, 681-683.
- Muller, R. U., & Kubie, J. L. (1987). The effects of changes in the environment on the spatial firing of hippocampal complex-spike cells. *Journal of Neuroscience*, *7*, 1951-1968.
- Mumby, D. G., & Pinel, J. P. J. (1994). Rhinal cortex lesions and object recognition in rats. *Behavioral Neuroscience*, *108*, 11-18.
- Mumby, D. G., Wood, E. R., & Pinel, J. P. J. (1992). Object recognition memory in rats is only mildly impaired by lesions of the hippocampus and amygdala. *Psychobiology*, *20*, 18-27.
- Mundy, M. E., Honey, R. C., Downing, P. E., Wise, R. G., Graham, K. S., & Dwyer, D. M. (2009). Material-independent and material-specific activation in functional MRI after perceptual learning *NeuroReport*, *20* 1397-1401.
- Murray, E. A., & Bussey, T. J. (1999). Perceptual-mnemonic functions of the perirhinal cortex. *Trends in Cognitive Sciences*, *3*, 142-151.
- Murray, E. A., Bussey, T. J., & Saksida, L. M. (2007). Visual perception and memory: a new view of medial temporal lobe function in primates and rodents. *Annual Review of Neuroscience*, *30*, 99-122.
- Murray, E. A., & Mishkin, M. (1986). Visual recognition in monkeys following rhinal cortical ablations combined with either amygdectomy or hippocampectomy. *Journal of Neuroscience*, 1991-2003.
- Murray, E. A., & Mishkin, M. (1998). Object recognition and location memory in monkeys with excitotoxic lesions of the amygdala and hippocampus. *Journal of Neuroscience*, *18*, 6568-6582.
- Nemanic, S., Alvarado, M. C., & Bachevalier, J. (2004). The hippocampal/parahippocampal regions and recognition memory: insights from visual paired comparison versus object-delayed nonmatching in monkeys. *Journal of Neuroscience*, *24*, 2013-2026.

- Norman, K. A. (2010). How hippocampus and cortex contribute to recognition memory: revisiting the complementary learning systems model. *Hippocampus*, *20*, 1217-1227.
- Norman, K. A., & O'Reilly, R. C. (2003). Modeling hippocampal and neocortical contributions to recognition memory: a complementary learning- systems approach. *Psychological Review*, *110*, 611-646.
- Nystrom, L. E., Braver, T. S., Sabbs, F. W., Delgado, M. R., Noll, D. C., & Cohen, J. D. (2000). Working memory for letters, shapes and locations: fMRI evidence against stimulus-based regional organization of human prefrontal cortex. *NeuroImage*, *11*, 424-446.
- O'Keefe, J. (1976). Place units in the hippocampus of the freely moving rat. *Experimental Neurology*, *51*, 78-109.
- O'Keefe, J., Burgess, N., Donnett, J. G., Jeffrey, K. J., & Maguire, E. A. (1998). Place cells, navigational accuracy, and the human hippocampus *Philosophical Transactions of the Royal Society London*, *353B*, 1333-1340.
- O'Keefe, J., & Dostrovsky, J. (1971). The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat. *Brain Research*, *34*, 171-175.
- O'Keefe, J., & Nadel, L. (1978). *The Hippocampus as a Cognitive Map*. Oxford: Oxford University Press.
- O'Neil, E. B., Cate, A. D., & Kohler, S. (2009). Perirhinal cortex contributes to accuracy in recognition memory and perceptual discriminations. *Journal of Neuroscience*, *29*, 8329-8334.
- Olman, C. A., Davachi, L., & Souheil, I. (2009). Distortion and signal loss in medial temporal lobe. *PLoS One*, *4*, e8160.
- Otten, L. J., Henson, R. N., & Rugg, M. D. (2001). Depth of processing effects on neural correlates of memory encoding: Relationship between findings from across- and within-task comparisons. *Brain*, *124*, 399-412.
- Otten, L. J., Henson, R. N., & Rugg, M. D. (2002). State-related and item-related neural correlates of successful memory encoding. *Nature Neuroscience*, *5*, 1339-1344.
- Otten, L. J., & Rugg, M. D. (2001). Task-dependency of the neural correlates of episodic encoding as measured by fMRI. *Cerebral Cortex*, *11*, 1150-1160.

- Otto, T., & Eichenbaum, H. (1992a). Complementary roles of the orbito-prefrontal cortex and perirhinal-entorhinal cortices in an odor-guided delayed nonmatching-to-sample task. *Behavioral Neuroscience*, *106*, 762-775.
- Otto, T., & Eichenbaum, H. (1992b). Neuronal activity in the hippocampus during delayed nonmatch to sample performance in rats: evidence for hippocampal processing in recognition memory. *Hippocampus*, *2*, 323-334.
- Owen, A. M. (1997). The functional organization of working memory processes within the human lateral frontal cortex: The contribution of functional neuroimaging. *European Journal of Neuroscience*, *9*(1329-1339).
- Paller, K. A., & Wagner, A. D. (2002). Observing the transformation of experience into memory. *Trends in Cognitive Sciences*, *6*, 93-102.
- Park, H., Uncapher, M. R., & Rugg, M. D. (2008). Effects of study task on the neural correlates of source encoding. *Learning and Memory*, *15*, 417-425.
- Park, S., & Chun, M. M. (2009). Different roles of the parahippocampal place area (PPA) and retrosplenial cortex (RSC) in panoramic scene perception. *NeuroImage*, *47*, 1747-1756.
- Parker, A., & Gaffan, D. (1998). Memory after frontal / temporal disconnection in monkeys: conditional and non-conditional tasks, unilateral and bilateral frontal lesions. *Neuropsychologia*, *36*, 259-271.
- Parks, C. M., & Yonelinas, A. P. (2008). Theories of recognition memory. In R. Menzel (Ed.), *Learning and memory: A comprehensive reference* (Vol. 2, pp. 11-24). Oxford: Elsevier.
- Peelen, M. V., & Downing, P. E. (2005). Within-subject reproducibility of category specific activation with functional MRI. *Human Brain Mapping*, *25*, 402-408.
- Penfield, W., & Milner, B. (1958). Memory deficit produced by bilateral lesions in the hippocampal zone. *AMA Archives of Neurology & Psychiatry*, *79*.
- Petrides, M. (1994). Frontal lobes of working memory: Evidence from investigations of the effects of cortical excisions in nonhuman primates. In F. Boller & J. Grafman (Eds.), *Handbook of Neuropsychology* (Vol. 9, pp. 59-82). New York: Elsevier.
- Pihlajamaki, M., Tanila, H., Kononen, M., Hanninen, T., Hamalainen, H., Soininen, H., & Aronen, H. J. (2004). Visual presentation of novel objects and newspatial arrangements of objects differentially activates the medial temporal lobe subareas in humans. *European Journal of Neuroscience*, *19*, 1939-1949.

- Press, G. A., Amaral, D. G., & Squire, L. R. (1989). Hippocampal abnormalities in amnesic patients revealed by high-resolution magnetic resonance imaging. *Nature*, *341*, 54-57.
- Preston, A. R., Bornstein, A. M., Hutchinson, B. J., Gaare, M. E., Glover, G. H., & Wagner, A. D. (2010). High-resolution fMRI of content-sensitive subsequent memory responses in human medial temporal lobe. *Journal of Cognitive Neuroscience*, *22*, 156-173.
- Prince, S. E., Dennis, N. A., & Cabeza, R. (2009). Encoding and retrieving faces and places: Distinguishing process- and stimulus-specific differences in brain activity. *Neuropsychologia*, *47*, 2282-2289.
- Quamme, J. R., Yonelinas, A. P., & Norman, K. A. (2007). Effect of unitization on associative recognition in amnesia. *Hippocampus*, *17*, 192-200.
- Rajaram, S. (1993). Remembering and knowing: Two means of access to the personal past. *Memory & Cognition*, *21*, 89-102.
- Rajaram, S., & Geraci, L. (2000). Conceptual fluency selectively influences knowing. *Journal of Experimental Psychology: Learning, Memory and Cognition*, *26*, 1070-1074.
- Ranganath, C. (2010). A unified framework for the functional organization of the medial temporal lobes and the phenomenology of episodic memory. *Hippocampus*, *20*, 1263-1290.
- Ranganath, C., Yonelinas, A. P., Cohen, M. X., Dy, C. J., Tom, S. M., & D'Esposito, M. (2004). Dissociable correlates of recollection and familiarity within the medial temporal lobes. *Neuropsychologia*, *42*, 2-13.
- Ratcliff, R., & Murdock, B. B. (1976). Retrieval processes in recognition memory. *Psychological Review*, *83*, 190-214.
- Ratcliff, R., Sheu, C., & Gronlund, S. D. (1992). Testing global memory models using ROC curves. *Psychological Review*, *99*, 518-535.
- Reinitz, M. T., Verfaellie, M., & Millberg, W. P. (1996). Memory conjunction errors in normal and amnesic subjects. *Journal of Memory and Language*, *35*, 286-299.
- Rempel-Clower, N. L., Zola, S. M., Squire, L. R., & Amaral, D. G. (1996). Three cases of enduring memory impairment after bilateral damage to the hippocampal formation. *Journal of Neuroscience*, *16*, 5233-5255.

- Ringo, J. L. (1996). Ringo, J. L. (1996) Stimulus specific adaptation in inferior temporal and medial temporal cortex of the monkey. *Behavioural Brain Research*, *76*, 191-197.
- Roediger, H. L., Zaromb, F. M., & Goode, M. K. (2008). A typology of memory terms. In R. Menzel (Ed.), *Learning and memory: A comprehensive reference* (Vol. 2, pp. 11-24). Oxford: Elsevier.
- Rogers, J. L., & Kesner, R. (2006). Lesions of the dorsal hippocampus or parietal cortex differentially affect spatial information processing. *Behavioural Neuroscience*, *120*, 852-860.
- Rogers, J. L., & Kesner, R. (2007). Hippocampal-parietal cortex interactions: Evidence from a disconnection study in the rat. *Behavioural Brain Research*, *179*, 19-27.
- Rotello, C. M., Macmillan, N. A., Reeder, J. A., & Wong, M. (2005). The remember response: Subject to bias, graded, and not a process-pure indicator of recollection. *Psychonomic Bulletin & Review*, *12*, 865-873.
- Rotello, C. M., & Zeng, M. (2008). Analysis of RT distributions in the remember-know paradigm. *Psychonomic Bulletin & Review*, *15*, 825-832.
- Rudebeck, S. R., & Lee, A. C. (2010). Investigating the interaction between spatial perception and working memory in the human medial-temporal lobe. *Journal of Cognitive Neuroscience*, *22*, 2823-2835.
- Russell, B. C., Torralba, A., Murphy, K. P., & Freeman, W. T. (2008). LabelMe: a database and web-based tool for image annotation. *International Journal of Computer Vision*, *77*, 157-173.
- Ryan, L., Cox, C., Hayes, S. M., & Nadel, L. (2008). Hippocampal activation during episodic and semantic memory retrieval: comparing category production and category cued recall. *Neuropsychologia*, *46*, 2109-2121.
- Saksida, L. M., & Bussey, T. J. (2010). The representational-hierarchical view of amnesia: Translation from animal to human. *Neuropsychologia*, *48*, 2370-2384.
- Sauvage, M. M., Fortin, N. J., Owens, C. B., Yonelinas, A. P., & Eichenbaum, H. (2008). Recognition memory: Opposite effects of hippocampal damage on recollection and familiarity. *Nature Neuroscience*, *11*, 19-18.

- Save, E., & Poucet, B. (2009). Role of the parietal cortex in long-term representation of spatial information in the rat. *Neurobiology of learning and memory*, *91*, 172-178.
- Saxe, R., Brett, M., & Kanwisher, N. (2006). Divide and conquer: a defense of functional localizers. *Neuroimage*, *30*, 1088-1096.
- Schacter, D. L., & Tulving, E. (1994). What are the memory systems of 1994? In D. L. Schacter & E. Tulving (Eds.), *Memory systems 1994* (pp. 1-38). Cambridge: MIT Press.
- Scoville, W. B., & Milner, B. (1957). Loss of recent memory after bilateral hippocampal lesions. *Journal of Neurology, Neurosurgery and Psychiatry*, *20*, 11-21.
- Shrager, Y., Gold, J. J., Hopkins, R. O., & Squire, L. R. (2006). Intact visual perception in memory-impaired patients with medial temporal lobe lesions. *Journal of Neuroscience*, *26*, 2235-2240.
- Simons, J. S., Graham, K. S., Galton, C. J., Patterson, K., & Hodges, J. R. (2001). Semantic knowledge and episodic memory for faces in semantic dementia. *Neuropsychology*, *15*, 101-114.
- Simons, J. S., & Mayes, A. (2008). What is the parietal lobe contribution to human memory? *Neuropsychologia*, *46*, 1739-1742.
- Simons, J. S., Peers, P. V., Hwang, D. Y., Ally, B. A., Fletcher, P. C., & Budson, A. E. (2008). Is the parietal lobe necessary for recollection in humans? *Neuropsychologia*, *46*, 1185-1191.
- Slotnick, S. D. (2010). "Remember" source memory ROCs indicate recollection is a continuous process. *Memory*, *18*, 27-39.
- Small, J. A., & Sandhu, N. (2008). Episodic and semantic memory influences on picture naming in Alzheimer's disease. *Brain and language*, *104*, 1-9.
- Smith, E. E., & Jonides, J. (1997). Working memory: A view from neuroimaging. *Cognitive Psychology*, *33*, 5-42.
- Smith, S. M. (2002). Fast and automated brain extraction. *Human Brain Mapping*, *17*(3), 143-155.
- Squire, L. R. (1992). Declarative and nondeclarative memory: Multiple brain systems supporting learning and memory. *Journal of Cognitive Neuroscience*, *4*, 232-243.

- Squire, L. R. (2004). Memory systems of the brain: A brief history and current perspective. *Neurobiology of Learning and Memory*, 82, 171-177.
- Squire, L. R., & Knowlton, B. J. (2000). The medial temporal lobe, the hippocampus, and the memory systems of the brain. In M. S. Gazzaniga (Ed.), *The New Cognitive Neuroscience*. Cambridge, MA: MIT Press.
- Squire, L. R., Schmolck, H., & Stark, S. (2001). Impaired auditory recognition memory in amnesic patients with medial temporal lobe lesions. *Learning and Memory*, 8, 252-256.
- Squire, L. R., Stark, C. E., & Clark, R. E. (2004). The medial temporal lobe. *Annual Review of Neuroscience*, 27, 279-306.
- Squire, L. R., Wixted, J. T., & Clark, R. E. (2007). Recognition memory and the medial temporal lobe: A new perspective. *Nature Reviews Neuroscience*, 8, 872-883.
- Squire, L. R., & Zola-Morgan, S. (1991). The medial temporal lobe memory system. *Science*, 253, 1380-1386.
- Staresina, B. P., & Davachi, L. (2006). Differential encoding mechanisms for subsequent associative recognition and free recall. *Journal of Neuroscience*, 26(36), 9162-9172.
- Staresina, B. P., & Davachi, L. (2008). Selective and shared contributions of the hippocampus and perirhinal cortex to episodic item and associative encoding. *Journal of Cognitive Neuroscience*, 20(8), 1478-1489.
- Stark, C. E., Bayley, P. J., & Squire, L. R. (2002). Recognition memory for single items and for associations is similarly impaired following damage to the hippocampal region. *Learning and Memory*, 9, 238-242.
- Stark, C. E., & Okado, Y. (2003). Making memories without trying: Medial temporal lobe activity associated with incidental memory formation during recognition. *Journal of Neuroscience*, 23, 6748-6753.
- Stark, C. E., & Squire, L. R. (2000). Intact visual perceptual discrimination in humans in the absence of perirhinal cortex. *Learning and Memory*, 7, 273-278.
- Stark, C. E., & Squire, L. R. (2003). Hippocampal damage equally impairs memory for single items and memory for conjunctions. *Hippocampus*, 13, 281-292.
- Stefanacci, L., Buffalo, E. A., Schmolck, H., & Squire, L. R. (2000). Profound amnesia following damage to the medial temporal lobe: A neuroanatomical

- and neuropsychological profile of patient E.P. *Journal of Neuroscience*, 20, 7024-7036.
- Suddendorf, T., & Busby, J. (2003). Mental time travel in animals? *Trends in Cognitive Sciences*, 7, 391-396.
- Suzuki, W. A. (2009). Perception and the medial temporal lobe: Evaluating the current evidence. *Neuron*, 61, 657-666.
- Suzuki, W. A., & Amaral, D. G. (1994). Perirhinal and parahippocampal cortices of the macaque monkey: cortical afferents. *Journal of Comparative Neurology*, 350, 497-533.
- Suzuki, W. A., & Baxter, M. G. (2009). Memory, perception, and the medial temporal lobe: A synthesis of opinions. *Neuron*, 61, 678-679.
- Suzuki, W. A., Zola-Morgan, S., Squire, L. R., & Amaral, D. G. (1993). Lesions of the perirhinal and parahippocampal cortices in the monkey produce long-lasting memory impairment in the visual and tactual modalities. *Journal of Neuroscience*, 13, 2430-2451.
- Tanaka, J. W., & Farah, M. J. (1991). Parts and wholes in face recognition. *Quarterly Journal of Experimental Psychology* 46A, 225-245.
- Taylor, K. A., Henson, R. N., & Graham, K. S. (2007). Recognition memory for faces and scenes in amnesia: Dissociable roles for medial temporal lobe structures. *Neuropsychologia*, 45, 2428-2438.
- Tsivilis, D., Vann, S. D., Denby, C., Roberts, N., Mayes, A. R., Montaldi, D., & Aggleton, J. P. (2008). A disproportionate role for the fornix and mammillary bodies in recall versus recognition memory. *Nature Neuroscience*, 11, 834-842.
- Tulving, E. (1972). Episodic and semantic memory. In E. Tulving & W. Donaldson (Eds.), *Organization of memory* (pp. 381-404). New York: Academic Press.
- Tulving, E. (1983). *Elements of episodic memory*. New York: Oxford University Press.
- Tulving, E. (1985). Memory and consciousness. *Canadian Psychology*, 26, 1-12.
- Turriziani, P., Fadda, L., Caltagirone, C., Giovanni, A., & Carlesimo, G. A. (2004). Recognition memory for single items and for associations in amnesic patients. *Neuropsychologia*, 42, 426-433.
- Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., . . . Joliot, M. (2002). Automated Anatomical Labeling of

Activations in SPM Using a Macroscopic Anatomical Parcellation of the MNI MRI Single-Subject Brain. *NeuroImage*, 15, 273-289.

- Uncapher, M. R., Otten, L. J., & Rugg, M. D. (2006). Episodic encoding is more than the sum of its parts: An fMRI investigation of multifeatured contextual encoding. *Neuron*, 52, 547-556.
- Uncapher, M. R., & Rugg, M. D. (2005). Encoding and the durability of episodic memory: a functional magnetic resonance imaging study. *Journal of Neuroscience*, 25, 7260-7267.
- Uncapher, M. R., & Rugg, M. D. (2009). Selecting for memory? The influence of selective attention on the mnemonic binding of contextual information. *Journal of Neuroscience*, 29, 8270-8279.
- Uncapher, M. R., & Wagner, A. D. (2009). Posterior parietal cortex and episodic encoding: Insights from fMRI subsequent memory effects and dual attention theory. *Neurobiology of Learning and Memory*, 91, 139-154.
- Ungerleider, L. G., & Haxby, J. V. (1994). 'What' and 'where' in the human brain. *Current Opinion in Neurobiology*, 4, 157-165.
- Vallar, G. (2006). Memory systems: The case of phonological short-term memory. A festschrift for cognitive neuropsychology. *Cognitive Neuropsychology*, 23, 135-155.
- Vann, S. D., Brown, M. W., Erichsen, J. T., & Aggleton, J. P. (2000). Fos imaging reveals differential patterns of hippocampal and parahippocampal subfield activity in response to different spatial memory tasks. *Journal of Neuroscience*, 20, 2711-2718.
- Vann, S. D., Tsivilis, D., Denby, C., Quamme, J. R., Yonelinas, A. P., Aggleton, J. P., . . . Mayes, A. R. (2009). Impaired recollection but spared familiarity in patients with extended hippocampal system damage revealed by 3 convergent methods. *PNAS*, 106, 5442-5447.
- Vargha-Khadem, F., Gadian, D. G., Watkins, K. E., Connelly, A., Van Paesschen, W., & Mishkin, M. (1997). Differential effects of early hippocampal pathology on episodic and semantic memory. *Science*, 277, 376-380.
- Victor, M., & Agamanolis, D. (1990). Amnesia due to lesions confined to the hippocampus: A clinical-pathologic study. *Journal of Cognitive Neuroscience*, 2, 246-257.

- Wagner, A. D., Schacter, D. L., Rotte, M., Koustaal, W., Maril, A., Dale, A. M., . . . Buckner, R. L. (1998). Building memories: Remembering and forgetting of verbal experiences as predicted by brain activity. *Science*, *21*, 188-191.
- Wagner, A. D., Shannon, B. J., & Buckner, R. L. (2005). Parietal lobe contributions to episodic memory retrieval. *Trends in Cognitive Sciences*, *9*, 445-453.
- Wais, P. E., Mickes, L., & Wixted, J. T. (2008). Remember/know judgements probe degrees of memory strength. *Journal of Cognitive Neuroscience*, *20*, 1-6.
- Wais, P. E., Squire, L. R., & Wixted, J. T. (2010). In search of recollection and familiarity signals in the hippocampus. *Journal of Cognitive Neuroscience*, *22*, 109-123.
- Wais, P. E., Wixted, J. T., Hopkins, R. O., & Squire, L. R. (2006). The hippocampus supports both the recollection and the familiarity components of recognition memory. *Neuron*, *49*, 459-466.
- Wan, H., Aggleton, J. P., & Brown, M. W. (1999). Different contributions of the hippocampus and perirhinal cortex to recognition memory. *Journal of Neuroscience*, *19*, 1142-1148.
- Weis, S., Specht, K., Klaver, P., Tendolkar, I., Willmes, K., Ruhlmann, J., . . . Fernandez, G. (2004). Process dissociation between contextual retrieval and item recognition. *NeuroReport*, *15*, 2729-2733.
- Weschler, D. (1945). A standardized memory scale for clinical use. *Journal of Psychology*, *19*, 87-95.
- Wheeler, M. E., & Buckner, R. L. (2004). Functional-anatomic correlates of remembering and knowing. *NeuroImage*, *21*, 1337-1349.
- Wilson, C. R., Gaffan, D., Mitchell, A. S., & Baxter, M. G. (2007). Neurotoxic lesions of ventrolateral prefrontal cortex impair object-in-place scene memory. *European Journal of Neuroscience*, *25*, 2514-2522.
- Winters, B. D., Forwood, S. E., Cowell, R. A., Saksida, L. M., & Bussey, T. J. (2004). Double dissociation between the effects of peri-postrhinal cortex and hippocampal lesions on tests of object recognition and spatial memory: heterogeneity of function. *Journal of Neuroscience*, *24*, 5901-5908.
- Wixted, J. T. (2007). Dual-process theory and signal-detection theory of recognition memory. *Psychological Review*, *114*, 152-176.
- Wixted, J. T., Mickes, L., & Squire, L. R. (2010). Measuring recollection and familiarity in the medial temporal lobe. *Hippocampus*, *20*, 1195-1205.

- Wixted, J. T., & Squire, L. R. (2004). Recall and recognition are equally impaired in patients with selective hippocampal damage. *Cognitive, Affective, and Behavioral Neuroscience, 4*, 58-66.
- Wixted, J. T., & Stretch, V. (2004). In defence of the signal detection interpretation of remember/know judgments. *Psychonomic Bulletin & Review, 11*, 616-641.
- Wolk, D. A., Dunfee, K. L., Dickerson, B. C., Aizenstein, H. J., & Dekosky, S. T. (2010). A medial temporal lobe division of labor: Insights from memory in aging and early Alzheimer disease. *Hippocampus*, [Epub March 15].
- Woolrich, M. W., Behrens, T. E. J., Beckmann, C. F., Jenkinson, M., & Smith, S. M. (2004). Multilevel linear modelling for fMRI group analysis using Bayesian inference. *NeuroImage, 21*, 1732-1747.
- Woolrich, M. W., Ripley, B. D., Brady, M., & Smith, S. M. (2001). Temporal autocorrelation in univariate linear modeling of fMRI data. *NeuroImage, 14*, 1370-1386.
- Yonelinas, A. P. (1994). Receiver-operating characteristics in recognition memory: Evidence for a dual-process model. *Journal of Experimental Psychology: Learning, Memory and Cognition, 20*, 1341-1354.
- Yonelinas, A. P. (1997). Recognition memory ROCs for item and associative information: The contribution of recollection and familiarity. *Memory and Cognition, 25*, 747-763.
- Yonelinas, A. P. (1999a). The contribution of recollection and familiarity to recognition and source-memory judgments: A formal dual-process model and an analysis of receiver operating characteristics. *Journal of Experimental Psychology: Learning, Memory and Cognition, 25*, 1415-1434.
- Yonelinas, A. P. (1999b). Recognition memory ROCs and the dual-process signal detection model: Comment on Glanzer, Kim, Hilford and Adams. *Journal of Experimental Psychology: Learning, Memory and Cognition, 25*, 514-521.
- Yonelinas, A. P. (2001a). Components of episodic memory: The contribution of recollection and familiarity. *Philosophical Transactions of the Royal Society London, B Biological Sciences, 356*, 1363-1374.
- Yonelinas, A. P. (2001b). Consciousness, control and confidence: The 3 C's of recognition memory. *Journal of Experimental Psychology: General, 130*, 361-379.

- Yonelinas, A. P. (2002). The nature of recollection and familiarity: A review of 30 years of research. *Journal of Memory and Language*, *46*, 441-517.
- Yonelinas, A. P., Dobbins, I. G., Szymanski, M. D., Dhaliwal, H. S., & King, L. (1996). Signal-detection, threshold, and dual process models of recognition memory: ROCs and conscious recollection. *Consciousness & Cognition*, *5*, 418-441.
- Yonelinas, A. P., & Jacoby, L. L. (1994). Dissociations of processes in recognition memory: Effects of interference and of response speed. *Canadian Journal of Experimental Psychology*, *48*, 516-534.
- Yonelinas, A. P., & Jacoby, L. L. (1995). The relation between remembering and knowing as bases for recognition: Effects of size congruency. *Journal of Memory and Language*, *34*, 622-643.
- Yonelinas, A. P., & Jacoby, L. L. (1996). Noncriterial recollection: Familiarity as automatic, irrelevant recollection. *Consciousness & Cognition*, *5*, 131-141.
- Yonelinas, A. P., Kroll, N. E. A., Dobbins, I. G., Lazzara, M. M., & Knight, R. T. (1998). Recollection and familiarity deficits in amnesia: Convergence of remember-know, process dissociation, and receiver operating characteristics data. *Neuropsychology*, *12*, 323-339.
- Yonelinas, A. P., Kroll, N. E. A., Dobbins, I. G., & Soltani, M. (1999). Recognition memory for faces: When familiarity supports associative recognition. *Psychonomic Bulletin & Review*, *6*, 418-661.
- Yonelinas, A. P., Kroll, N. E. A., Quamme, J. R., Lazzara, M. M., Sauve, M. J., & Widaman, K. F. (2002). Effects of extensive temporal lobe damage or mild hypoxia on recollection and familiarity. *Nature Neuroscience*, *5*, 1236-1241.
- Yonelinas, A. P., Otten, L. J., Shaw, K. N., & Rugg, M. D. (2005). Separating the brain regions involved in recollection and familiarity in recognition memory. *Journal of Neuroscience*, *25*, 3002-3008.
- Yonelinas, A. P., & Parks, C. M. (2007). Receiver operating characteristics (ROCs) in recognition memory: A review. *Psychological Bulletin*, *133*, 800-832.
- Yonelinas, A. P., Sauve, M. J., & Knight, R. T. (2004). Mild hypoxia disrupts recollection, not familiarity. *Cognitive, Affective, and Behavioral Neuroscience*, *4*, 393-400.

- Yonelinas, A. P., Widaman, K. F., Mungas, D., Reed, B., Weiner, M. W., & Chui, C. H. (2007). Memory in the aging brain: Doubly dissociating the contribution of the hippocampus and the entorhinal cortex. *Hippocampus*, *17*, 1134-1140.
- Zhu, X. O., Brown, M. W., & Aggleton, J. P. (1995). Neuronal signalling of information important to visual recognition memory in rat rhinal and neighbouring cortices. *European Journal of Neuroscience*, *7*, 753-765.
- Zhu, X. O., McCabe, B. J., Aggleton, J. P., & Brown, M. W. (1996). Mapping recognition memory through the differential expression of the immediate early gene c-fos induced by novel or familiar visual stimulation. *NeuroReport*, *7*, 1871-1875.
- Zhu, X. O., McCabe, B. J., Aggleton, J. P., & Brown, M. W. (1997). Differential activation of the hippocampus and perirhinal cortex by novel visual stimuli and a novel environment. *Neuroscience Letters*, *229*, 141-143.
- Zola-Morgan, S., Clower, R. P., Rempel, N. L., & Squire, L. R. (1993). Damage to the perirhinal cortex exacerbates memory impairment following lesions to the hippocampal formation. *Journal of Neuroscience*, *13*, 251-265.
- Zola-Morgan, S., Squire, L. R., & Amaral, D. G. (1986). Human amnesia and the medial temporal region: Enduring memory impairment following a bilateral lesion limited to field CA1 of the hippocampus. *Journal of Neuroscience*, *6*, 2950-2967.
- Zola-Morgan, S., Squire, L. R., Amaral, D. G., & Suzuki, W. A. (1989). Lesions of perirhinal and parahippocampal cortex that spare the amygdala and hippocampal formation produce severe memory impairment. *Journal of Neuroscience*, *9*, 4355-4370.
- Zola-Morgan, S., Squire, L. R., & Mishkin, M. (1982). The neuroanatomy of amnesia: amygdala-hippocampus versus temporal stem. *Science*, *218*, 1337-1339.
- Zola-Morgan, S., Squire, L. R., & Ramus, S. J. (1994). Severity of memory impairment in monkeys as a function of locus and extent of damage within the medial temporal lobe memory system. *Hippocampus*, *4*, 483-495.
- Zola-Morgan, S., Squire, L. R., Rempel, N. L., Clower, R. P., & Amaral, D. G. (1992). Enduring memory impairment in monkeys after ischemic damage to the hippocampus. *Journal of Neuroscience*, *12*, 2582-2596.

Zola, S. M., Squire, L. R., Teng, E., Stefanacci, L., Buffalo, E. A., & Clark, R. E. (2000). Impaired recognition memory in monkeys after damage limited to the hippocampal region. *Journal of Neuroscience*, 20, 451-463.

