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Category-Specific Item Recognition and the Medial Temporal Lobe

Christopher B. Martin
The University of Western Ontario

Supervisor
Dr. Stefan Köhler
The University of Western Ontario

Graduate Program in Psychology
A thesis submitted in partial fulfillment of the requirements for the degree in Doctor of Philosophy
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CATEGORY-SPECIFIC ITEM RECOGNITION AND
THE MEDIAL TEMPORAL LOBE

(Thesis format: Integrated Article)

by

Christopher B. Martin

Graduate Program in Psychology

A thesis submitted in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy

The School of Graduate and Postdoctoral Studies
Western University
London, Ontario, Canada

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Abstract

Much neuropsychological and neuroimaging research has been focused on the contributions of different medial temporal lobe (MTL) structures to recognition memory. The majority of these studies have linked perirhinal cortex (PrC) to item recognition, whereas the hippocampus and parahippocampal cortex (PhC) have primarily been associated with the recollection of contextual detail pertaining to a specific prior stimulus encounter. Here, I report results from three fMRI studies that examined the neural correlates of item recognition with a specific focus on the relationship between such signals and category-specific effects in the MTL. In Chapter 2, I reveal that category-specific representations in both PrC and PhC can be brought to bear on item recognition decisions. In Chapter 3, I examined the specific stimulus properties that determine the relative contributions of PrC and PhC to item recognition, with a focus on landmark suitability. The results from this study revealed item recognition signals for non-landmark objects in PrC and landmarks in PhC. In Chapter 4, I focused specifically on face recognition to characterize the manner in which PrC codes item-recognition signals and to further explore the issue of category-specificity with independent functional localizer data. Results from this study indicate that item recognition signals in PrC can be distributed across voxels with directionally heterogeneous response profiles. Further, these data also revealed that the voxels comprising these patterns respond preferentially to faces under passive viewing conditions. Taken together, these findings suggest that item recognition signals are represented in a distributed, category-specific manner within both PrC and PhC.

Keywords

Recognition Memory, Item Recognition, Familiarity, Medial Temporal Lobe, Perirhinal Cortex, Parahippocampal Cortex , Hippocampus, fMRI, Multi-Voxel Pattern Analysis, Category-Specificity

Co-Authorship Statement

All projects in my thesis were carried out under the supervision of my advisor, Dr. Stefan Köhler. The study presented in Chapter 2 was published in *The Journal of Neuroscience* (Martin et al., 2013). Adam McLean and Dr. Edward O’Neil co-authored the paper and provided assistance with experimental design and data analysis. Additionally, Victoria Barkley provided assistance with data collection. Chapter 3 is currently in preparation for publication together with Dr. Köhler. Lastly, the research presented in Chapter 4 was conducted in collaboration with Dr. Paul Gribble, Dr. Rosemary Cowell, and Jessey Wright. The work presented benefited greatly from statistical advice and theoretical guidance from each. This work is currently prepared for submission. Lastly, all projects comprising my thesis were advanced through many insightful considerations from, as of yet, unmentioned members of the Köhler lab including Dr. Ben Bowles, Devin Duke, and Dr. Chris Fiacconi. The written material in this thesis is largely my own work, but was also shaped by extensive feedback and input from my advisor, Dr. Stefan Köhler.

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List of Abbreviations and Symbols

aHC	Anterior Hippocampus
ANOVA	Analysis of Variance
ATFP	Anterior Temporal Face Patch
BIC	Binding of Items and Contexts
BOLD	Blood-Oxygen Level Dependent
CRAFT	Convergence, Recollection, and Familiarity Theory
d'	Discriminability Index
EEG	Electroencephalography
ErC	Entorhinal Cortex
F	Familiar
fMRI	Functional Magnetic Resonance Imaging
FOV	Field of View
GLM	General Linear Model
HC	Hippocampus
HRF	Hemodynamic Response Function
ISI	Inter-Stimulus Interval
LIP	Lateral Intraparietal Area
MR	Magnetic Resonance
MRI	Magnetic Resonance Imaging
ms	Millisecond
MTL	Medial Temporal Lobe
MVPA	Multi-Voxel Pattern Analysis
pHC	Posterior Hippocampus
PhC	Parahippocampal Cortex
PrC	Perirhinal Cortex
R	Recollection
ROI	Region of Interest
s	Second
SEM	Standard Error of the Mean
SVM	Support Vector Machine
T1	Anatomical Magnetic Resonance Image
T2*	Functional Magnetic Resonance Image
TE	Echo Time
TR	Repetition Time
VTC	Ventral Temporal Cortex

Chapter 1

1 General Introduction

Declarative memory is the capacity for the conscious recovery of facts and personally experienced events (Milner et al., 1998). Recognition memory, a widely studied example of declarative memory, refers to the ability to distinguish between previously encountered and novel aspects of our environment, a critical component of adaptive human behaviour. To illustrate, we often rely upon landmark recognition while navigating to a restaurant and, upon arrival, we rely on face recognition to find a friend in a crowded dining room. Although we seldom reflect on our remarkable ability to do so, evidence from research attempting to identify the capacity limits of item recognition suggests that we are capable of discriminating between thousands of previously studied target objects and novel lures across varying degrees of perceptual and semantic similarity (Brady et al., 2008).

There is broad consensus in the cognitive neuroscience of memory literature that recognition memory is supported by two component processes: item recognition and recognition associated with the recovery of contextual details from a specific prior stimulus encounter (Cohen and Eichenbaum, 1993; Aggleton and Brown, 1999; Eichenbaum et al., 2007; Squire et al., 2007). The most fundamental difference between these recognition processes pertains to the nature of the processing that gives rise to each. Namely, item recognition is based on a memory signal pertaining to an object itself, such as the perceptual features of an individual's face. By contrast, the recovery of episodic contextual detail is associative in nature as it involves retrieval of information that is independent of a target stimulus. That is to say, for example, we can put a name to a face based on a single prior encounter. While the existence of these component processes is not in question, how to best characterize their cognitive and neural mechanisms remain the subject of much debate.

At a phenomenological level, a number of influential theoretical models of recognition memory have mapped item recognition and the recovery of contextual detail onto subjective experiences of familiarity and recollection, respectively (Aggleton and Brown,

1999; for review, see Brown and Aggleton, 2001; Yonelinas, 2002; Eichenbaum et al., 2007; Squire et al., 2007; Montaldi and Mayes, 2010). Specifically, familiarity supports item recognition in the absence of the retrieval of any contextual information.

Recollection refers to the retrieval of associative information related to episodic contextual details. At a cognitive level, a number of theorists have suggested that familiarity-based item recognition and recollection are qualitatively different. On these accounts, familiarity is thought to be a relatively fast process based on a continuous memory signal that can vary in strength, whereas recollection is purported to reflect a slower threshold process (see Yonelinas, 2002, for review). However, other influential proposals challenge the notion that the differences between these processes are qualitative in nature (Squire et al., 2007; Wixted and Squire, 2011).

At a neural level, research aimed at characterizing and dissociating the neural correlates of familiarity-based item recognition and the recollection of episodic contextual information has proven particularly controversial. Beginning with Scoville and Milner's (1957) seminal work on patient HM, lesion research in other cases and in non-human species, as well as functional magnetic resonance imaging (fMRI) studies in healthy individuals have firmly established the link between declarative long-term memory and the medial temporal lobes (MTL). However, a consensus regarding how to best characterize the functional contributions of different MTL structures to item recognition and recollection is still lacking (Aggleton and Brown, 2006; Eichenbaum et al., 2007; Henke, 2010; Squire et al., 2007; Ranganath and Ritchey, 2012). Discussions concerning such contributions have focused primarily on the hippocampus (HC), perirhinal cortex (PrC), and parahippocampal cortex (PhC). While not universally accepted, a number of widely influential accounts of MTL organization suggest that PrC supports familiarity-based item recognition, whereas the HC and/or PhC support the encoding and retrieval of contextual details. At the same time, however, there are also findings that point to category-specific effects in PrC and PhC that are difficult to reconcile with these claims (e.g., Davachi, 2006; Murray et al., 2007; Graham et al., 2010; Staresina et al., 2011). Interestingly, while categorical effects in more posterior aspects of occipitotemporal cortex have been well characterized in non-mnemonic task contexts, it remains unclear how such findings map onto the proposed distinction between item and context

representations in PrC and PhC. Critically, as item-based recognition memory signals reflect the familiarity of a stimulus itself, rather than any episodic contextual information from a prior stimulus encounter, the nature of the pertinent object category may play an important role in their neural organization.

At the broadest level, my thesis is focused on assessing the neural correlates of familiarity-based item recognition and examining how category-specific effects may relate to the functional contributions of different MTL structures in this regard. Toward this end, I employed multi-voxel pattern analysis (MVPA) to decode familiarity-based item recognition decisions from distributed fMRI BOLD responses within the MTL. To gain leverage on questions concerning category-specificity I employed visually presented stimuli drawn from a number of discrete object categories. The results presented in Chapters 2, 3, and 4 have potentially important implications for a number of influential models of MTL organization and functioning. Based on these data, I will argue that representations in both PrC and PhC can be brought to bear on familiarity-based item recognition decisions, and that these representations are organized in a category-specific manner. To frame the rationale and goals of my thesis I begin with a brief review pertinent models of MTL organization before highlighting an apparent gap between such models and our understanding of categorical representations in the ventral visual pathway more broadly. Lastly, I review the limited extant evidence that speaks to the issue of category-specific item recognition signals in human MTL.

1.1 MTL Structures and Connectivity

The central tenets of many theories concerning MTL contributions to recognition memory are predicated on differential connectivity between MTL structures and more posterior aspects of the ventral and dorsal visual processing pathways (Aggleton and Brown, 1999; Eichenbaum et al., 2007; Montaldi and Mayes, 2010). Connectivity within the MTL is organized in a hierarchical manner with PrC and PhC providing inputs to entorhinal cortex (ErC), which in turn provides inputs to the HC. Perirhinal and parahippocampal projections remain segregated in lateral and medial aspects of ErC, respectively (Suzuki and Amaral, 1994). In addition to inputs from ErC, the HC also receives a limited number of inputs directly from PrC and PhC (Lavanex and Amaral,

2000). Importantly, PrC and PhC are also densely connected, though these connections are largely non-reciprocal; PrC receives considerably more input from PhC than it returns (Suzuki and Amaral, 1994; Suzuki and Naya, 2014).

Although a number of cortical and subcortical regions are directly connected with ErC and the HC, the majority of information enters the MTL from unimodal and polymodal association regions via projections to PrC and PhC. The majority of these inputs are from visual processing regions in the ventral (i.e., ‘what’) and dorsal (i.e., ‘how/where’) visual pathways (Mishkin and Ungerleider, 1982; Goodale and Milner, 1992). The ventral visual pathway constitutes an occipitotemporal network and is thought to represent object quality or identity. The response selectivity of neurons within the ventral visual pathway is hierarchically organized; cells in posterior regions such as V1 exhibit small receptive fields with selectivity for simple perceptual features (e.g. line orientations; Hubel and Wiesel, 1968), whereas cells in anterior regions such as area TE in the macaque exhibit large receptive fields with selectivity for object-level representations. The discovery of intrinsic feed-forward and feed-backward connectivity within this network has guided the proposal that information is transformed and represented within a series of recurrent loops with multiple levels of inter-activity (Kravitz et al., 2013). In contrast to the ventral visual pathway, the dorsal pathway comprises an occipitoparietal network that serves to transform real-world object metrics (e.g., size, distance, rate of acceleration) into motoric commands that allow for visually guided action, such as eye movements, reaching, and grasping (Goodale and Milner, 1992). Notably, processing regions in the ventral and dorsal pathways differentially project to PrC and PhC.

Perirhinal cortex receives the large majority of its inputs from anterior aspects of the ventral visual pathway, whereas PhC is more broadly connected to regions within both the ventral and dorsal pathways. Examination of neuroanatomical connectivity in macaques has revealed that well over half of the inputs to PrC come from the unimodal visual area TE and rostral aspects of TEO, regions of the ventral visual stream that are recognized as critical for object perception (Suzuki and Amaral, 1994; Suzuki and Naya, 2014). As area TE has historically been considered to be the anterior most extent of the ventral visual pathway, its extensive connectivity with PrC suggests that PrC may further

process or transform representations from TE in the support of object recognition. Similarly to PrC, PhC also receives substantial inputs from the ventral visual stream including area TEO, V4, and caudal aspects of TE. However, in contrast to PrC, it is also innervated by regions in the dorsal visual pathway such as the cingulate, retrosplenial cortex, and areas 7a and LIP in the posterior parietal lobe (Suzuki and Amaral 1994). This pattern of differential connectivity has informed the proposal that, within the domain of vision, PrC and PhC represent objects and visuospatial information such as scenes, respectively (Mishkin and Ungerleider, 1982).

1.2 The MTL and Long-Term Declarative Memory

Scoville and Milner's (1957) seminal research with patient HM, together with the torrent of human neuropsychological and animal lesion research that followed, firmly established the link between long term declarative memory and the MTL. To treat intractable epilepsy, HM underwent a bilateral resection of his MTL that affected the majority of the amygdala, ErC, and the HC (Corkin et al., 1997). Subsequently, he suffered from profound anterograde amnesia. Anterograde amnesia, as a result of a neurological condition, refers to a deficit in forming new long-term declarative memories. For example, despite a relative preservation of his ability to remember events that had taken place prior to surgery, HM was unable to learn new word pairs or recognize people that he encountered subsequent to his resection. Importantly, however, amnesic individuals such as HM are capable of learning in the context of non-declarative memory tasks. This ability is often indexed by decreased reaction times or improved accuracy following procedural training. For example, HM benefited from practice on a procedural mirror-tracing task (Milner, 1962), evidence that pointed to a critical dissociation between declarative and non-declarative procedural memory.

Although the impairment in forming new memories is the hallmark of anterograde amnesia there are three other characteristics that have been noted in research with HM and other similar patients with MTL lesions. The first is that the impairment is multimodal, i.e., declarative memory for information is affected regardless of sensory modality and material type (Milner, 1972; Squire, 2004). Another characteristic typical of MTL damage is that immediate, or short term, memory, such as processing assessed

with digit span, remains broadly intact (Milner et al., 1998; Squire, 2004; but see Ranganath and Blumenfeld, 2005, for evidence that supports a different view). Finally, the memory impairment is present despite largely preserved perceptual and intellectual functioning (Squire et al., 2004; but see Buckley et al., 2008).

In response to the findings in HM, several researchers worked to develop animal models in non-human primates and rats that would mirror the memory impairments seen in humans with MTL lesions. The majority of these studies examined the effects of lesion location and extent on object recognition in the context of either delayed match to sample or non-match to sample tasks. Much of this work was initially guided by the assumption that the HC in particular supports long-term declarative memory. However, early results suggested that recognition memory impairments following selective hippocampal lesions were less pronounced than those associated with less selective lesions that also included the amygdala (Mishkin, 1978) or adjacent MTL cortex (i.e., ErC, PrC, and PhC; Zola-Morgan et al., 1994). This pattern of results was generally consistent with evidence from human neuropsychological research demonstrating that patients with damage limited to the HC have less severe memory impairments than those with damage that also includes aspects of PrC, ErC, and PhC (Zola-Morgan et al., 1986; Rempel-Clower et al., 1996; Corkin et al., 1997; Stefanacci et al., 2000). Ultimately, these lines of research informed the development of a unitary model of MTL functioning which maintains that the HC, PrC, ErC, and PhC form an integrated declarative memory system with each structure contributing to declarative memory in a similar manner (Squire and Zola-Morgan, 1991; Zola-Morgan et al., 1994; Squire et al., 2004). On this account, the distinction between familiarity-based item recognition and recollection is thought to be quantitative in nature, reflecting differences in memory signal strength rather than independent cognitive processes. Moreover, as part of an integrated memory system each MTL structure is purported to play a role in supporting both component processes (Squire et al., 2004; Squire et al., 2007). However, results from subsequent animal lesion research pointed to the possibility that there is functional specialization among MTL structures with each making unique contributions to recognition memory. Ultimately, advocates of unitary models of MTL functioning acknowledged the importance of functional specialization in

the MTL, but maintain that it cannot be characterized by the distinction between familiarity and recollection (Wixted and Squire, 2011).

1.3 Dual-Process Models of Recognition Memory and MTL Organization

Despite evidence suggesting that the severity of recognition memory impairments is closely related to the extent of MTL lesions, further animal research revealed that item memory impairments were obtained only when lesions to the HC were accompanied by secondary damage to MTL cortical regions, an unforeseen consequence of the surgical procedure used to lesion the HC (Murray and Mishkin, 1986; Zola-Morgan and Squire, 1986). Subsequent research directly assessed the effects of MTL lesions that ostensibly spared the HC and found that combined PrC and PhC resections resulted in item recognition deficits (Zola-Morgan et al., 1989), as did resection of PrC and ErC (Eacott et al., 1994; Gaffan and Murray, 1992; Meunier et al., 1993). Of most importance for theoretical models of MTL organization, Meunier et al. (1993) revealed item recognition deficits following selective PrC lesions that were comparable to those obtained with PrC and ErC lesions; selective ErC lesions minimally affected performance on a delay non-match to sample task. Together, these findings suggest that PrC, rather than the HC and/or amygdala, is critical for item recognition memory.

The accumulation of animal lesion evidence pointing to distinct contributions of different MTL structures to recognition memory engendered the development of models of MTL organization that attribute specific mnemonic functions to different structures. A number of similar theories concerning the functional relationship between recognition memory and MTL organization, though subtly distinct from one another, can be classified as dual-process models. Such models are predicated on the notion that familiarity-based item recognition and the recollection of contextual details associated with the previous presentation of a test cue are functionally distinct processes that are supported by different MTL structures. That is to say, this class of models emphasizes qualitative differences between familiarity and recollection both in cognitive terms and in the way these processes are supported by MTL structures.

Aggleton and Brown (1999) first proposed that there is a division of labour within the MTL whereby PrC supports item recognition based on the familiarity of the stimulus itself and the HC supports the associative processing related to recollection. This initial proposal was informed by evidence obtained with human and animal lesion studies, electrophysiological recordings from both rats and monkeys, and fMRI with healthy humans (Brown and Aggleton, 2001; Eichenbaum et al., 2007). While a complete review of this literature is beyond the scope of my thesis, I will briefly review evidence from a number of relevant neuropsychological studies (see Section 1.6 for related fMRI findings). Importantly, dual-process models of MTL organization make very specific predictions concerning the nature of recognition memory deficits associated with selective damage to different MTL structures. Specifically, such accounts posit that patients with damage limited to the HC should exhibit impairments in recollection with spared familiarity-based item memory. By contrast, patients with damage limited to PrC should exhibit deficits related to item familiarity despite a preserved ability to recollect contextual detail regarding a prior stimulus encounter.

1.4 Dual-Process Models of Recognition Memory and MTL Organization: Neuropsychological Evidence

A number of neuropsychological investigations in patients with selective MTL damage have sought to test predictions derived from dual-process and unitary memory strength models of MTL organization. While the evidence remains controversial (Wixted and Squire 2011), a substantial number of findings from research in patients with selective HC lesions support dual-process models by revealing selective recollection impairments that leave familiarity-based item recognition intact (Vargha-Khadem et al. 1997; Mayes et al. 2002; Yonelinas et al., 2002; Bastin et al., 2004; Quamme et al., 2004; Aggleton et al. 2005; Holdstock et al., 2008; Turriziani et al. 2008; Jäger et al. 2009; Bowles et al. 2010). Patient KN, for example, suffered from persistent anterograde amnesia associated with meningitis related bilateral hippocampal atrophy (Aggleton et al., 2005); volumetric analysis of MRI data revealed approximately 45% volume reductions in KN's hippocampi bilaterally, whereas surrounding neocortical tissue, including PrC, remained intact. As predicted by dual-process models, KN showed selective recollection

impairments for words with intact familiarity across two different experimental paradigms that required either subjective phenomenological reports of recognition experience or ratings of memory confidence.

While results from a number of studies have linked selective recollection impairments to MTL damage restricted to the HC, broader recognition impairments that affect the accuracy of both recollection and familiarity judgments have been reported in association with MTL lesions that include both the HC as well as aspects of surrounding MTL cortex (Yonelinas et al., 2002; Knowlton and Squire, 1995). In other words, restricted damage to the HC frequently results in impaired recollection with intact familiarity-based item recognition, whereas broader MTL damage that affects both the HC and PrC results in deficits that manifest in both component processes. This pattern of results has been interpreted as evidence in support of the notion that the HC and PrC are functionally independent. However, dissociating the functional role of PrC from the HC by way of a true double dissociation has proven to be difficult due to the typical nature and extent of naturally occurring MTL damage or surgical excisions. Unlike the HC, which is particularly vulnerable to insults or damage caused by anoxia, epilepsy, or encephalitis, selective damage to MTL cortex, including PrC, is quite rare.

Results from a single-case study conducted with patient NB provide further support for the dual-process model, and complement those reported in patients with HC lesions, by demonstrating that selective familiarity impairments can also be observed in association with an MTL lesion (Bowles et al., 2007; Bowles et al., 2010). NB underwent a rare unilateral surgical resection of the left anterior temporal lobe for treatment of intractable temporal-lobe epilepsy caused by a mass in the left amygdala. Her surgical resection involved the most anterior extent of lateral and medial temporal cortex in the left hemisphere; critically, as confirmed by post-surgical MR volumetry, it included large aspects of PrC, ErC, and the amygdala but spared the HC entirely. Across four experiments using verbal material as memoranda, conducted with three different methodological approaches that have been developed to specifically probe familiarity and recollection (remember-know paradigm, receiver operating characteristics of confidence-based recognition decisions, and a response deadline procedure), it was revealed that NB

has impairments in familiarity assessment with preserved recollection. This deficit manifested not as a phenomenological absence of feelings of familiarity, but as an impaired discrimination process with reduced accuracy that was observed in the context of overall normal recognition performance. Importantly, more recent research conducted with NB has revealed that the accuracy of her familiarity judgments for non-verbal stimuli is within the range of healthy controls (Martin et al., 2011). These results suggest NB's familiarity deficit does not reflect a more general inability to make subjective meta-memory judgments. Moreover, they also indicate that her selective impairment is material specific. These data are reviewed in more detail in Section 1.11.

Additional follow-up work (Bowles et al., 2010) directly compared NB with a group of patients who had also been treated surgically for intractable temporal-lobe epilepsy, but with a unilateral intervention that targeted the amygdala and HC, while aiming to spare surrounding neocortical structures, including PrC. In this group, an individual with a left-sided lesion was identified who showed a selective recollection impairment at a comparable level of memory strength (i.e., overall recognition performance) as the selective familiarity impairment reported in NB. Importantly, this double dissociation cannot be attributed to a potential confound related to differences in overall memory strength, a criticism previously related to neuroanatomical dissociations between familiarity-based recognition and recollection (e.g., Squire et al., 2007; Wixted, 2007).

When considered together, evidence obtained from neuropsychological investigations in patients with MTL lesions provides considerable support for dual-process accounts of MTL organization, with findings that point to dissociable roles for PrC and the HC in supporting familiarity-based item recognition and recollection, respectively. However, the literature does present some inconsistencies in that recognition impairments in patients with selective HC damage are not always limited to recollection (Manns et al., 2003; Squire et al., 2004; Wais et al., 2006). Differences related to lesion extent and documentation, the selection of patients, and overall memory impairment have been suggested to account for findings in patients in whom these impairments were not selective (for discussion, see Holdstock et al. 2008; Bowles et al. 2010). These discrepant findings may also relate to the extent to which lesions differentially affect either the

anterior or posterior HC, or different hippocampal subfields (see Poppenk et al., 2013, for related proposals). Nevertheless, the cognitive neuroscience models of recognition memory that map familiarity-based item recognition and recollection onto separate MTL structures remain contentious.

1.5 Three-Component Models of MTL Organization

It has recently been suggested that dual-process models require extension and further refinement in order to fully characterize MTL contributions to recognition memory (Eichenbaum et al., 2007; Diana et al., 2007; Ranganath et al., 2010; Montaldi and Mayes, 2010). The binding of items and contexts model (BIC; Eichenbaum et al., 2007; Diana et al., 2007; Ranganath, 2010) of MTL organization is a particularly promising three-component model that has broad explanatory power with respect to many empirical findings related to recognition memory. The BIC model differs from earlier dual-process models in two regards. First, it specifies separate roles for the HC, PrC, and PhC in episodic memory based on differential connectivity between these structures and more posterior visual processing regions. Second, the BIC model also emphasizes differences in information content between PrC and PhC, rather than focusing exclusively on process-related differences between these structures. Specifically, within this framework, the purported contribution of a given MTL structure to recognition memory is predicated on the informational content that it represents and the extent to which such information is required to perform a particular task (Ranganath, 2010).

As PrC receives the majority of its input from regions within the ventral visual stream known to be critical for object perception (e.g., area TE/TEO in the macaque; Suzuki and Amaral, 1994; Ranganath and Ritchey, 2012; Suzuki and Naya, 2014), the BIC model suggests that it plays a critical role in item recognition. In this context, the term item refers to discrete objects, faces, or words that are processed at the center of attention. Importantly, however, PrC is thought to support item recognition based on the familiarity of a stimulus itself, as well as the recognition of item-item associations when discrete items are processed in a unitized manner, a claim that has been corroborated by empirical evidence linking item-item associations (Quamme et al., 2007; Haskins et al., 2008) and the recollection source memory related to item information (Staresina and Davachi, 2006,

2008), to activity in PrC. That is to say, PrC is thought to support both familiarity- and recollection-based recognition when the content in question pertains to an item representation. By contrast, the role of PhC is purported to be related to the representation of contextual information as it receives input from both the ventral (e.g., V4 and caudal aspects of TE/TEO) and dorsal (e.g., retrosplenial and posterior parietal cortices) visual processing streams (Suzuki and Amaral, 1994; Kravitz et al., 2011; Ranganath and Ritchey, 2012). Within the BIC framework, contextual information is defined as visual, spatial, temporal, or semantic detail that is peripheral to items at the center of attention during encoding. For example, context could refer to non-target items in a visual array, thoughts one had about a target item or its temporal sequence, semantic associations related to objects that often co-occur with a target item, or the spatial location of a target item (Ranganath, 2010; Aminoff et al., 2013). As encoding and retrieval of contextual detail is necessarily associative in nature, the role of PhC in recognition memory is purported to be linked to recollection, although the model does allow for potential familiarity signals for context in PhC as well. To my knowledge, however, no neuropsychological or fMRI study to date has revealed an empirical link between PhC and the familiarity of contextual information. Lastly, the HC is thought to support the binding of item information with contextual detail. On this account, item and context representations are purported to remain segregated in PrC and PhC, respectively, prior to their convergence in the HC, where they are linked into discrete episodic representations. Given the associative nature of this item-context binding, the HC is thought to support recollection.

The Convergence, Recollection, and Familiarity Theory (CRAFT; Montaldi and Mayes, 2010) is a second three-component model of MTL organization that also builds upon dual-process predecessors. Similar to BIC, CRAFT also specifies particular roles for PrC, PhC, and the HC in episodic memory and links these roles to differences in information content. Specifically, PrC is thought to represent item information and within domain item-item associations (e.g., two words), PhC is thought to represent context and within domain context-context associations, and the HC is purported to bind items with contexts as well as across domain items (e.g., a name and a face) or contexts. Beyond the distinction between within- and between-domain associations, CRAFT also deviates from

the BIC model in how familiarity and recollection map onto PrC and PhC. Namely, CRAFT theorists maintain that PrC and PhC represent information in a manner that supports familiarity-based recognition of items and contexts, respectively, but not recollection. Recall that on the BIC model both structures can support familiarity-based recognition and recollection. Montaldi and Mayes (2010) argue that because PrC and PhC have similar cytoarchitectonic structures they likely represent and process information in a comparable manner. However, both PrC and PhC differ in this regard from the HC, pointing to the potential for fundamentally different processing. Specifically, the HC is thought to perform rapid pattern separation of bound item-context representations in a manner that subsequently allows for recollection, whereas PrC and PhC are unable to encode pattern separated item and context information, thus representing information that supports familiarity-based recognition.

1.6 Three-Component Models of MTL Organization: fMRI Evidence

In addition to the neuropsychological research reviewed in section 1.4, a number of fMRI investigations have also examined the neural correlates of recognition memory. Importantly, the unitary memory strength model, dual-process models, the BIC model, and CRAFT make different predictions concerning differential fMRI BOLD responses in PrC, PhC, and HC in relation to familiarity-based item recognition and recollection. Pertinent fMRI studies have probed familiarity and recollection using either subjective reports of either familiarity- or recollection-based recognition, source memory judgments that assess recognition of a target item as well as the ability to recall contextual detail from the initial encounter, or recognition confidence ratings that index the certainty with which participants feel an item is old or new. In the context of experiments that have employed these paradigms, fMRI BOLD responses related to recollection have been isolated by contrasting recollected trials with those judged as being familiar [$R > F$], source memory correct versus incorrect [Source Correct $>$ Incorrect], and highest confidence responses versus all lower confidence ratings [e.g., $5 > 1-4$]. By contrast, familiarity related activity is assessed by contrasting correct familiar judgments with target items called ‘new’ [$F < Miss$], trials on which a target item is correctly identified

but not the source with misses [Target Correct + Source Incorrect < Miss], and by identifying regions in which changes in BOLD response correlate with changes in confidence levels after excluding the highest response option.

Evidence obtained across many studies using the paradigms noted above converges in a remarkably consistent manner with respect to the neural correlates of recollection and familiarity, although these findings have not gone unchallenged (Wixted and Squire, 2011). Specifically, most fMRI studies that have examined recognition memory report differential activity related to recollection at both the time of encoding and retrieval in the HC and PhC. Critically, however, these regions are generally insensitive to differences related to familiarity-based recognition (Eldridge et al., 2000; Davachi et al., 2003; Kahn et al., 2004; Ranganath et al., 2004; Weis et al., 2004; Dolcos et al., 2005; Uncapher and Rugg, 2005; Woodruff et al., 2005; Yonelinas et al., 2005; Montaldi et al., 2006; Daselaar et al., 2006; Uncapher et al., 2006; Vilberg and Rugg, 2007; Wang et al., 2014; see Diana et al., 2007, for review). In contrast to results obtained in the HC and PhC, activity in PrC has been demonstrated to be sensitive to familiarity-based item recognition, but not the recollection of contextual detail (Henson et al., 1999; Davachi et al., 2003; Ranganath et al., 2004; Weis et al., 2004; Uncapher and Rugg, 2005; Yonelinas et al., 2005; Daselaar et al., 2006; Montaldi et al., 2006; Kensinger and Schacter 2006; Uncapher et al., 2006; Yassa and Stark, 2008; Kafkas and Montaldi, 2012; Wang et al., 2014; see Diana et al., 2007, for review).

Rather than detailing the experimental design and specific results from each of these studies, I will elaborate on just one that has figured prominently in the literature. Ranganath et al. (2004) scanned participants during the encoding stage of a recognition memory task and in a subsequent un-scanned test stage asked that they discriminate between previously studied and novel words. During the test stage, participants indicated how confident they were that each item was studied and also performed a two alternative forced-choice source memory judgment that probed recollection of the encoding task associated with each trial. Scanned encoding trials were then scored according to subsequent memory judgments and whole-brain voxel-wise contrasts revealed that left PrC was the only MTL structure in which activity linearly indexed recognition

confidence ratings (i.e., a graded familiarity signal). By contrast, the right HC and right PhC were the only MTL structures that showed differential effects between correct and incorrect source memory judgments (i.e., recollection).

The results from Ranganath et al. (2004), together with those not reviewed in further detail (see above), are largely consistent with predictions derived from dual-process models of MTL organization regarding PrC and the HC. Specifically, evidence from the majority of fMRI studies link PrC to familiarity-based item recognition and the HC to the recovery of episodic contextual detail. However, in addition to the HC, these data also implicate PhC in the recovery of contextual detail. With respect to competing three-component models of MTL organization, the overall pattern of results obtained with fMRI studies favours the BIC model over CRAFT as differential activity in PhC is typically observed in relation to the encoding and retrieval of recollection or the recovery of source detail, not familiarity-based context recognition.

In addition to informing the development of the theoretical models of MTL organization, results from these fMRI investigations have also guided proposals concerning the mechanism by which familiarity-based item recognition signals are coded in PrC. Specifically, the observation that familiarity signals measured at the time of retrieval tend to manifest in fMRI BOLD responses as a relative decrement in activity has been taken as evidence favouring the notion that it is a decrease in PrC activity that codes for stimulus familiarity (c.f., Yassa and Stark, 2008; Kafkas and Montaldi, 2012). Interestingly, such findings are consistent with results from neurophysiological data obtained with single-cell recordings from PrC in both macaques and rats. Specifically, these studies most typically reveal a decrease in neural spiking for repetition of visually presented stimuli (Xiang and Brown, 1998; cf. Thome et al., 2012). However, as will be discussed in Chapter 4, there are a number of challenges associated with mapping neurophysiological recordings and fMRI BOLD responses onto one another.

By linking the functional contributions of MTL structures to differences in informational content, rather than mnemonic processes as such, the BIC model of MTL organization can account for much, though not all, extant fMRI and neuropsychological data that

speak to the issue of functional specialization pertaining to familiarity-based item recognition and recollection of contextual detail. Importantly, however, the neural correlates of familiarity-based item recognition have primarily been probed using words as memoranda. Accordingly, no systematic effort has been made to examine potential differences between contributions of MTL structures to recognition memory in relation to stimulus content. This point is particularly pertinent for discussions concerning the roles of PrC and PhC, as fMRI data obtained in non-mnemonic task contexts point to category-specific differences between these structures in relation to visually presented objects. How these categorical effects relate to the distinction between item and context representations remains unclear.

1.7 Representational Account of MTL Functioning

Classically, the MTL has been characterized as a dedicated declarative memory system, a bias reflected in each of the theories reviewed thus far. However, the representational account of MTL functioning challenges theoretical frameworks that ascribe purely mnemonic functions to MTL structures. At its core, the representational account suggests that the MTL supports not only long-term memory, but short-term memory, implicit memory, and perception, as well. Moreover, the specific contributions of different MTL structures to both memory and perception is determined by the type of visual content in question (Murray and Bussey, 1999; Bussey and Saksida, 2007; Graham et al., 2010). Specifically, PrC is thought to code for complex object representations whereas the HC and PhC are thought to represent scenes (Graham et al., 2006; Lee et al., 2006; Taylor et al., 2007; Lee et al., 2008; Barense et al., 2010). Notably, however, discussions pertaining to the proposed interface between memory and perception in the MTL have focused primarily on the distinction between PrC and the HC.

Critically, PrC is purported to generate highly integrated representations of complex, multi-feature objects. These representations code not only the co-occurrence of features comprising an object (e.g., eyes, nose, and mouth), but also their unique configuration (e.g., what distinguishes one face from another). In this regard, object representations in PrC are thought to differ from those in earlier regions of the ventral visual stream (e.g., lateral occipital complex) which are less integrated or even coded at the individual

feature level (Bussey and Saksida, 2002; Cowell et al., 2006); the level of object feature integration is thought to increase as information progresses rostrally along the ventral visual stream with PrC at the apex. This hierarchical framework assumes that object representations in PrC are recruited only when task demands require discrimination between complex objects that are highly similar, and therefore, are discriminable only at the level of feature conjunctions (i.e., categorized stimuli), rather than any one single feature. If the objects in question are not sufficiently complex and/or have limited feature overlap, it is assumed that discriminations can be resolved based on less integrated or feature level representations at earlier stages of the ventral visual pathway. The representational account suggests that the HC and PhC generate highly integrated scene representations in a manner that is comparable to that of objects in PrC. Importantly, integrated object representation in PrC and scene representations in either the HC or PhC can be brought to bear on both mnemonic and perceptual discriminations in a task dependent manner. Put another way, the representational account suggests that there may not be a sharp distinction between memory and perception as discriminations at either level are predicated on common representations.

Proponents of representational accounts maintain that the memory deficits associated with MTL damage reflect the consequence of an inability to form new, and to access previously stored, conjunctive representations of objects in PrC and scenes in the HC and PhC. In other words, the model predicts category-specific impairments associated with MTL damage that selectively affects either PrC or the HC and PhC. With respect to the distinction between familiarity-based item recognition and recollection, the model predicts that object representations in PrC and scene representations in the HC and PhC support both component processes.

1.8 Representational Account of MTL Functioning: Neuropsychological and fMRI Evidence

While development of the representational account was guided primarily by animal lesion studies, predictions derived from this model have also been tested with neuropsychological research conducted in humans. Such approaches have focused on characterizing perceptual deficits in patients that have either selective HC lesions or

broader MTL damage that includes aspects of the HC, PrC, and PhC. At the outset, it should be noted that results favouring a representational account of MTL function have not gone unchallenged (Levy et al., 2005; Shrager et al., 2006; Baxter, 2009; Suzuki, 2009). Here, however, I will highlight results from only a few exemplary studies that provide support for this model (see Graham et al., 2010, for review).

Lee et al. (2005) examined performance on a perceptual discrimination task using a simultaneous match to sample paradigm in healthy control participants, patients with selective hippocampal damage, and patients with broader MTL damage that included PrC. The task required participants to judge which of two images was most similar to a simultaneously presented sample image; the similarity between each option and the sample image was manipulated through image morphing with one option adopting relatively more features from the sample. When compared to age-matched controls, patients with hippocampal damage exhibited deficits limited to the discrimination of scenes, whereas patients with broader MTL damage were impaired at discriminations of scenes, faces, and objects. This pattern of results is consistent with the representational account as it not only implicates MTL structures in perceptual judgments in the absence of long-term declarative memory demands, but it does so in a category-specific manner. Moreover, both patient groups performed as well as controls when discriminating colors and abstract art that could be resolved based on a simple perceptual feature. Lee et al. (2006) have replicated these findings using different experimental procedures for scenes and faces in neurological patients with more pronounced atrophy of the HC than surrounding neocortical structures (i.e., Alzheimer's disease) and those with more significant damage to PrC than the HC (i.e., semantic dementia patients).

In addition to neuropsychological investigations, a number of studies have also evaluated the representational account using fMRI in healthy humans. For example, Barense et al. (2010) compared PrC activation during difficult and easy oddity discriminations for faces, objects, and scenes. In this task, stimulus triplets were presented, two of which were identical, and participants were required to identify the oddball. In the easy condition, all stimuli were presented with viewpoint held constant. As such, the target could be identified based on overall differences in item shape or contrast whereas the

difficult condition required feature integration. In the difficult condition, viewpoint varied across stimuli in the triplet and required consideration of integrated feature conjunctions. Comparison of BOLD responses in each condition, within each stimulus class, revealed PrC involvement for perceptual judgments pertaining to objects and faces, but not scenes. Lee et al., (2008) have revealed similar effects in PrC for faces and in the HC for scenes in the context of a comparable oddity paradigm.

O'Neil et al., (2009) directly examined the role of PrC when perceptual and mnemonic discriminations are made for morphed faces, using similar stimulus arrays for each condition. The memory task required that participants identify a previously studied face from an array that included the simultaneous presentation of two lures that varied with respect to perceptual similarity with the target. The perceptual discrimination task required selection of the odd item from the stimulus triplet display. Critically, both tasks were found to activate PrC similarly, compared to a control task that could be solved based upon a simple perceptual feature (i.e., a luminance discrimination task).

When considered together, the pattern of results obtained across neuropsychological and fMRI investigations does indeed suggest that PrC and the HC play a critical role not only in declarative memory tasks but in perceptual discrimination, as well. Perhaps more important for current consideration, however, are predictions concerning category-specific recognition memory effects pertaining to objects and scenes in these structures. While many of the core principles of the representational account have been carefully tested, the notion that recognition memory signals may be category-specific has not been the subject of systematic investigation. Given that memory and perception may indeed be closely related at the level of MTL processing, hypotheses regarding category-specific item recognition signals are likely to benefit from consideration of category-specific responses in more posterior aspects of the ventral visual stream and the MTL.

1.9 Category-Specific Responses in Ventral Temporal Cortex

Efficient categorization of stimuli is among the most fundamental functions of our visual system. Evidence obtained over decades of neuropsychological and fMRI research

indicates that the ventral visual pathway is critically important for object recognition and categorization (Goodale and Milner, 1992; Mishkin and Ungerleider, 1982). Given the broad implications associated with understanding object recognition, these lines of research have generated a massively large, yet nuanced literature that cannot be fully reviewed here. Rather, I will provide only a brief summary of robust findings related to categorical representations in ventral temporal cortex (VTC) that are particularly relevant to the rationale and goals of this thesis. At the broadest level, fMRI research has revealed two types of categorical responses in VTC (see Op de Beeck et al., 2008; Grill-Spector and Weiner, 2014, for review). The first comprise contiguous regions of cortex that respond preferentially to stimuli from a specific category (e.g., faces) as compared to stimuli from other categories (e.g., scenes). The second type of categorical representations are distributed across the entirety of VTC and coded at a population level.

Discrete category selective regions of cortex have been identified for numerous types of stimuli including faces (Kanwisher et al., 1997), scenes (Epstein et al., 1998), words (Cohen et al., 2000), and body parts (Peelen and Downing, 2005). These regions are typically contiguous voxel clusters functionally defined based on differential BOLD responses and often encompass more than one distinct anatomically defined structure. Parahippocampal place area, for example, is comprised of the posterior extent of the parahippocampal cortex and adjacent lingual gyrus and is defined as the contiguous cluster of voxels that preferentially respond to scenes as compared to faces, objects, and scrambled scenes. Importantly, fMRI findings suggesting that specific areas of VTC support specialized visual processing of categorical stimuli is consistent with neuropsychological evidence linking damage in different aspects of VTC to various forms of visual agnosia (i.e., the inability to recognize stimuli from specific categories; for comprehensive review see Farah, 2004). For example, prosopagnosia, perhaps the most well-known form of agnosia, refers to an inability to recognize faces despite a preserved ability to name inanimate objects, and can be associated with damage to the fusiform gyrus (e.g., Moscovitch et al., 1997). While agnosia for multiple stimulus categories are often comorbid, careful consideration of lesion overlap across individuals suggests that category-specific forms of agnosia can be linked to focal damage in regions of VTC that correspond to functionally defined regions in healthy individuals (Milner and

Goodale, 1995). Together, these lines of research have informed proposals suggesting that categorical perception is sub-served by visual modules that are specialized for processing specific types of stimuli.

In contrast to evidence supporting a modular view of visual perception and object categorization, the introduction of multi-voxel pattern analysis (MVPA) has also revealed overlapping categorical representations that are distributed across broad swaths of VTC, including voxels with no clear categorical preference. These analysis approaches can be used to ask whether the patterns of activation associated with stimuli from one specific category are more similar to one another than they are to those corresponding to stimuli from a different category. Seminal work conducted by Haxby et al. (2001), was among the first MVPA studies to reveal these distributed regularities in VTC using stimuli from eight distinct categories, including faces and various classes of man-made objects.

Importantly, this study revealed categorical sensitivity across visually responsive voxels in VTC even after exclusion of regions that showed category-selective responses, i.e., accurate classification of face stimuli even after excluding voxels that responded maximally to faces, for example. Further, stimuli from non-preferred categories could also be classified in discrete, classically defined category-selective regions. This finding has since been replicated using both fMRI (Spiridon and Kanwisher, 2002; Carlson et al., 2003; O'Toole et al., 2005) and single-cell recordings in macaques (Kiani et al., 2007). Notably, striking similarities have been reported between the representational structure of these distributed responses across humans and macaques (Kriegeskorte et al., 2008). Moreover, these cross-species data revealed that this categorical representational structure is not present in early or intermediate visual areas (V1-4) in either humans or monkeys. Biologically plausible computational models have also been developed that further support the notion of distributed and overlapping categorical representations in VTC (Cowell and Cottrell, 2013).

Ultimately, a categorical representational structure that is distributed across VTC and coded at the population level can accommodate the observation that humans and other species are able to recognize and categorize stimuli from thousands of categories at varying levels of abstraction (i.e., exemplar, basic, subordinate, and superordinate)

despite the fact that there are relatively few regions dedicated to processing specific categories of stimuli. As it relates to recognition memory, however, it is not clear how these category specific responses in the ventral visual stream map onto models of MTL organization that emphasize a distinction between items and contexts in PrC and PhC, respectively. This issue is even more striking when considered in the context of research that implicates both PrC and PhC in object processing.

1.10 Category-Specific Responses in the MTL

Although it has been suggested that PrC constitutes the anterior most aspect of the ventral visual stream (Murray and Bussey, 1999; Bussey and Saksida, 2007; Graham et al., 2010), fMRI investigations of categorical representations have primarily focused on more posterior aspects of VTC. Recently, however, a number of studies have specifically examined content-specific responses in MTL with a particular focus on identifying categorical dissociations between PrC and PhC. Although the MTL is known to play a critical role in recognition memory, this line of research concerning categorical effects has not been directly linked to specific mnemonic processes.

In addition to the face-selective regions that have been identified in more posterior VTC (e.g., fusiform face area), results from recent fMRI and animal neurophysiological research indicate that aspects of PrC may also exhibit specialization for face processing. Specifically, examination of the face processing network in the macaque has implicated a contiguous patch in a ventral aspect of the anterior temporal lobe (Freiwald and Tsao, 2010; Moeller et al., 2008; Mur et al., 2010; Pinsk et al., 2009; Rajimehr et al., 2009; Tsao et al., 2003; Tsao et al., 2008). Targeted assessment of face selectivity in humans has been probed using mnemonic tasks including 1-back identity tasks (Mundy et al., 2012; Nasr and Tootell, 2012; Rossion et al., 2012), and non-mnemonic tasks such as gender discrimination or passive viewing conditions (Mundy et al., 2012; Rajimehr et al., 2009). Together, these lines of research converge in revealing a region in the vicinity of PrC that is functionally comparable to that revealed in non-human primates (Nasr and Tootell, 2012; Rajimehr et al., 2009; Rossion et al., 2012; Tsao et al., 2008; Von Der Heide et al., 2013). Interestingly, MVPA of fMRI data has also revealed distributed

categorical information in PrC with evidence for a potential specialized role related to faces, as compared to either scenes, words, or sounds (Liang et al., 2013).

As noted in section 1.9, early research on categorical perception linked PhC to the processing of scene stimuli (i.e., the parahippocampal place area; Epstein and Kanwisher, 1998). Indeed, obtaining differential responses to scenes as compared to faces, tools, or scrambled scenes in posterior aspects of PhC is one of the most robust fMRI effects in the literature. The initial link between PhC and scene processing was one line of evidence that informed the notion that this structure represents contextual detail relevant for episodic recollection (Davachi, 2006; Eichenbaum et al., 2007). However, results from subsequent investigations of category preference in PhC have revealed differential responses not only to content that can serve as contextual information, such as scenes, but also to some categories of objects that can potentially serve as target items in a recognition memory task, such as buildings (Aguirre et al., 1998; Epstein and Kanwisher, 1998; Janzen and van Turrenout, 2004; Epstein, 2005; Cate et al., 2011). A number of fMRI studies have since sought to identify the stimulus properties that modulate PhC responses to objects.

While the object properties that evoke differential responses in PhC in the absence of mnemonic demands are only beginning to be understood, evidence from a number of studies suggests that landmark suitability may be a critical determinant (Mullally and Maguire, 2011; Konkle and Oliva, 2012; Troiani et al., 2014). Specifically, objects that are large and typically fixed in location are suitable landmarks as these properties confer potential navigational relevance. For example, Troiani et al. (2014) examined PhC responses to objects that were independently rated along a number of dimensions (i.e., real-world size, visual size, fixedness, placeness, context, and distance) in the context of an experiment that asked participants to press a button each time a stimulus was presented. Results from a factor analysis revealed that PhC responses to objects loaded primarily on visual size and the landmark suitability of an object (i.e., the extent to which an object is large, fixed in place, and defines a physical space). This pattern of results is consistent with previous research which suggested that PhC represents objects that define

a three-dimensional space that one could operate within by virtue of being large and fixed in location (Mullally and Maguire, 2011).

In general, and to the extent that faces can be considered discrete items, evidence from research linking PrC to face processing is consistent with both the BIC model and representational account of MTL functioning. They are also consistent with the notion that PrC plays a critical role in face and object perception. However, the observation of object-specific representations in PhC raises interesting questions regarding the proposal that this structure supports only contextual information and that PrC supports familiarity-based item recognition for objects from all stimulus categories. The implications of these category-specific effects on distinctions between PrC and PhC at the level of items and contexts, or familiarity and recollection remain poorly understood. Given that extant fMRI studies of recognition memory have primarily employed words as stimuli (for review, see Diana et al., 2007; Kim, 2013; cf. Montaldi et al., 2006), whether objects that are differentially represented in PhC in non-mnemonic task contexts are also associated with familiarity signals in PhC remains unknown. In fact, few efforts have been made to systematically probe the relationship between stimulus content and familiarity-based item recognition.

1.11 Evidence of Material-Specific Familiarity Signals in PrC

Given that the controversy over whether familiarity-based item recognition and recollection are supported by different MTL structures has dominated the discussion regarding functional specialization within the MTL over recent years, very few studies have systematically examined the relationship between stimulus content and the neural correlates of familiarity-based item recognition. However, a much older neuropsychological literature has been concerned with the question of whether left versus right-sided MTL structures differ in their functional role (for reviews, see Smith, 1989; Lee et al., 2002; Saling, 2009). The most influential account of lateralization in the MTL builds on the notion of material-specificity and entails that hemispheric differences in MTL functioning are determined by the nature of the stimuli processed in declarative long-term memory (Milner, 1972); left MTL structures are thought to be specialized for

memory processing of verbal materials whereas right MTL structures make differential contributions to processing of materials that cannot easily be verbalized. Overall, the link between left sided lesions and verbal-memory deficits appears to be more consistent across neuropsychological studies, in particular those conducted in patients with temporal lobe epilepsy, than that between right-sided lesions and deficits in memory for non-verbal material (e.g., Lee et al., 2002). However, even for verbal memory impairments, the laterality literature is by no means conclusive (for discussions, Blaxton and Theodore, 1997; Dobbins et al., 1998; Saling, 2009).

Much of the literature on lateralization and material specificity predates our current understanding of recognition memory in terms of two independent processes with distinct neural mechanisms in the MTL. As such, the question of whether item recognition and recollection are lateralized in specific ways has received significantly less systematic investigation than examining differential contributions of HC as compared to neighbouring neocortical structures to these two processes. Research from several studies in patients with selective recollection impairments that are associated with unilateral HC lesions suggests that this component process may not be clearly lateralized (Peters et al., 2009; Bowles et al., 2010; but see, Moscovitch and McAndrews, 2002; Bird et al., 2007). By contrast, data from two recent studies in patients with large, unilateral temporal-lobe lesions suggest that the processes supporting familiarity-based item recognition may be more clearly lateralized than those supporting recollection (Cohn et al., 2009; Aly et al., 2010). Critically, however, in both studies these familiarity impairments were observed in the context of accompanying broad recollection impairments.

To determine whether recognition impairments that are selective for familiarity-based item recognition are material-specific we recently examined whether NB's familiarity impairment, associated with a left MTL resection that included PrC (see section 1.4), was limited to verbal stimuli or generalizes across materials (Martin et al., 2011). Towards this end, I administered three different recognition tasks using aurally presented pronounceable non-words, faces, and abstract designs as stimuli. Familiarity and recollection were specifically probed by asking participants to indicate whether their subjective recognition experience associated with each trial during a recognition test were

based on familiarity of the stimulus itself or recollection of contextual detail. We found that NB exhibited a deficit in overall recognition of aurally presented pronounceable non-words that reflected a specific impairment of familiarity assessment with preservation of recollective processes. Examination of recognition memory for faces and abstract designs did not reveal any impairment. Importantly, this pattern was observed even though task difficulty, as reflected in overall recognition performance, was matched between the tasks with auditory pronounceable non-words and faces.

This pattern of results suggests that stimulus material is a factor that influences whether familiarity impairments will be observed with unilateral lesions. More broadly, these findings suggest that the neural mechanisms that support familiarity assessment in the temporal lobe operate in a manner that is tied to the specific stimulus class being assessed. While these data provide a promising starting point, they do not speak to questions related to potential category-specific differences between structures within the MTL in each hemisphere, namely PrC and PhC, and how they relate to familiarity-based item recognition in particular.

1.12 Goals of Current Studies

My thesis describes research I conducted with the aim of addressing the relationship between familiarity-based item recognition signals and category-specific effects in the MTL. Within this context, I have also examined and characterized the manner in which such signals are reflected in fMRI BOLD responses. At the broadest level, the experiments presented here were designed to answer three questions.

- 1) As they relate to recognition memory, do PrC and PhC make category-specific contributions to familiarity-based item recognition?

In Chapter 2, I present an fMRI study that sought to evaluate the BIC model's strong claim that PrC supports item recognition for stimuli from all categories. To evaluate this possibility I employed faces, chairs, and buildings as stimuli. It was hypothesized that activity in PrC would be associated with the familiarity of faces, whereas activity in PhC would be associated with the familiarity of buildings even in the absence of recovery of

episodic contextual detail. No strong a priori predictions were made concerning the familiarity of chairs. To anticipate my findings, MVPA revealed face familiarity signals in right PrC, but not PhC. By contrast, I found evidence for familiarity signals pertaining to buildings in right PhC, but not PrC. Lastly, the familiarity of chairs was associated with distributed patterns of activation in both PrC and PhC.

- 2) What specific stimulus properties determine the relative contributions of PrC and PhC to item-based recognition memory?

In Chapter 3, I present results from an experiment that follows directly from results reported in Chapter 2. The primary objective of this study was to 1) replicate our previous results pointing to the coding of item recognition signals for buildings in PhC, and 2) assess the stimulus properties that push such familiarity signals toward either PrC or PhC. For the latter purpose, I focused specifically on landmark suitability while holding size constant. Towards this end, buildings, trees, and airplanes were used as stimuli. Decoding results revealed above chance classification of familiarity-based item recognition judgments for buildings and trees from patterns of activity distributed across PhC, but not PrC. By contrast, classifier accuracy was above chance when decoding recognition decisions for airplanes from distributed activity patterns in PrC.

- 3) Are item-based recognition signals in PrC coded in a distributed, category-specific manner?

The research presented in Chapter 4 aimed to address novel questions concerning the distributed nature of face familiarity signals in PrC and the extent to which they can be characterized as content specific. I focused specifically on PrC as familiarity-based item recognition signals in this structure have been widely characterized and it has been linked to face processing in non-mnemonic task contexts. Interestingly, results obtained using MVPA revealed that the familiarity of faces can be reflected in patterns of activation that are distributed across voxels with heterogeneous response profiles. Moreover, through comparison with activity from an independent functional localizer scan, my results indicate that familiarity signals pertaining to faces are category-specific, despite being

coded in a pattern that extend beyond the contiguous patch of voxels within PrC that preferentially responded to faces.

1.13 References

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Chapter 2

2 Distinct Familiarity-Based Response Patterns for Faces and Buildings in Perirhinal and Parahippocampal Cortex

2.1 Introduction

The functional organization of the medial temporal lobes (MTL) remains a topic of intense debate in neuroscience. Much pertinent research in human and non-human species has focused on recognition memory, i.e., the ability to discriminate between previously encountered and novel stimuli, and the question of whether different MTL structures make distinct functional contributions. An influential view is that the hippocampus (HC) plays a specific role in the encoding and subsequent recovery of episodic contextual information about a specific prior stimulus encounter, whereas perirhinal cortex (PrC) supports recognition based on the familiarity of the item itself (Aggleton and Brown, 1999; Eichenbaum et al., 2007; Mayes et al., 2007). However, there are also findings that point to category-specific contributions of different MTL structures to recognition memory (Davachi, 2006; Murray et al., 2007; Graham et al., 2010). An important, currently unresolved question is how category-specific effects relate to the distinction between item- and contextually-based recognition processes. This issue is of particular relevance for characterizing the functional contributions of the perirhinal and parahippocampal cortices (PhC; Ranganath and Ritchey, 2012).

In the visual modality, the strongest category-specific neural responses have been observed for faces and scenes. Differential fMRI responses to faces are typically most pronounced in aspects of the lateral occipital and posterior fusiform gyrus (e.g., Kanwisher et al., 1997; see Gobbini and Haxby, 2007 for review), but have also been reported more rostrally in PrC (Tsao et al., 2008; Nasr and Tootell, 2012; O'Neil et al., 2013). Differential responses to scenes, by contrast, have predominantly been found in posterior aspects of PhC (Epstein and Kanwisher, 1998; Epstein, 2008). Scene specific

responses in PhC have informed the proposal that this structure represents episodic context in recognition memory and recall (Davachi, 2006; Eichenbaum et al., 2007). This role of PhC has been considered as distinct from both the role of PrC in the representation of objects, and from the role of the HC in item-context binding (Diana et al., 2007; Eichenbaum et al., 2007).

Interestingly, fMRI research has also revealed that preferential PhC responses extend beyond scenes to certain types of objects, including buildings (Aguirre et al., 1998; Cate et al., 2011). While the exact object characteristics that ‘drive’ PhC responses are only beginning to be understood, initial findings suggest that PhC is preferentially tuned to objects that are large (Konkle and Oliva, 2012), that evoke a sense of three-dimensional space (Mullally and Maguire, 2011), and/or that have navigational relevance (Janzen and van Turrenout, 2004; Troiani et al., 2012). That PhC responds not only to scenes but also to certain types of objects is of direct relevance to its proposed role in recognition memory. Specifically, the summarized findings raise the question of whether the role of PhC in recognition memory is indeed limited to representing episodic contextual information, or whether it also represents item-based familiarity for certain types of objects. Phenomenologically, buildings, like any other objects, can be recognized as ‘old’, even when episodic contextual detail about a specific prior stimulus encounter is absent. Corresponding item-based familiarity signals in PhC would be of broader theoretical significance towards understanding MTL organization, as they could suggest that familiarity is not invariably supported by PrC.

Here, we employed high-resolution fMRI in combination with multi-voxel pattern analyses (MVPA) to examine distributed patterns of activity in MTL structures that carry information about the perceived familiarity of three categories of objects, namely faces, buildings, and chairs.

2.2 Materials and Methods

2.2.1 Participants

Nineteen right-handed participants took part in the study (21-30 years of age, mean age = 25.2 years; 12 females). They were screened for the absence of a history of neurological

disorders. Data from one participant were excluded from all analyses due to excessive head movement (> 5 mm along one axis) during scanning. Participants received financial compensation for their participation and provided informed consent according to procedures approved by the University of Western Ontario Health Sciences Research Ethics Board.

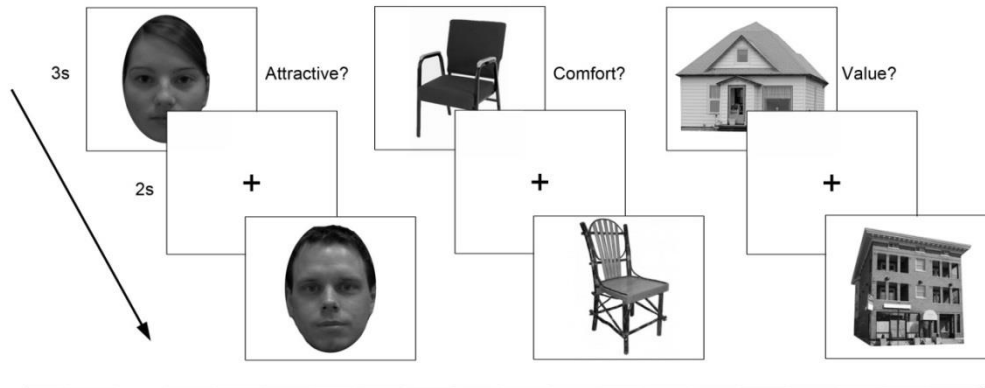
2.2.2 Stimuli and Procedure

Grayscale images depicting exemplars from three different object categories (faces, chairs, and buildings) were used as stimuli. Images of chairs and buildings were obtained from the internet using Google Image Search. Images of faces were obtained from a database we acquired for another study (O'Neil et al., 2009). All visual background was removed from the target object depicted in each image and replaced by an artificial, homogenous background without any space-defining features (see Fig. 2.1). For example, sidewalks, lawns, and any visible horizon were removed from each image depicting a building. Presented in this manner, all items fulfill the definition of an object as being a discrete entity bounded by a single contour that does not have background elements or a horizon, in line with previous research that aimed to characterize the response properties of PhC regions (Troiani et al., 2012). Image size was constrained by a 375 x 250 pixel bounding box and each object image was scaled to fit this box, with at least one dimension corresponding to its limits. Final item selection was optimized based on behavioural pilot data so as to match recognition accuracy and maximize the proportion of familiarity-based recognition responses across the three object categories. For each category, three sets of 40 items were selected. Two of these sets served as items presented prior to scanning during a study session and as corresponding targets in the subsequent recognition-memory test during scanning; items from the third set served as novel lures in the recognition task. Assignment of the three item sets as targets or lures was counterbalanced across participants.

All participants completed an initial study session outside of the scanner that was preceded by a brief practice phase. The study session was separated into six blocked sequences of 40 trials, with blocks corresponding to the two sets of items from each of the three categories. Blocks were presented in an ABCCBA order, with each stimulus

category corresponding to one of the letters. Stimuli were presented for 3000ms each with a 2000ms ISI and participants were asked to rate the relative attractiveness, comfort, or value for faces, chairs, and buildings, respectively, using a five-point scale. Refer to Figure 2.1 for a schematic representation of the experimental design.

Encoding Stage



Scanned Test Stage

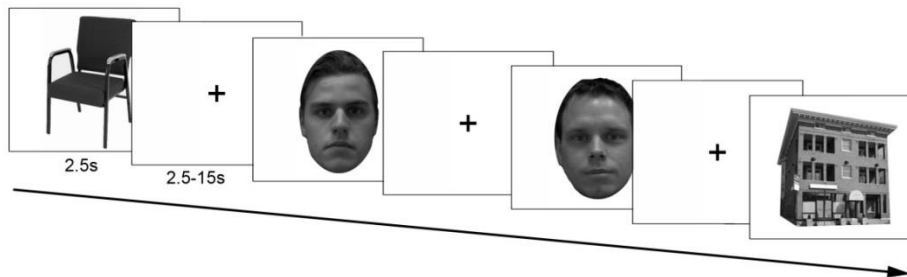


Figure 2.1 Experimental task design. During encoding, participants rated the relative attractiveness, comfort, or value for faces, chairs, and buildings, respectively. In the subsequent scanned recognition-test stage, participants provided a rating of perceived item familiarity. They were asked to avoid voluntary attempts to recollect contextual details pertaining to a specific prior item encounter, but were offered an opportunity to indicate recollection when it occurred involuntarily.

Following a delay of approximately one hour that allowed for scanning preparation, participants completed a recognition memory test consisting of the 80 previously studied targets and 40 lures from each category, for a total of 360 trials. Items were distributed over eight functional runs, each comprised of 45 trials with 10 previously studied and 5 novel items from each stimulus class. Each stimulus was presented for 2500 ms (corresponding to the length of one TR), with a jittered fixation-baseline separating trials. Baseline fixation ranged from 2.5s to 15s and the order of trials and jitter were optimized within each run, using the OptSeq2 algorithm (<http://surfer.nmr.mgh.harvard.edu/optseq/>). Each of the three counterbalanced versions of the experiment used a unique jitter sequence and trial order. Participants viewed the stimulus displays through a mirror at a distance that yielded an approximate object size of 18 x 13° visual angle. Participants were asked to make recognition judgments with one of five different response options using an MRI-compatible keypad.

For their recognition judgments, participants were instructed to focus on their experienced item familiarity and provide a rating of perceived strength on a scale between one (least familiar) and four (most familiar). They were asked to respond quickly and avoid intentional attempts to recollect contextual details pertaining to a specific prior item encounter; however, they were offered an opportunity to indicate recognition based on spontaneous, involuntary recollection with a separate response button when it occurred. Pertinent prior fMRI research suggests that participants can strategically control the extent to which they attempt to retrieve contextual details in recognition decisions (Dobbins and Han, 2006; Quamme et al., 2010; the specific instructions were guided by those provided by Montaldi et al., 2006; see also Migo et al., 2012 for further rationale). Participants were informed that, despite their efforts to focus on familiarity, spontaneous recollection could be expected to occur on some trials. Recollection of contextual details was defined as any situation that involved conscious awareness of information about the past item encounter that was not included in the stimulus itself, such as internal thoughts and associations that were formed during the initial item encounter, or related uncontrolled external events (e.g., a knock on the door during that item's presentation at study). Participants were familiarized with these response options in a practice phase that required them to justify any recollection

response with a description of the contextual detail retrieved. They were also informed that two thirds of the items to be presented had been encountered in the study phase.

2.2.3 fMRI Acquisition Protocol

All MRI data were acquired on a 3-Tesla Siemens TIM MAGNETOM Trio scanner with a high-resolution fMRI protocol optimized for MTL examination. Functional MRI volumes were collected using a T2*-weighted single-shot gradient-echo-planar acquisition sequence [TR = 2500 ms, TE = 26 ms, slice thickness = 2 mm, in-plane resolution = 2 X 2 mm, FOV = 220 mm X 220 mm, matrix size 110 X 110 mm, flip angle = 90°]. Each functional volume included 37 contiguous slices collected in an interleaved manner. For each experimental run, 176 volumes were collected. To optimize MR signal in the anterior temporal lobes, a transverse orientation was chosen with the effort to include the entire temporal lobes and as much visual cortex as possible. This slice selection resulted in full coverage of the ventral aspects of occipital and full coverage of the entire temporal lobes in all participants, with exclusion of the most superior aspects of frontal, parietal, and occipital cortices. A saturation band was applied during functional runs in order to minimize artifacts related to eye-movements and the sinus cavity. T1-weighted anatomical images were obtained using an ADNI MPRAGE sequence [192 slices, time to repetition (TR) = 2300 ms, field of view (FOV) = 240 X 256 mm, matrix size = 240 X 256, flip angle = 9 mm, echo time (TE) = 4.25 ms, 1 mm isotropic voxels].

2.2.4 fMRI Data Pre-Processing

fMRI data were pre-processed in native space using BrainVoyager QX version 2.3 (Brain Innovation). Functional images were slice-scan time corrected, 3-D motion corrected with reference to the functional volume taken just prior to the anatomical scan, and high-pass filtered using a linear trend and a Fourier basis set of 2 cycles/run. Images were then co-registered with the anatomical image, aligned with the AC-PC plane, and smoothed using a three-dimensional Gaussian kernel with a full-width at half maximum of 3 mm. Functional data were convolved using a standard double gamma hemodynamic response function (Friston, 1998). Participant-specific GLMs of these data allowed for extraction of z -scored trial-specific beta estimates in all voxels of interest. Beta estimates derived

from a modeled HRF were chosen as target measure for the MVPA (i.e., as classifier input) because they are particularly well suited to account for overlap in the hemodynamic response in fast-event related designs (Misaki et al., 2010). Changes in mean intensity across runs were modeled by including them as predictor of no interest in the participant-specific GLMs.

2.2.5 Anatomical ROI Definition

The main structures of interest in our investigation were PrC, PhC, and the HC. To conduct our MVPA, we obtained anatomically defined ROIs in native MRI space with manual tracing separately in each participant, using an established MR-based protocol that specifies anatomical landmarks for demarcation of these MTL structures and their boundaries (Pruessner et al., 2000, 2002). Specifically, we obtained ROIs for PrC, PhC, anterior HC (aHC), posterior HC (pHC), and the entire HC in each hemisphere. Entorhinal cortex was identified at the time of tracing to aid in the identification of anatomical landmarks but was not considered for the functional analyses. The distinction between anterior and posterior HC was introduced based on recent findings pointing to distinct functional specialization, and followed the protocol described by Poppenk and Moscovitch (2011) with the uncal apex serving as the critical boundary. Figure 2.2 depicts a graphical representation of these ROIs in a representative participant.

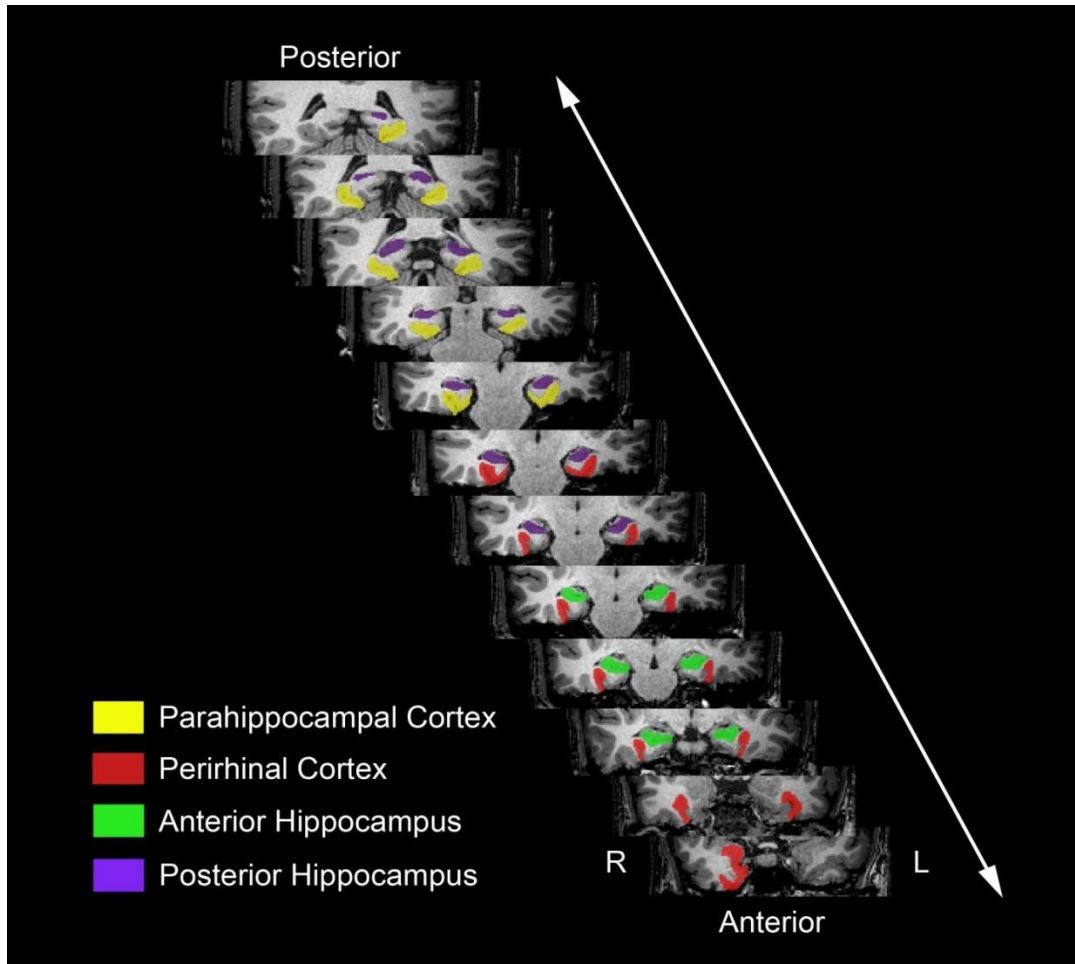


Figure 2.2 Coronal structural MRI slices from a representative participant with anatomically defined ROIs used for MVPA of fMRI data.

2.2.6 Multivariate Pattern Analysis of fMRI Data

MVPA (see Norman et al., 2006; Kriegeskorte and Bandettini, 2007; Tong and Pratte, 2012, for reviews and rationale) was employed to address two different types of questions. First, we used it to determine whether distributed patterns of activity could be identified in any of the MTL structures examined that distinguished between the stimulus categories (i.e., faces, chairs, and buildings). Second, and more importantly, it allowed us to examine whether distributed patterns of activity could be identified that reflected a memory signal, i.e., differences between familiar and novel stimuli within a given stimulus category. In these analyses, we specifically focused on perceived familiarity or novelty given that our main interest was in understanding the role of MTL structures in explicit recognition judgments. To the extent that the response distribution for items perceived as familiar or novel (i.e., familiarity levels 3, 4 versus familiarity levels 1, 2, respectively) varied within participants, and to the extent that such unequal item distributions can introduce unwanted classification biases, we introduce a sampling procedure that matched item numbers of perceived familiar and novel trials within each stimulus category. This sampling procedure operated in pseudo-random manner and underwent 10 iterations, with the provision that all trials be included in the classification analysis at least one time. It reduced the number of trials in the condition with the larger number (familiar or novel) so that it corresponded with the number in the other condition of interest. For example, if one participant had 50 ‘familiar’ and 42 ‘novel’ responses for faces, the number of ‘familiar’ trials included in the classification analysis for faces was reduced to 42. We decided to use 10 different sampling iterations in each familiar/novel classification based on initial pilot analyses in two participants, which showed that classifier performance did not differ statistically when more sampling iterations (up to 100) were included.

Pattern classification analyses were conducted using the Princeton MVPA toolbox (<http://www.pni.princeton.edu/mvpa>) and custom MATLAB code (The MathWorks, Natick, MA). As a first step, we performed feature selection in order to reduce noise in the functional data. For each ROI in each participant separately, the subset of voxels that appeared most informative for classification based on initial univariate GLM were

selected (ANOVA; see Norman et al., 2006 for discussion). Specifically, a one-factorial ANOVA, with number of conditions being equal to the number of conditions pertinent for the classification at hand (two or three), was conducted on the beta weights of all voxels in each ROI and in each cross-validation. For all familiar-novel classifications this analysis was also performed separately for each of the 10 iterations of item sampling. The resulting *F*-values were then rank-ordered across all voxels, and the voxels corresponding to the top 10% of that ranking were selected for the MVPA-based classification. Note that with this type of feature selection, the number of voxels considered for classifier training still scales with the overall size of the ROI. To illustrate the outcome of this feature selection, the number of voxels (2x2x2 mm in size), averaged across participants, that were included in the subsequent MVPA for each ROI were: right PrC 55.1, left PrC 54.9, right PhC 41.2, left PhC 41.2, right aHC 26.2, left aHC 24.3, right pHC 30.5, and left pHC 30.0.

A linear support vector machine (SVM; libSVM, <http://www.csie.ntu.edu.tw/~cjlin/libsvm>) was used for classification of the beta-values for the various experimental conditions, with a linear kernel function and a constant cost parameter of $C = 1$. The SVM was trained on all trials minus one from each of the conditions that were included in the analysis at hand; those trials not included in the training data set subsequently served as test trials for assessment of classification performance. This procedure was repeated multiple times such that every trial served as the test stimulus for classification, providing a *k*-fold cross validation (Duda, 2001; Chadwick et al., 2010), where *k* reflects the number of trials that were included in the relevant analysis. For each trial in the test set, the classifier provided probability estimates that reflected the likelihood that the activity pattern across voxels associated with that trial corresponded to each of the different conditions included in the classification. These estimates were expressed in a binary manner such that classification was either correct (i.e., when the ‘true’ experimental condition was assigned the highest probability) or incorrect. Classification accuracy was then calculated based on the percentage of test trials that were classified correctly in this binary schema. This calculation was performed and averaged across all 10 sampling iterations in the familiar/novel classifications to provide an unbiased performance estimate.

Finally, we also conducted additional cross-classification analyses to probe whether any decision boundary yielding above-chance classification between familiar/novel trials in a stimulus category might also allow for successful classification between familiar and novel trials from other stimulus categories. The MVPA cross-classification procedure used for this purpose employed the same linear SVM, cross-validation technique, and sampling procedure described above. However, the sampling procedure was performed in order to equate the number of trials across four, rather than two, conditions (i.e., novel and familiar trials from two stimulus categories).

To obtain inferential statistics, we primarily examined whether classification performance was above chance (0.5 or 0.33 depending on whether two or three conditions were included, respectively), focusing on each ROI independently. For this purpose, we employed a single sample *t*-test to test against a population mean of chance level, applying Bonferroni correction based on the number of independent comparisons made (i.e., the number of ROIs examined).

2.3 Results

2.3.1 Behavioural Performance

Raw percentages of the different recognition-response types for each stimulus category are presented in Table 2.1. Visual inspection of these data demonstrates that recognition decisions for previously studied items were based more frequently on familiarity (F3 and F4 collapsed; $M = 40.2\%$, 41.0% , and 43.5% for faces, chairs, and buildings, respectively) than on recollection (R; $M = 11.2\%$, 12.9% , and 12.5% for faces, chairs, and buildings), as intended. Overall recognition performance, i.e., the ability to distinguish between previously studied items and novel lures, irrespective of subjective recognition experience, was quantified using the discriminability index d' , which considers hits and false alarms in the context of signal-detection theory, considering F3, F4 and R as 'old' responses. Familiarity estimates were calculated using d' based on F1, F2, F3, and F4 responses, and corrected assuming independence between familiarity and recollection (Yonelinas, 1999). A one-way ANOVA conducted on these measures revealed that performance was closely matched across stimulus categories; there were no

significant differences between categories for overall discrimination ($F_{2,51} = .81, p = .45$), estimates of familiarity ($F_{2,51} = .45, p = .64$), nor for estimates of recollection (R hits minus R false alarms; $F_{2,51} = .01, p = .99$). Although performance levels were low, due to the high similarity between all items within each stimulus category, familiarity discrimination was above chance for each category (all t_{17} 's $> 8.4, p$'s $< .001$). We note that the limited number of R responses observed in the present study (collapsed across hits and false alarms $M = 9.56, 11.67, \text{ and } 11.06$ for faces, chairs, and buildings, respectively) did not allow for any investigation of fMRI responses associated with recollection.

With respect to reaction times, a 2 x 3 ANOVA (response type x stimulus category) revealed neither a main effect of category ($F_{2,102} = 2.00, p = .14$) nor a significant interaction ($F_{2,102} = 2.13, p = .12$), providing further evidence that all three stimulus categories were matched behaviourally. This analysis did reveal a significant main effect of response type ($F_{2,102} = 44.39, p < .001$), with recollection responses ($M = 1336.2 \text{ ms}, SD = 233.9 \text{ ms}$) being faster than judgments of familiarity (F1-F4; $M = 1648.8 \text{ ms}, SD = 261.4 \text{ ms}$).

Table 2.1 Recognition-response distribution and discrimination estimates for each stimulus category.

Stimulus Category	Percentage responses to studied items					Percentage responses to novel items					Discrimination	
	1	2	3	4	R	1	2	3	4	R	Recognition d'	Familiarity d'
Faces												
Mean	21.9%	26.7%	20.8%	19.4%	11.2%	42.9%	30.9%	16.3%	8.0%	2.0%	.76	.64
SEM	3.1%	2.1%	1.4%	2.1%	2.0%	5.1%	3.1%	1.8%	1.9%	0.9%	.08	.08
Chairs												
Mean	21.4%	24.6%	20.7%	20.3%	12.9%	46.5%	26.8%	15.4%	7.8%	3.5%	.76	.66
SEM	2.5%	1.5%	2.1%	1.8%	3.6%	3.4%	2.2%	1.4%	1.6%	1.2%	.06	.06
Buildings												
Mean	24.3%	19.7%	18.4%	25.1%	12.5%	48.0%	25.4%	14.2%	10.2%	3.1%	.84	.73
SEM	3.5%	1.4%	1.7%	2.5%	2.6%	5.6%	2.6%	2.5%	1.6%	1.1%	.07	.07

2.3.2 fMRI Results - Between Category Classification

With our MVPA, we first sought to determine whether distributed patterns of activity across voxels in any of the anatomically defined ROIs in the MTL could discriminate between the three stimulus categories. For this purpose, we considered all novel trials regardless of the recognition responses provided by the participants, with an equal number of trials for each stimulus category. The one-sample t-tests conducted with Bonferroni correction for 8 comparisons (i.e., ROIs), revealed that classification performance was above chance in right PrC ($t_{17} = 3.96, p < .01$ corrected), left PrC ($t_{17} = 4.56, p < .01$ corrected), right PhC ($t_{17} = 12.89, p < .001$ corrected), left PhC ($t_{17} = 9.13, p < .001$ corrected), and right pHC ($t_{17} = 3.46, p < .05$ corrected), with all other regions (left aHC, right aHC, and left pHC) showing classifier accuracy not significantly greater than chance (all p 's $> .37$). While these data point to category-specific representations in some MTL regions, they do not allow for any inferences as to whether all stimulus categories can be discriminated from one another. Figure 2.3 presents the results of additional analyses that focused on pair-wise classifications. Activation patterns in right PrC ($t_{17} = 3.82, p < .01$ corrected), left PrC ($t_{17} = 3.19, p < .05$ corrected), right PhC ($t_{17} = 12.04, p < .001$ corrected), left PhC ($t_{17} = 7.25, p < .001$ corrected) were sensitive to differences between faces and buildings (p 's for remaining ROIs were $> .11$). These regions were also sensitive to differences between faces and chairs (right PrC $t_{17} = 3.46, p < .05$ corrected; left PrC $t_{17} = 5.67, p < .001$ corrected; right PhC $t_{17} = 7.31, p < .001$ corrected; left PhC $t_{17} = 7.14, p < .001$ corrected). Another region that showed above-chance classification for these categories was the right pHC ($t_{17} = 3.66, p < .05$ corrected; all other p 's $> .41$). Lastly, for discriminations between buildings and chairs, classifiers for activation patterns in right PrC ($t_{17} = 3.19, p < .05$ corrected), right PhC ($t_{17} = 5.41, p < .001$ corrected), and left PhC ($t_{17} = 6.06, p < .001$ corrected) produced above chance performance (all other p 's $> .30$). Together, these results revealed evidence for category-specific representations reflected in sensitivity to differences between all pairs of stimulus categories in PrC as well as in PhC, with the most clear-cut pattern emerging in the right hemisphere. Evidence for category-specific representations in the hippocampus was limited.

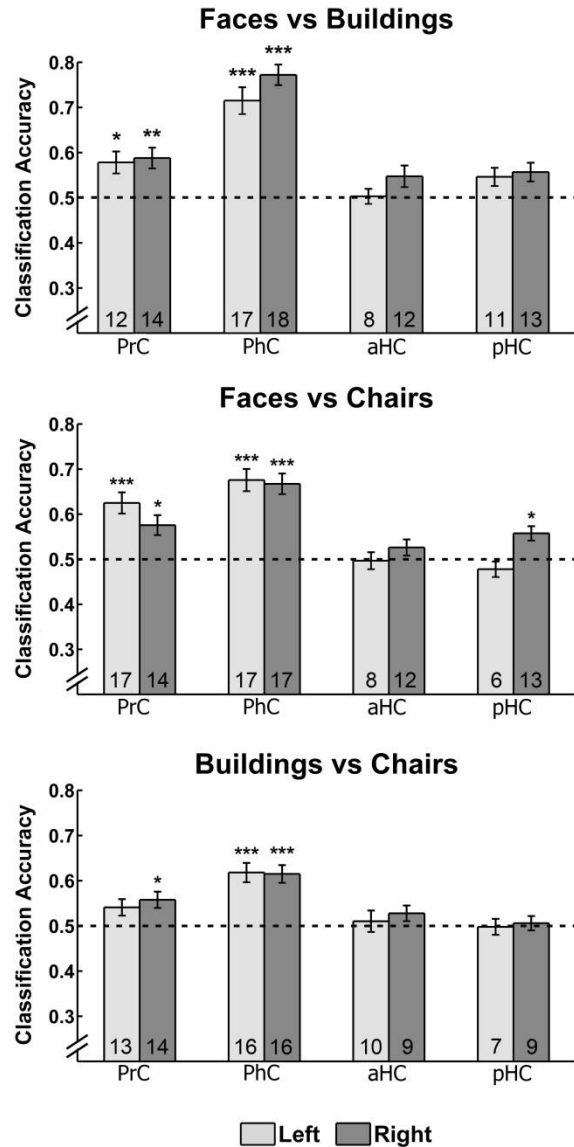


Figure 2.3 Pairwise MVPA classification of different stimulus categories in left and right PrC, PhC, aHC, and pHC. Classification was based on examination of all trials in which novel stimuli were presented. Dashed lines indicate chance level for classification. Numbers within bars represent the number of participants for whom classification performance was numerically above chance level. All error bars indicate the SEM calculated across participants. * $p < .05$, ** $p < .01$, *** $p < .001$.

2.3.3 fMRI Results - Within Category Classification of Familiar and Novel Trials

While the previous analyses revealed category-specific effects in both PrC and PhC, their selective focus on novel items does not speak to mnemonic signals as such. In other words, the results of these analyses do not imply that these structures carry information about the perceived familiarity of items in any of the relevant categories. Therefore, we next examined whether subjectively perceived familiarity would also be reflected in patterns of activity in PrC and PhC that are category specific. For these analyses, trials were considered regardless of objective item status and were collapsed across familiarity ratings F1 and F2 (novelty or low familiarity) and contrasted with familiarity ratings F3 and F4 (high familiarity). This approach ensured that SVM training could be based on a sufficiently large number of trials (≥ 24) for the familiarity-based classification in each category and individual participant. The average number of trials included for the classification of faces, chairs, and buildings at each familiarity level (i.e., low versus high) was 39.8, 39.7, and 38.3, respectively. The results of these analyses are presented in Figure 2.4. We found evidence for activation patterns that reflected subjectively perceived familiarity in both PrC and PhC, but not in the HC in either hemisphere. Specifically, in right PrC, patterns of activity could be classified according to subjective familiarity with above-chance accuracy for faces ($t_{17} = 4.77, p < .001$ Bonferroni corrected for 3 comparisons, i.e., number of stimulus categories) and chairs ($t_{17} = 3.47, p < .01$ corrected), but not for buildings ($t_{17} = .17, p = .87$). Notably, classifier accuracy for both faces and chairs was significantly greater than for buildings in right PrC ($t_{34} = 3.83, p < .01; t_{34} = 2.68, p < .05$, respectively; corrected). By contrast, in right PhC, patterns of activity could be classified according to subjective familiarity with above-chance accuracy for buildings ($t_{17} = 3.91, p < .01$ corrected) and chairs ($t_{17} = 5.27, p < .001$ corrected), but not faces ($t_{17} = 1.20, p = .25$). Classifier accuracy for both buildings and chairs was significantly greater than for faces in right PhC ($t_{34} = 2.42, p < .05; t_{34} = 2.48, p < .05$, respectively; corrected). In the left hemisphere, classifier performance in PrC did not exceed chance level for any stimulus category (faces, $t_{17} = 1.15, p = .26$; chairs, $t_{17} = 1.95, p = .06$; buildings, $t_{17} = .44, p = .67$). Classification accuracy was above chance in

left PhC for chairs ($t_{17} = 3.53, p < .01$), but not faces ($t_{17} = .05, p = .96$) or buildings ($t_{17} = .72, p = .48$).

Critically, in the HC, we found no evidence for patterns of activation that allowed for classification based on subjective familiarity for any stimulus category. This held regardless of whether we assessed the posterior or the anterior portion of the HC, and regardless of whether we did this in right or the left hemisphere (all p 's $> .15$). One issue to consider in these analyses is that the four hippocampal ROIs were generally smaller than those in PrC and PhC. Moreover, in as much as they focused only on the anterior or posterior section separately, they would not capture diagnostic patterns that might be distributed across the entire HC. Accordingly, we also determined whether results would differ if we examined the whole HC in a single analysis (for each hemisphere). Note that in these analyses the right hippocampal ROIs were on average, and in the majority of the participants, numerically larger than the ROIs for right PrC and for right PhC. Still, we found no evidence for patterns of responses in the right HC that allowed for classification based on subjective familiarity for faces ($M = .50, SEM = .01$), chairs ($M = .49, SEM = .01$), or buildings ($M = .50, SEM = .02$). Similarly, we found no such evidence when the HC was considered as a whole in the left hemisphere for faces ($M = .49, SEM = .01$), chairs ($M = .50, SEM = .01$), or buildings ($M = .49, SEM = .01$).

Although our primary interest was in perceived familiarity, we also explored whether patterns of responses in any ROI would allow for successful classification based on objective item status (i.e., previously studied vs. new items irrespective of recognition response). No significant effects were revealed for any stimulus category in any region examined (PrC, PhC, anterior HC, posterior HC, entire HC in left or right hemisphere; all p 's $> .05$, uncorrected). These divergent results for classification based on perceived (i.e., subjective) familiarity versus objective item status mirror previous fMRI findings obtained with MVPA for the whole brain in the context of recognition memory for faces (Rissman et al., 2010).

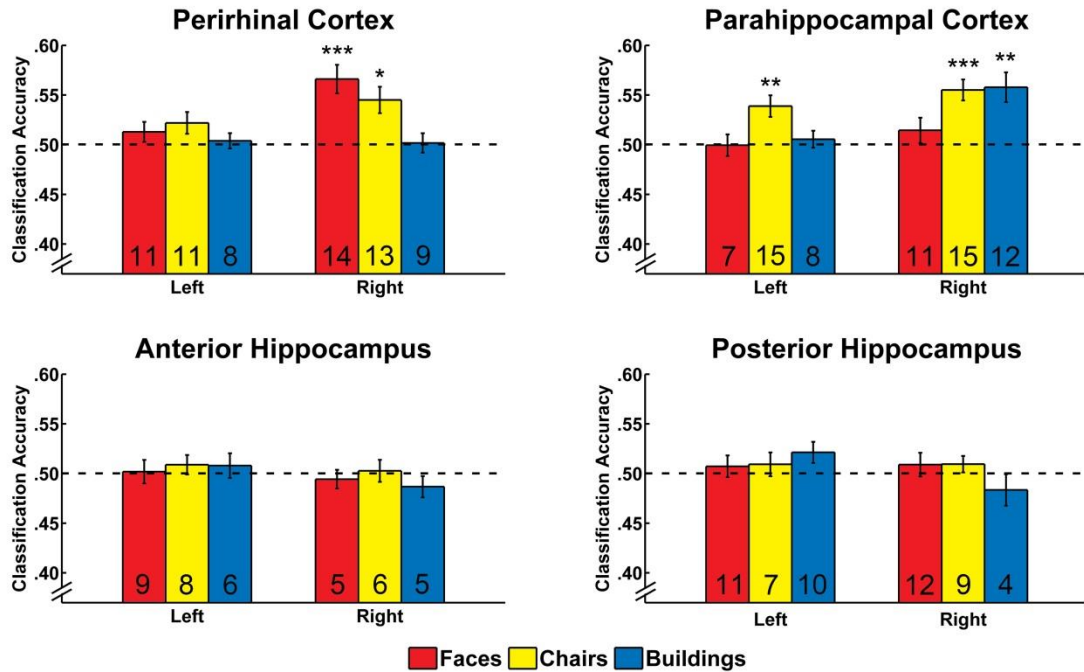


Figure 2.4 MVPA classification of perceived familiar versus novel trials for the three different stimulus categories in left and right PrC, PhC, aHC, and pHC. Dashed lines indicate chance level. Numbers within bars represent the number of participants for whom classification performance was numerically above chance level. All error bars indicate the SEM calculated across participants. * $p < .05$, ** $p < .01$, *** $p < .001$.

2.3.4 fMRI Results - Between Category Cross-Classification and Voxel Overlap Analysis

Given that our MVPA revealed signals related to subjectively perceived familiarity for two stimulus categories in both PrC (faces and chairs) as well as PhC (buildings and chairs), an important question that arises is whether the patterns of activity that could be classified successfully are indeed category-specific. The analyses conducted so far would not rule out, for example, that above chance classifier performance in right PrC for faces and chairs is based on a common familiarity signal. Likewise, they do not rule out that the familiarity signal for buildings and chairs in PhC is shared. To address category specificity of the observed familiarity signals more directly, we first explored the extent of overlap between voxels that contribute to the classification of familiar and novel responses in one stimulus category, and those that contribute to classification in the other. Towards this end we examined overlap at the level of voxels that were selected in the initial feature-selection procedure to be the most informative for use in the SVM. We found that 52% of the voxels in right PrC that entered the classification analysis for faces also entered the classification for chairs (and vice versa). The corresponding averaged value for overlap in right PhC in the context of classification of buildings and chairs was 53%. These results suggest that the distributed memory representations for the categories supported by each of these MTL structures show partial overlap. In the next step, we examined this issue more formally with inferential statistics by conducting a cross-classification analysis for faces and chairs in right PrC, and for buildings and chairs in right PhC. If familiarity-based classification in PrC, for example, is based on strongly overlapping distributed representations for faces and chairs, these analyses should reveal that the pattern of activity that distinguishes between familiar and novel faces can also be used to discriminate between familiar and novel chairs, and vice versa. The classification accuracies we obtained for these cross-classification analyses in right PrC and right PhC are presented in Figure 2.5. Again, these analyses were conducted using the item-sampling procedure described previously, which matched item numbers across both stimulus class and recognition responses (with 33.7 trials included on average). Critically, cross-classification was at chance in right PrC when the linear decision boundary of the SVM trained on faces was used to classify familiar and novel chairs ($M = .50$; $p > .45$

uncorrected) as well as when the SVM trained on chairs was used to classify familiar and novel faces ($M = .49$ $p > .58$). Cross-classification performance for buildings and chairs in right PhC was equally unsuccessful ($M = .52$, $p > .18$ and $M = .51$ $p > .32$). These data suggest that the distributed patterns of voxels that contribute to classification of familiar versus novel faces and chairs in PrC, and those that contribute to classification of familiar versus novel buildings and chairs in PhC show some specificity within each of these structures.

In the interest of completeness, we also conducted the remaining cross classification analyses that can be brought to bear on our data in right PrC and right PhC (i.e., cross-classification involving buildings in PrC and faces in PhC). None of these analyses revealed any significant effects (all p 's $> .11$, uncorrected).

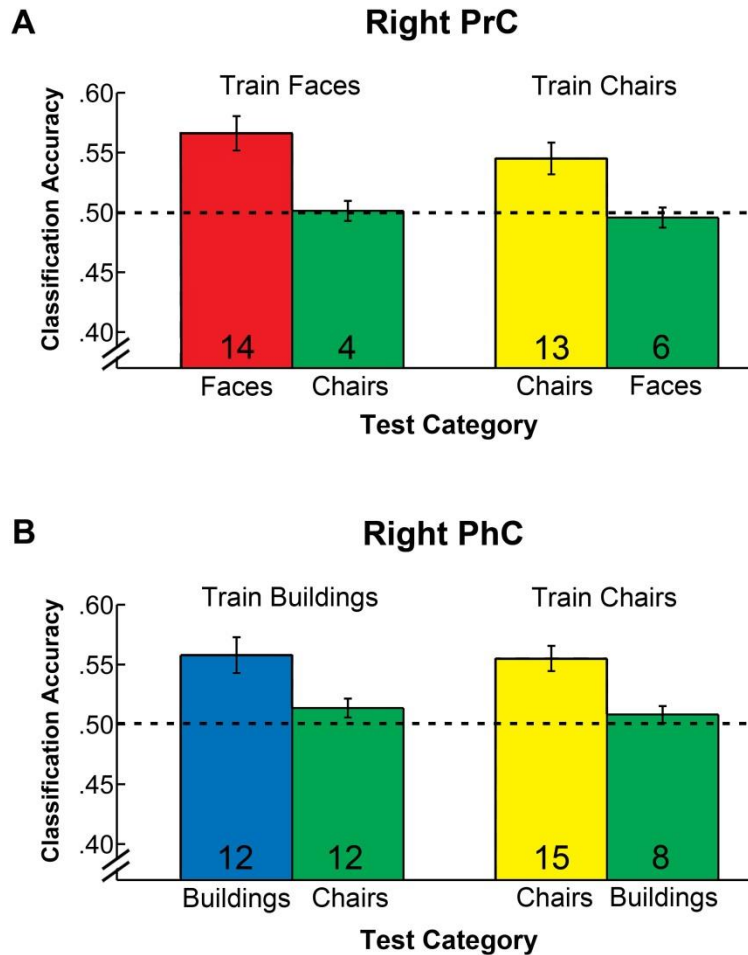


Figure 2.5 MVPA cross-classification for the two stimulus categories for which reliable familiarity-based classification was found in right PrC and PhC. Within-category classification performance is shown for reference in the left column of each data pair as displayed in Figure 4. Cross classification data are displayed in green in the right column. A Classification and cross classification of familiarity signals for faces and chairs in PrC B Classification and cross classification of familiarity signals for buildings and chairs in PhC. Dashed lines indicate chance performance level. Numbers within bars represent the number of participants for whom classification performance was numerically above chance level. All error bars indicate the SEM calculated across participants. Cross classification performance did not exceed chance level in any condition.

2.4 Discussion

In the current study we examined distributed patterns of activity in the MTL that are associated with the perceived familiarity of faces, buildings, and chairs. Our primary analyses of interest focused on patterns of activity that distinguished between subjectively experienced familiar or novel items in each object category. In right PrC, MVPA revealed such familiarity signals for faces but not buildings. In right PhC, by contrast, we observed familiarity signals for buildings but not faces. Familiarity signals for chairs were present in both structures, but shared limited overlap with the patterns we observed for faces and buildings. Contrasting with these findings for PrC and PhC, we found no evidence for familiarity signals in the HC for any of the object categories examined.

A number of studies have previously documented category specific responses in the MTL (e.g., Litman et al., 2009; Preston et al., 2010; Staresina et al., 2011), some of which were also based on MVPA of fMRI data (Diana et al., 2008; Liang et al., 2013). As in the literature on category-specific effects in the ventral visual stream more broadly, the most widely used comparison in these studies has been between faces and scenes. In research concerned with item-based familiarity, such comparisons can pose challenges for interpretation. When a scene (such as a bedroom), is endorsed as being familiar, the response may be based on individual objects (e.g., furniture), the spatial relationships among these objects, or the geometric properties of the background (e.g., shape and size of the room). Unless the relationships between target scenes and their distractors are systematically manipulated (e.g., Cleary et al., 2012), the source of information in the stimulus display that guides the memory judgment is unknown and may even vary from trial to trial (see Preston et al., 2010; Martin et al., 2012 for discussion).

In the present study, we addressed the potential role of PhC in item familiarity by examining familiarity signals for items from three different object categories, all of which were presented without any scene context. Results from our initial examination of MVPA classification (when only novel stimuli were considered) revealed that patterns of activity in both PrC and PhC were sensitive to differences among all three object categories, and that the most consistent differences were present in the right hemisphere. Critically,

patterns of activity that gave rise to reliable classification of memory signals, more specifically item-based familiarity, revealed noticeable functional differences between both structures. In right PrC, familiarity signals could be classified reliably only for faces and chairs. In right PhC, by contrast, familiarity signals could be classified reliably only for buildings and chairs. This pattern of findings suggests that PhC, like PrC, carries information about the familiarity of objects. However, both structures differ in their response profile across the three different object categories examined here. To the extent that these results were obtained with analyses that excluded any recollection-based behavioural responses, this difference in neural response profile cannot be captured with reference to the distinction between items and episodic-context.

The preferential responses in PrC and PhC we observed for faces and buildings in familiarity-based judgments are consistent with findings from prior research in other tasks. For example, recent evidence from fMRI studies in human and non-human primates points to the presence of a cortical patch in rostral aspects of the collateral sulcus that shows preferential responses to faces even during passive viewing (Tsao et al., 2008; Rajimehr et al., 2009; Ku et al., 2011; Nasr and Tootell, 2012). Other studies have revealed preferential responses to buildings in PhC (Aguirre et al., 1998; Cate et al., 2011; Maguire et al., 2001; Nasr and Tootell, 2012), and have shown adaptation effects in perceptual judgments (Pourtois et al., 2008).

That familiarity signals for chairs were found to be present in PrC as well as in PhC suggests that reference to stimulus category alone may ultimately be insufficient to account for the difference in response profiles exhibited by both structures. What other factors might determine whether reliable familiarity signals are observed in PrC or PhC then? The current findings would be consistent with the idea that these structures are differentially sensitive to specific stimulus dimensions that are often correlated in various object categories (Op de Beeck et al., 2008). Based on the characterization of PhC responses in other studies, we speculate that critical dimensions may include the size, mobility, and sense of space that objects evoke (Mullally and Maguire, 2011; Cate et al., 2011; Konkle and Oliva, 2012; Troiani et al., in press). From a functional perspective, these dimensions are essential determinants of the navigational relevance of objects

(Janzen and van Turenout, 2004; Troiani et al., in press). In such a framework, PhC may carry familiarity signals for objects that tend to be large, immobile, and evoke a sense of three-dimensional space. Conversely, PrC may carry familiarity signals for objects that are smaller in real world size and are not tied to a specific geographical location. Familiarity for chairs would be represented in both PrC and PhC because chairs are characterized by some stimulus attributes that ‘drive’ PrC and others that ‘drive’ PhC. Namely, like faces, they are not tied to a specific location. Like buildings, they can evoke a sense of surrounding three-dimensional space (Mulluly and Maguire, 2011). An account that makes reference to object dimensions, rather than categories, could also explain why the voxels within each structure that carry information about the familiarity for one object category, although not allowing for cross classification, show some overlap with those that are diagnostic for the familiarity of another. Given that fMRI studies in recognition memory have most commonly focused on verbal stimuli, with no systematic manipulation of specific features of the referent objects, we acknowledge, however, that extant evidence that speaks to this proposal is currently limited.

Another explanation as to why certain types of objects preferentially engage PhC invokes the degree to which different objects elicit contextual associations. In particular, it has been suggested that PhC is involved in representing contextual associations for those objects (e.g., pillow) that are typically encountered in the same context (e.g., bed or bedroom; Bar and Aminoff, 2003). These types of contextual associations can be seen as semantic in nature, in that they specify a typical context that may or may not hold for any specific episodic encounter. It seems unlikely that such semantic contextual associations would be of diagnostic value in familiarity-based recognition memory decisions that require discrimination between studied and non-studied exemplars within restricted object categories, such as the buildings used in the current study. While some buildings may be more likely to elicit such contextual associations than others, these associations, to the extent that they become conscious at the time of encoding and retrieval, would be captured with recollective rather than familiarity-based responses. Taken together with other recent evidence showing that the contextual effects in PhC reported by Bar and Aminoff (2003) may in fact reflect scene imagery (Epstein and Ward, 2008), or the sense of surrounding space that some objects evoke (Mullully and Maguire, 2011), these

considerations argue against the idea that the differences in item-based familiarity signals we observed for PhC and PrC reflect differential influences of semantic contextual associations.

In the current study, the primary focus of analysis centered on discrete MTL structures that were defined anatomically. Another approach in the literature has been to examine functional gradients that cross the boundary of both structures in the parahippocampal region (e.g., Litman et al., 2009; Staresina et al., 2011; Liang et al., 2013). We focused on differences between discrete structures because our primary objective was to evaluate theoretical claims regarding differences in functional properties between PrC and PhC that have been proposed to be present at this neuroanatomical scale (Eichenbaum et al., 2007; Graham et al., 2010). These models of functional MTL organization have typically been informed by differences in cytoarchitectonic composition and anatomical connectivity of PrC and PhC (e.g., Lavenex and Amaral, 2000; Manns and Eichenbaum, 2006). In the future, it will be important to develop and test models of MTL organization that directly map distributed patterns of mnemonic signals to more fine grained neuroanatomical subdivisions in neocortical MTL structures (e.g., Ding and Van Hoesen, 2010), and to corresponding differences in connectivity.

Concerning HC function, we observed that distributed patterns of activation in this structure did not allow for any reliable classification of familiarity signals. These results held across both hemisphere and across anterior and posterior aspects of the HC, irrespective of stimulus category. Inasmuch as the patterns probed were specific to trials that were not accompanied by recollection of episodic contextual information, this finding is consistent with the influential idea that the HC does not support item-based familiarity (Aggleton and Brown, 1999). We recognize, however, that considered in isolation this hippocampal finding reflects a null effect. As such, it is amenable to alternate interpretations, and could also be accommodated by the proposal that the HC only carries memory representations of high strength, which are associated with high levels of behavioural accuracy (Squire and Wixted, 2007). Nevertheless, we note that recent data from intracranial EEG recordings strongly argue against a single-process account of medial temporal lobe organization that attributes functional differences

between PrC and the HC to any differential sensitivity of both structures to a unidimensional strength signal (Staresina et al., 2012; see also Horner et al., 2012).

In conclusion, our findings indicate that both PrC and PhC contribute to the assessment of item familiarity. They show that the role of PhC is not limited to representing information about context, and that PrC is not involved in representing familiarity for all object categories. Considered within the larger literature reviewed, these findings suggest that a comprehensive model of MTL organization for PrC, PhC, and the HC will ultimately require consideration of representational distinctions that include, but go beyond the division between item and context information.

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Chapter 3

3 Parahippocampal and Perirhinal Cortex Differentially Support Item Recognition Memory for Objects With and Without Navigational Relevance

3.1 Introduction

Recognition memory refers to the ability to discriminate between previously encountered and novel stimuli and is known to be critically dependent on the medial temporal lobes (MTL). However, the question of whether different MTL structures make distinct functional contributions to recognition memory remains a topic of intense debate in neuroscience (Montaldi and Mayes, 2010; Ranganath, 2010; Wixted and Squire, 2011). The binding of items and contexts (BIC) model purports that perirhinal cortex (PrC) supports item recognition, parahippocampal cortex (PhC) supports the encoding and retrieval of episodic contextual details, and the hippocampus (HC) serves to bind items and contexts into discrete episodic events (Eichenbaum et al., 2007; Diana et al., 2007; Ranganath, 2010). However, there are also findings that point to category-specific contributions of different MTL structures to recognition memory (Davachi, 2006; Murray et al., 2007; Graham et al., 2010). An important, currently unresolved question is how category-specific effects relate to the distinction between item- and contextually-based recognition processes. This issue is of particular relevance for characterizing the functional contributions of PrC and PhC (Ranganath and Ritchey, 2012).

One of the most robust category-specific effects in the visual modality is differential responses to scenes in posterior aspects of PhC (Epstein and Kanwisher, 1998; Epstein, 2008). These scene specific responses have informed the proposal that PhC represents episodic context in recognition memory and recall (Davachi, 2006; Diana et al., 2007; Eichenbaum et al., 2007). Interestingly, however, fMRI research conducted in non-mnemonic task contexts has also revealed that preferential PhC responses extend beyond scenes to objects from specific categories, such as buildings (Aguirre et al., 1998; Cate et

al., 2011). Initial evidence from research aimed at identifying the object properties that ‘drive’ PhC responses suggest that PhC is preferentially tuned to objects that are large (Konkle and Oliva, 2012), that evoke a sense of three-dimensional space (Mullally and Maguire, 2011), and/or that have navigational relevance (Janzen and van Turrenout, 2004; Troiani et al., 2012; Bastin et al., 2013). Evidence linking PhC responses to certain types of objects is of direct relevance to its proposed role in recognition memory. Namely, this observation raises the question of whether the role of PhC in recognition memory is indeed limited to representing episodic contextual information, or whether it also supports familiarity-based item recognition for some categories of objects. Importantly, objects that evoke differential responses in PhC can indeed be recognized as ‘old’, even in the absence of episodic contextual detail about a specific prior stimulus encounter. Corresponding item-based familiarity signals in PhC would be of broader theoretical significance towards understanding MTL organization, as they could suggest that familiarity is not invariably supported by PrC.

Recent fMRI research has indeed examined the relationship between category-specific effects and familiarity-based item recognition signals in the MTL. Specifically, Martin et al. (2013) employed multi-voxel pattern analysis (MVPA) to decode item recognition decisions pertaining to faces, buildings, and chairs from patterns of activation in PrC and PhC. Results from this experiment revealed category-specific item recognition signals in both structures, even in the absence of retrieval of episodic contextual detail. Specifically, above chance classifier performance was obtained in right PrC for faces, but not buildings. By contrast, the perceived familiarity of buildings, but not faces, could be decoded from activity patterns in right PhC. Evidence of item recognition signals for chairs was present in both structures, but shared little overlap with the patterns observed for faces and buildings on a more fine-grained scale. This pattern of results provides initial evidence suggesting that item recognition signals in PrC and PhC are represented in a category-specific manner. However, that familiarity signals for chairs were observed in both structures suggests that reference to stimulus category alone may ultimately be insufficient to account for the difference in response profiles exhibited by PrC and PhC.

The primary aim of the current study was to replicate our previous results linking PhC to item recognition (Martin et al., 2013) and, more importantly, identify the object properties that determine whether item recognition signals are coded in PrC or PhC. Specifically, we used MVPA to examine whether the extent to which objects are fixed in location plays a critical role, while holding real-world size constant. Towards this end, we employed images depicting buildings, trees, and planes as stimuli. At a functional level, the navigational utility of an object is primarily determined by its mobility; objects that are fixed in location (e.g., buildings and trees) necessarily have more navigational relevance than those that are not (e.g., planes). However, object fixedness is often highly correlated with real-world size (Mullally and Maguire, 2011; Troiani et al., 2012), a dimension that has been linked to differential responses to objects in PhC (Konkle and Oliva, 2012). Critically, as stimuli selected for the current study were matched across categories with respect to perceived real-world size, we were able to specifically probe the importance of fixedness in determining whether PrC or PhC code item familiarity. Demonstrating that item recognition signals in PrC and PhC are dissociable for objects that are either fixed in location or not would strongly argue for the role of potential navigational relevance as a critical determinant.

3.2 Materials and Methods

3.2.1 Participants

Twenty right-handed participants took part in the fMRI study (21-29 years of age, mean age = 24.3 years). They were screened for the absence of a history of neurological disorders. Additionally, twenty participants (21-28 years of age, mean age = 24.1 years), six of whom also participated in the fMRI study, provided relative real-world size estimates for all stimuli in an independent behavioural rating task. Participants received financial compensation for their participation and provided informed consent according to procedures cleared by the University of Western Ontario Health Sciences Research Ethics Board.

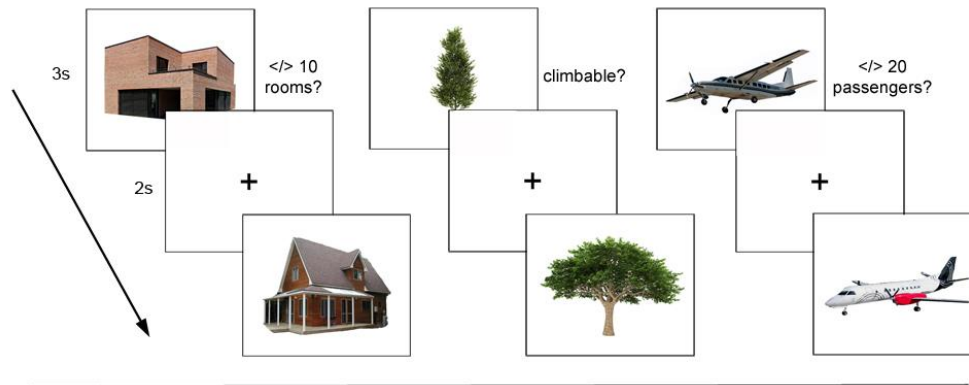
3.2.2 Stimuli and Procedure

The stimuli employed in the current study consisted of 360 colour images depicting objects that were evenly distributed across three categories: buildings, trees, and planes. All images were obtained from the internet using Google Image Search; building stimuli were full color versions of those used in Martin et al. (2013). All stimuli were initially selected from a larger pool of images following a series of behavioural pilot experiments intended to optimize experimental design with respect to difficulty and the extent to which recognition was based on familiarity judgments across categories. In line with previous research, objects were defined as discrete entities bounded by a single contour that does not have background elements or a horizon (Troiani et al., 2012; Bastin et al., 2013). Accordingly, target objects were cropped from their natural background in their original form and placed on a homogenous white background without cues providing information related to size, distance, or horizon (see Figure 3.1). Specifically, all objects were depicted in the absence of contextual visual detail such as ground, horizon, and other non-target objects or features. All objects were proportionally scaled in a manner that ensured at least one dimension corresponded to the limits of a 375 x 250 pixel white background. Behavioural size ratings were obtained for all 360 stimuli to ensure that all categories were matched on this dimension. Participants were asked to rate the relative real-world size of the object depicted in each image on a 1-10 scale (1 = the smallest object, 10 = the largest object). Notably, all stimulus categories were matched with respect to perceived real-world size (buildings, $M = 6.69$, $SD = 1.81$; trees, $M = 5.61$, $SD = 1.76$; planes, $M = 6.38$, $SD = 1.69$; $F_{2,57} = 2.01$, $p = .14$). These data suggest that any potential differences observed between categories at the level of behavioural recognition performance or decoding performance are not attributable to variation in size across categories.

For the purpose of counterbalancing in our fMRI experiment, stimuli from each category were divided into three sets of 40 items. Two of these sets were presented during an initial encoding stage and served as target items in the subsequently scanned recognition memory test stage. Items comprising the third set were presented as lures during the test stage. Assignment of item sets as targets or lures was counterbalanced

across participants. Prior to the scanned recognition test stage of the experiment, all participants completed an initial encoding session. Objects were presented in one of six encoding blocks with each block corresponding to one set of target items. The order in which categories appeared was counterbalanced across participants. Stimuli were presented for 3000ms each and separated by a 2000ms fixation. Participants were asked to focus on the size and form of the object depicted in each trial and rate whether each building had more or less than 10 interior rooms, whether each tree was climbable, and whether each plane could seat more or fewer than 20 passengers. Refer to Figure 3.1 for a schematic representation of the experimental design.

Encoding Stage



Scanned Test Stage

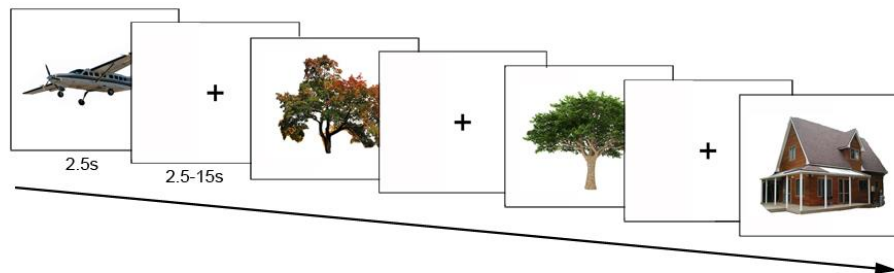


Figure 3.1 Experimental task design. During encoding, participants rated whether buildings had more or less than ten interior rooms, whether trees were climbable, and whether planes could seat more or less than 20 passengers. In the subsequent scanned recognition-test stage, participants provided a rating of perceived item familiarity. They were asked to avoid voluntary attempts to recollect contextual details pertaining to a specific prior item encounter, but were offered an opportunity to indicate recollection when it occurred involuntarily.

The initial encoding stage and subsequent test stage were separated by approximately one hour to allow for administration of test instructions, completion of a brief practice test, and scanning preparation. Participants were asked to indicate their recognition judgments using one of five response options corresponding to sure novel, unsure novel, unsure familiar, sure familiar and recollection. The differences between these response options were made clear through detailed instruction with a particular emphasis on the distinction between familiar responses and recollection. Toward this end, recollection was defined as recognition that was accompanied by conscious retrieval of contextual detail from the initial item encounter (i.e., during the encoding stage of the experiment). Participants were told that such retrieval could reflect cognitive context (e.g., trial unique internal thoughts and associations that were formed during the initial item encounter), temporal context (e.g., which trial preceded or followed a given object presentation), or environmental context (e.g., a passing voice that could be heard from the testing room). Familiarity was defined as an acontextual impression of oldness pertaining to the perceptual details of an object itself. Participants were asked to focus on evaluating the perceived familiarity of each stimulus and discouraged from intentionally attempting to recollect contextual details. To optimize the proportion of familiarity-based judgments we asked that participants respond quickly and in an intuitive manner. At the same time, however, participants were encouraged to indicate recognition based on spontaneous, involuntary recollection when it did occur. This specific procedure was adapted from previous fMRI research that focused on familiarity-based responding (Montaldi et al., 2006; see also Migo et al., 2012, for further rationale). Participants were not provided any information pertaining to the relative proportion of targets and lures presented during the recognition test stage. Immediately prior to scanning, all participants completed a brief practice test that required justification for any recollection response with a description of the contextual detail retrieved.

The scanned recognition test stage comprised 360 trials (80 targets and 40 lures from each category) evenly divided over eight runs of functional data acquisition. Stimuli were presented for 2500 ms, with a jittered fixation-baseline separating trials (fixation ranged between 2.5s and 15s). Trial order and jitter interval were optimized for each run using the OptSeq2 algorithm (<http://surfer.nmr.mgh.harvard.edu/optseq/>), with unique

sequences and timing across counterbalanced versions of the experiment. Participants viewed the stimuli through a mirror at a distance that yielded an approximate object size of $18 \times 13^\circ$ visual angle. Recognition responses were recorded using an MRI-compatible keypad.

3.2.3 fMRI Acquisition Protocol

All MRI data were acquired on a Siemens 3-Tesla Magnetom Prisma scanner with a high-resolution fMRI protocol optimized for MTL examination. Functional MRI volumes were collected using a T2*-weighted single-shot gradient-echo-planar acquisition sequence [TR = 2500 ms, TE = 26 ms, slice thickness = 2 mm, in-plane resolution = 2×2 mm, FOV = 220 mm X 220 mm, flip angle = 90°]. Each functional volume included 37 contiguous slices collected in an interleaved manner. For each experimental run, 176 volumes were collected. To optimize MR signal in the anterior temporal lobes, a transverse orientation was chosen with the effort to include the entire temporal lobes and as much visual cortex as possible. This slice selection resulted in full coverage of the ventral aspects of occipital and full coverage of the entire temporal lobes in all participants, with exclusion of the most superior aspects of frontal, parietal, and occipital cortices. A saturation band was applied during functional runs in order to minimize artifacts related to eye-movements and the sinus cavity. T1-weighted anatomical images were obtained using an ADNI MPRAGE sequence [192 slices, TR = 2300 ms, TE = 4.25 ms, 1 mm isotropic voxels, FOV = 240 X 256 mm, flip angle = 9°].

3.2.4 fMRI Data Pre-processing

fMRI data were pre-processed using BrainVoyager QX version 2.8 (Brain Innovation). Functional images were slice-scan time corrected, 3-D motion corrected with reference to the functional volume taken just prior to the anatomical scan, and high-pass filtered using a linear trend and a Fourier basis set of 2 cycles/run. Images were then co-registered with the anatomical image, aligned with the AC-PC plane, and smoothed using a three-dimensional Gaussian kernel with a full-width at half maximum of 3 mm. Functional data were convolved using a standard double gamma hemodynamic response function (Friston, 1998). Participant-specific GLMs of these data allowed for extraction of trial-

specific beta estimates in all voxels of interest. Beta estimates derived from a modeled HRF were chosen as target measure for the MVPA (i.e., as classifier input) because they are particularly well suited to account for overlap in the hemodynamic response in fast-event related designs (Misaki et al., 2010).

3.2.5 Anatomical ROI Definition

Our primary interest in the current paper centered on patterns of activity related to item recognition in anatomically defined PrC and PhC. However, we also considered activation patterns in the HC and entorhinal cortex (ErC), as well. To conduct MVPA, we considered distributed patterns of activation within ROIs that were defined in native MRI space based on anatomical demarcations detailed in established tracing protocols (Pruessner et al., 2000, 2002; Franko et al., 2012). All ROIs were manually traced in each participant separately. Specifically, we obtained ROIs for PrC, PhC, anterior HC (aHC), and posterior HC (pHC) in each hemisphere. The posterior extent of PhC ROIs was defined using anatomical landmarks described by Frankó et al. (2012). The distinction between anterior and posterior HC was introduced based on recent evidence suggesting distinct functional specialization across the long axis of the HC, and followed the protocol described by Poppenk and Moscovitch (2011) with the uncal apex serving as the critical boundary.

In addition to conducting MVPA using patterns of activation distributed across either PrC or PhC in their entirety, we also tested for the presence of familiarity signals along an anterior-posterior gradient of non-overlapping ROIs within these structures. For the purpose of these analyses we focused specifically on the right hemisphere. Toward this end, complete PrC and PhC ROIs were parsed in a manner that honoured the anatomical boundary between these structures and also ensured that each resultant ROI within the gradient had approximately the same number of voxels. Moreover, voxels comprising all gradient ROIs were independent with the boundary between the last slice of a given ROI and the first slice of the next (along the anterior-posterior axis) being entirely non-overlapping. In satisfying these criteria, PrC was divided into four distinct ROIs and PhC was parsed into three sub-sections for each participant independently. A one-way

ANOVA conducted on the number of voxels across gradient ROIs revealed no significant differences ($F_{6,133} = .57, p = .74$).

3.2.6 Multivariate Pattern Analysis of fMRI Data

MVPA was performed to examine the extent to which distributed patterns of activation within each of the ROIs considered were reliably discriminable at the level of 1) distinctions between stimulus categories and 2) within-category differences that reflect familiarity-based item recognition. To address questions related to stimulus category we considered only those patterns of activation obtained during presentation of objectively novel lures, irrespective of subjective memory judgments. As trials were not defined in relation to subjective responses, results from these analyses reflect differences in activation patterns corresponding to presentation of all 40 novel lures from each stimulus category.

Given the primary objective of the current study, i.e., to determine whether distributed patterns of activity within each ROI differentiate between recognition decisions for each stimulus category, we focused on perceived familiarity. Toward this end, we collapsed across both accuracy and levels of familiarity and novelty (i.e., ‘unsure’ and ‘sure’) to obtain patterns of activation comprising a familiar class of trials (hits and false alarms for both familiarity response options) and a novel class of trials (correct rejections and misses for both novel response options). Given that an unequal number of trials between classes can bias classification outcome we also implemented a pseudo-random sampling procedure that equated the number of trials corresponding to each class across runs. Specifically, familiar and novel trials were sampled so as to equate the number of trials both within and between runs, using the run with the fewest number of trials in either class as baseline. This procedure was repeated over 10 iterations to ensure that all trials for a given participant were included in the classification analysis at least one time. Specifically, 10 separate instances of the classification analysis (i.e., cross-validated classifier train-test) were completed and inferential statistical analyses were performed on classifier accuracy averaged over these 10 iterations.

Pattern classification analyses were conducted using the Princeton MVPA toolbox (<http://www.pni.princeton.edu/mvpa>) and custom MATLAB code (The MathWorks, Natick, MA). Feature selection, beyond that of selecting voxels within anatomically defined ROIs, was guided by voxel-wise measures of discriminability. Specifically, voxel-wise *t*-tests were conducted between beta values across trials from each class to identify features that, on their own, best discriminated between the pertinent classes at hand. Voxels were then rank-ordered based on absolute obtained *t*-values and the top 10% were selected for inclusion in the classification analysis irrespective of spatial proximity, direction of differential responses, or *t*-value magnitude. Averaged across participants, this procedure yielded the following number of functional voxels in each ROI: right PrC 52.5, left PrC 50.63, right PhC 46.2, left PhC 44.5, right ErC 30.2, left ErC 30.2, right aHC 24.3, left aHC 23.3, right pHC 28.4, and left pHC 29.5.

No additional feature selection was performed for the purpose of MVPA within gradient ROIs (i.e., ROIs along the anterior-posterior axis of right PrC and right PhC).

Accordingly, classification results for these analyses were based on all voxels within each ROI. Right PrC ROIs, from anterior to posterior, consisted of 142.9, 145.5, 136.9, and 139.0 voxels. Right PhC ROIs, from anterior to posterior, consisted of 133.7, 140.1, and 132.5 voxels.

The extent to which distributed patterns of activation could discriminate between pairs of classes of interest was formally assessed through implementation of a linear support vector machine (SVM; libSVM, <http://www.csie.ntu.edu.tw/~cjlin/libsvm>) with a linear kernel function and a constant cost parameter of $C = 1$. For the purpose of cross validation, the SVM was initially trained using data from all but one run, with trials from the run held out serving as test data for classification. This train-test procedure was fully cross validated with each run being held out one time. For each test trial, the classifier returned a probability estimate that reflected the likelihood that the observed activity pattern corresponded to either of the classes pertinent to the analysis at hand. However, these probability estimates were considered in a winner takes all manner; classification was either correct (i.e., when the ‘true’ experimental condition was assigned the highest probability) or incorrect. Averaged across all 10 iterations, classifier accuracy reflects the

percentage of test trials that were classified correctly in this binary manner, for each participant separately. To obtain inferential statistics, we examined whether classifier performance, averaged across all participants, was above chance (i.e., 0.5). For this purpose, we employed a single sample t -test using a Bonferroni correction based on the number of independent comparisons made (i.e., the number of ROIs examined).

Lastly, for ROIs in which familiarity-based classification was significantly greater than chance for more than one stimulus category, we also conducted cross-classification analyses to test for the presence of a familiarity signal that is common to multiple object categories. With this approach, a SVM decision boundary was initially established based on familiar and novel trials in one stimulus category and subsequently used to classify familiar and novel trials from a second category. Cross-classification employed the same linear SVM, cross-validation technique, and sampling procedure described above. However, the sampling procedure was performed in order to equate the number of trials across four, rather than two, conditions (i.e., novel and familiar trials from two stimulus categories).

3.3 Results

3.3.1 Behavioural Performance

Response percentages corresponding to each of the recognition response options are presented in Table 3.1. Target object recognition was primarily driven by familiarity-based responses (collapsed across ‘unsure’ and ‘sure’ response options; $M = 48.3\%$, 61.5% , and 48.3% for buildings, trees, and planes, respectively), as compared to recollection (R; $M = 6.8\%$, 7.1% , and 8.2% for buildings, trees, and planes, respectively). Overall recognition performance, i.e., the ability to discriminate between targets and lures irrespective of subjective recognition experience, was quantified using the discriminability index d' . Estimates were derived using hits and false alarm rates in the context of signal-detection theory through consideration of ‘old’ responses collapsed across the ‘unsure familiar’, ‘sure familiar’ and ‘R’ response options. In contrast, familiarity estimates were calculated using d' based on hits and false alarm rates corresponding to collapsed familiarity responses, and corrected for independence

between familiarity and recollection (Yonelinas, 1999). A one-way ANOVA conducted on these measures revealed that performance was closely matched across stimulus categories; there were no significant differences between categories for overall discrimination ($F_{2,57} = .82, p = .44$), estimates of familiarity ($F_{2,57} = .35, p = .71$), nor for estimates of recollection (R hits minus R false alarms; $F_{2,57} = .120, p = .31$). Although performance levels were low, due to the high similarity between all items within each stimulus category, familiarity discrimination was above chance for each category (all t_{19} 's $> 7.33, p$'s $< .001$). We note that the limited number of R responses observed in the present study (collapsed across hits and false alarms $M = 5.9, 6.7, \text{ and } 6.5$ for buildings, trees, and planes, respectively) did not allow for any investigation of fMRI responses associated with recollection.

Table 3.1 Recognition-response distribution and discrimination estimates for each stimulus category

Stimulus Category	Percentage responses to studied items					Percentage responses to novel items					Discrimination	
	1	2	3	4	R	1	2	3	4	R	Recognition d'	Familiarity d'
Buildings												
Mean	15.5%	29.4%	28.7%	19.6%	6.8%	29.4%	39.0%	21.9%	8.1%	1.5%	.64	.57
SEM	2.6%	2.3%	2.6%	2.2%	2.0%	3.8%	3.2%	2.0%	1.5%	0.7%	.06	.06
Trees												
Mean	10.2%	21.2%	30.6%	30.9%	7.1%	20.1%	32.3%	26.7%	17.9%	3.0%	.59	.56
SEM	2.3%	2.4%	2.4%	2.2%	2.0%	2.3%	3.7%	2.3%	2.7%	1.2%	.07	.07
Planes												
Mean	14.8%	28.7%	27.5%	20.8%	8.2%	29.6%	38.9%	22.4%	8.6%	0.5%	.73	.64
SEM	2.5%	3.2%	2.4%	3.3%	2.2%	3.5%	3.8%	2.4%	2.0%	0.4%	.10	.09

With respect to response latencies (refer to Table 3.2), a 3 x 3 ANOVA [response type (novel, familiar, recollection) x stimulus category (buildings, trees, planes)] was conducted after collapsing across objective item status (i.e., target or lure) and response options (novel = ‘unsure novel’ and ‘sure novel’; familiar = ‘unsure familiar’ and ‘sure familiar’). This specific approach was implemented to match that employed for the purpose of classification of fMRI data (see below). This analysis revealed a main effect of response ($F_{2,171} = 13.43, p < .001$) but not stimulus category ($F_{2,171} = .93, p = .40$). The interaction between response and stimulus category was not significant ($F_{4,171} = .61, p = .66$), providing further evidence that all three stimulus categories were matched behaviourally. Post-hoc analyses revealed that the main effect of response type was driven primarily by shorter response latencies for recollection responses as compared to either novel ($t_{59} = -5.19, p < .001$) or familiar ($t_{59} = -5.08, p < .001$) responses. Response latencies for novel and familiar did not differ from one another ($t_{59} = .18, p = .85$).

Table 3.2 Recognition response latencies for each stimulus category

Response	Novel	Familiar	Recollection
Buildings	1774 (91)	1956 (84)	1554 (99)
Trees	1830 (97)	1889 (85)	1671 (105)
Planes	1880 (132)	2006 (131)	1549 (132)

3.3.2 fMRI Results - Between Category Classification

Our first analyses of fMRI data were conducted to evaluate the extent to which information pertaining to stimulus category, rather than recognition memory decision per se, could be decoded from distributed patterns of activity across voxels in each anatomically defined ROI. Specifically, we focused on activity corresponding to all objectively novel trials (i.e., lures) from each stimulus classes (i.e., buildings vs. trees vs. planes), regardless of the recognition responses provided by the participants. One-sample *t*-tests were conducted with a Bonferroni corrected threshold, based on 10 comparisons (i.e., ROIs), for the purpose of establishing significance of decoding accuracy (chance performance = .33). Classifier performance was above chance in right PrC ($t_{19} = 5.89, p < .01$ corrected), left PrC ($t_{19} = 4.01, p < .01$ corrected), right PhC ($t_{19} = 10.17, p < .001$ corrected), and left PhC ($t_{19} = 8.44, p < .001$ corrected), with classifier accuracy not differing from chance in any other structure (right and left ErC, aHC, pHC; all p 's $> .10$).

To determine whether activity related to each stimulus category could be discriminated from all other categories we next performed additional analyses that assessed pair-wise classifications. Classification results are presented in Figure 3.2. We obtained above chance classification when discriminating between activation patterns associated with buildings and trees in right PrC ($t_{19} = 3.32, p < .01$ corrected), left PrC ($t_{19} = 4.37, p < .001$ corrected), right PhC ($t_{19} = 12.77, p < .001$ corrected), left PhC ($t_{19} = 6.83, p < .001$ corrected). Classifier accuracy was not significantly greater than chance in any of the remaining ROIs (all p 's $> .17$). The same regions were also sensitive to differences between buildings and planes (right PrC $t_{19} = 7.26, p < .001$ corrected; left PrC $t_{19} = 6.54, p < .001$ corrected; right PhC $t_{19} = 8.41, p < .001$ corrected; left PhC $t_{19} = 8.86, p < .001$ corrected). No other structures yielded above chance decoding (all other p 's $> .11$). Lastly, classifier accuracy was also above chance in right PrC ($t_{19} = 4.81, p < .001$ corrected), left PrC ($t_{19} = 5.98, p < .001$ corrected), right PhC ($t_{19} = 7.12, p < .001$ corrected), and left PhC ($t_{19} = 7.76, p < .001$ corrected) when discriminating between planes and trees (all other p 's $> .15$). When considered together, these results suggest that PrC and PhC do indeed carry information pertaining to stimulus category. Conversely, we found little evidence for category-specific representations in either ErC or the HC.

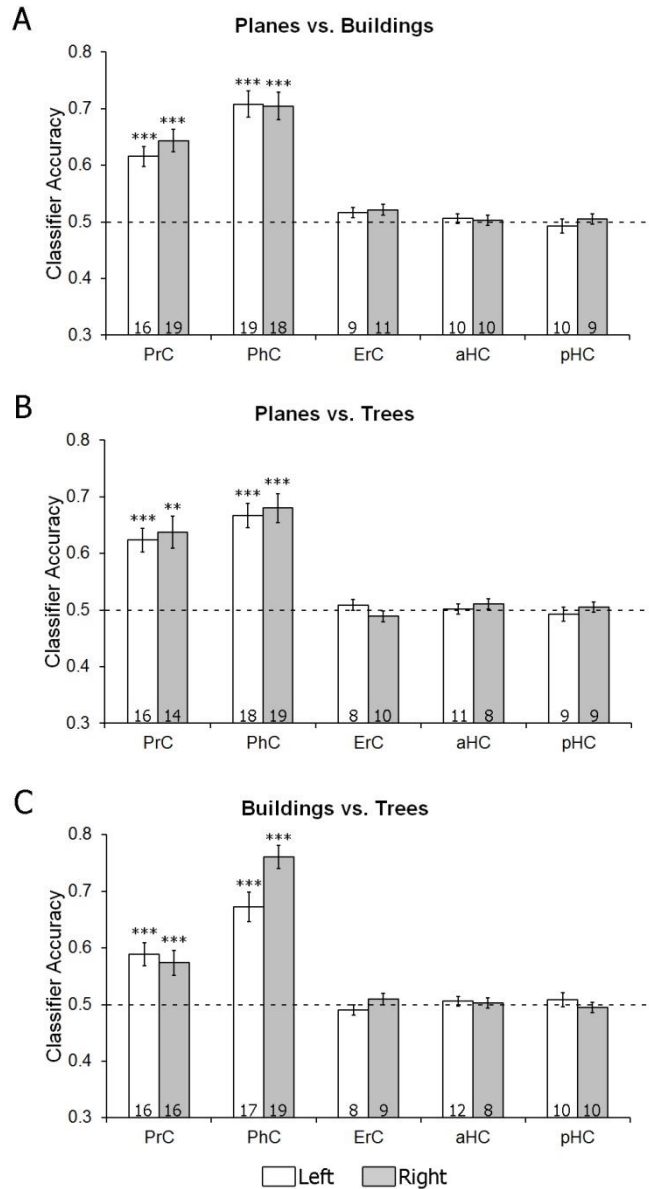


Figure 3.2 Pairwise MVPA classification of different stimulus categories in left and right PrC, PhC, aHC, and pHC. Classification was based on examination of all trials in which novel stimuli were presented. Dashed lines indicate chance level for classification. Numbers within bars represent the number of participants for whom classification performance was numerically above chance level. All error bars indicate the SEM calculated across participants. * $p < .05$, ** $p < .01$, *** $p < .001$.

3.3.3 fMRI Results - Within Category Classification of Familiar and Novel Trials

We next examined whether we could accurately decode item recognition decisions from activation patterns in any of our MTL ROIs. Two classes of trials were initially defined for each stimulus category by collapsing across novelty ('sure novel' and 'unsure novel') and familiarity ratings ('sure familiar' and 'unsure familiar'), regardless of objective item status. Across participants, the average number of trials from each class (i.e., familiar and novel) included for the classification of buildings, trees, and planes was 49.3, 42.1, and 42.9, respectively, with a minimum of 19 and maximum of 58 trials. Our first analysis focused specifically on the patterns of activation that were obtained following feature selection of voxels (i.e., top 10% based on voxel-wise ability to discriminate between classes) drawn from the entirety of each anatomically defined ROI. Decoding accuracies for PrC and PhC are presented in Figure 3.3. We found evidence for activation patterns that reflected subjectively perceived familiarity in both PrC and PhC, but not in ErC, aHC, or pHC in either hemisphere. Specifically, in right PrC, patterns of activity could be classified according to subjective familiarity for planes ($t_{19} = 5.28, p < .001$ Bonferroni corrected for 3 comparisons, i.e., number of stimulus categories), but not for buildings ($t_{19} = -.20, p = .42$) or trees ($t_{19} = .35, p = .37$). Classifier accuracy for planes was significantly greater than that obtained for buildings or trees in right PrC ($t_{19} = 4.63, p < .001$; $t_{19} = 4.11, p < .001$, respectively; corrected). By contrast, familiarity could successfully be decoded from patterns of activity obtained in right PhC for buildings ($t_{19} = 7.71, p < .001$ corrected) and trees ($t_{19} = 5.92, p < .001$ corrected), but not planes ($t_{19} = .92, p = .18$). Classifier accuracy for both buildings and trees was significantly greater than that obtained for planes in right PhC ($t_{19} = 4.31, p < .001$; $t_{19} = 2.84, p < .05$, respectively; corrected). In the left hemisphere, classifier performance in PrC did not exceed chance level for any stimulus category (buildings, $t_{19} = -.79, p = .42$; trees, $t_{19} = .27, p = .40$; planes, $t_{19} = .68, p = .25$). Classification accuracy was above chance in left PhC for buildings ($t_{19} = 5.99, p < .001$ corrected), but not trees ($t_{19} = 1.19, p = .14$) or planes ($t_{19} = .92, p = .19$). While our results point to category-specific item recognition signals in PrC and PhC, we were unable to decode familiarity in either right or left ErC, aHC, or pHC for any stimulus category (all p 's $> .07$). Similarly, classifier accuracy did

not exceed chance levels in the HC for any stimulus category when considered in its entirety rather than as an anterior and posterior segment independently (all p 's > .38).

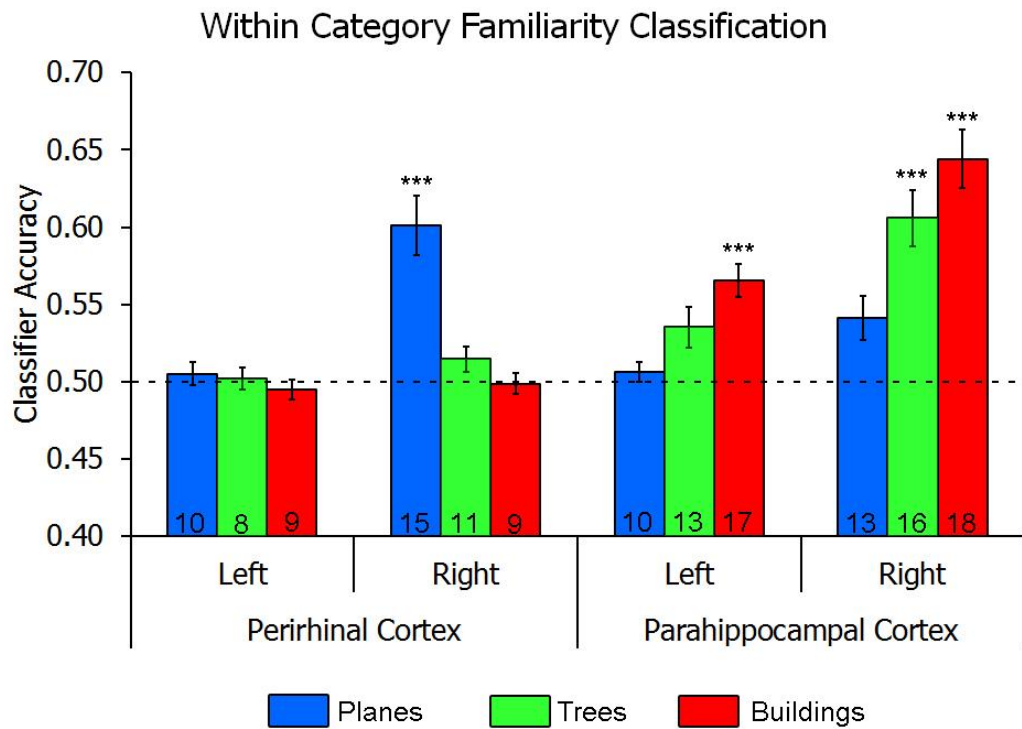


Figure 3.3 MVPA classification of perceived familiar versus novel trials for the three different stimulus categories in left and right PrC and PhC. Dashed lines indicate chance level. Numbers within bars represent the number of participants for whom classification performance was numerically above chance level. All error bars indicate the SEM calculated across participants. *** $p < .001$.

To further characterize the manner by which category specific item recognition signals are reflected in activity patterns within PrC and PhC we also examined whether such information would also be carried in sub-structure ROIs along an anterior-posterior gradient within each. This approach was guided by previous fMRI research that has revealed differential responses to varying types of stimulus content (e.g., objects and scenes) across an anterior-posterior gradient that encompasses PrC and PhC in both mnemonic (Staresina et al., 2011) and non-mnemonic task contexts (Litman et al., 2009; Liang et al., 2013). As previously noted, each anatomically defined ROI was further segmented into a subset of smaller ROIs that were all comparable in size (from anterior to posterior: PrC1, PrC2, PrC3, PrC4, PhC1, PhC2, and PhC3). We focused specifically on activity in the right hemisphere, given that our initial results primarily implicated right PrC and PhC. Classifier accuracy obtained for each of these ROIs was based on activity distributed across all voxels without any additional feature selection (i.e., 100% of voxels within each region). Decoding results are presented in Figure 3.4. Statistical significance was established using a Bonferroni correction for seven comparisons (i.e., the number of ROIs). Classification was significantly greater than chance when decoding the familiarity of planes from activity in PrC2 ($t_{19} = 6.13, p < .001$ corrected), PrC3 ($t_{19} = 5.67, p < .001$ corrected), PrC4 ($t_{19} = 6.86, p < .001$ corrected), and PhC1 ($t_{19} = 5.22, p < .001$ corrected). No other regions yielded above chance classification for planes (all p 's $> .11$). The same analysis conducted with data corresponding to familiar and novel trees revealed above chance classification in PhC1 ($t_{19} = 5.53, p < .001$ corrected), PhC2 ($t_{19} = 6.95, p < .001$ corrected), and PhC3 ($t_{19} = 5.80, p < .001$ corrected). Classifier accuracy for trees was not greater than chance in any of the PrC ROIs (all p 's $> .14$), nor the anterior most region of PhC (PhC1, $p > .09$). Lastly, the perceived familiarity of buildings was successfully decoded from activity patterns in PhC2 ($t_{19} = 5.07, p < .001$ corrected) and PhC3 ($t_{19} = 9.16, p < .001$ corrected), but not any of the remaining ROIs (all p 's $> .06$).

Lastly, in addition to assessing perceived familiarity, we also examined whether response patterns in any ROI would allow for successful classification based on objective item status (i.e., targets vs. lures irrespective of recognition response). In line with results from our previous investigation (Martin et al., 2013) and those reported for faces uses whole brain MVPA by Rissman et al. (2010), we did not find any significant effects for any

stimulus category in any region examined (PrC, PhC, ErC, aHC, pHC, entire HC in either the left or right hemisphere; all p 's > .09, uncorrected).

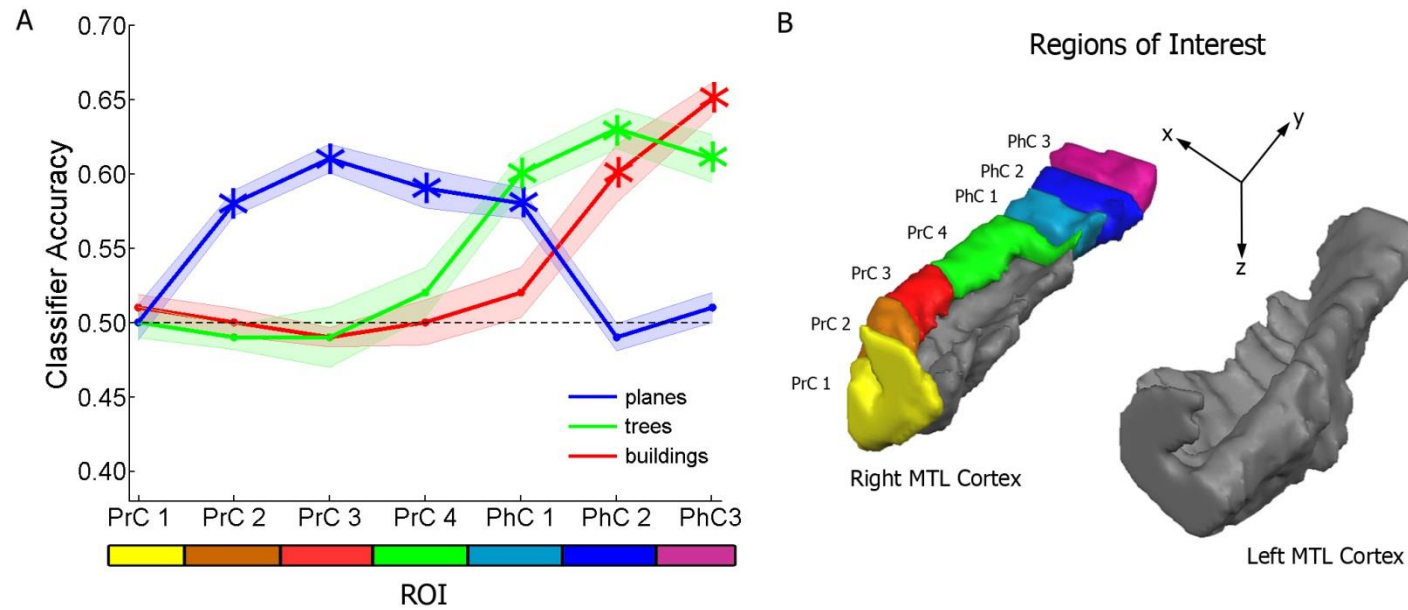


Figure 3.4 MVPA classification of perceived familiar versus novel trials for the three different stimulus categories across an anterior-posterior gradient encompassing right PrC and PhC. A) Classifier accuracies obtained for planes, trees, and buildings in each of seven ROIs in right PrC and PhC. Dashed lines indicate chance level. B) Depiction of ROI segments in a representative participant. * $p < .001$.

3.3.4 fMRI Results – Correlations Between Behavioural Recognition Accuracy and fMRI Classifier Performance

We next examined whether any of the different types of classification reported show a relationship to the accuracy of memory decisions when inter-individual differences are considered. Note that all classification analyses presented are based on the outcome of recognition decisions regardless of their accuracy, an analyses approach that maximized the number of trials on which training of the classifier could be based. To get leverage in answering questions about behavioural performance, we assessed the relationship between the accuracy of recognition decisions (i.e., familiarity-based d') and classifier accuracy across participants. These analyses revealed significant positive correlations between behavioural performance and classifier accuracy for planes in right PrC [$r(18) = .46, p < .05$] and buildings in right PhC [$r(18) = .59, p < .01$]. For trees, the correlation between classification accuracy in PhC and behavioural performance was in the expected direction, but did not reach statistical significance [$r(18) = .33, p < .10$].

3.3.5 fMRI Results - Between Category Cross-Classification of Familiar and Novel Trials and Voxel Overlap Analysis

Decoding from activity patterns in right PhC revealed signals related to subjectively perceived familiarity for both buildings and trees. Accordingly, it is critical to determine whether this pattern of results reflects a shared, stimulus general familiarity signal, or whether there is indeed evidence to support the notion that item recognition signals are coded in a category specific manner. To address this issue, we first evaluated the extent to which voxels with diagnostic relevance for the classification of familiar and novel trials overlapped between categories. Specifically, we examined overlap at the level of voxels that were selected in the initial feature-selection procedure to be the most informative for use in the SVM; recall that only 10% of all voxels within each region were selected for each cross-validated step of classification. To minimize the influence of noise, only those voxels that were selected in at least six of the 10 classification iterations were considered. The extent of voxel overlap for voxels with diagnostic relevance for decoding recognition decisions for buildings and trees from activity within right PhC is depicted for a representative participant in Figure 3.5. This approach revealed that 43%

of the voxels in right PhC with diagnostic relevance in the context of SVM optimization for classification of buildings were also included in the classification analysis for trees. In the opposite direction, 54% of the voxels that were selected for classification of familiar and novel trees were also selected for the corresponding analysis for buildings. These results indicate that the distributed memory representations in PhC that reflected the familiarity of buildings and trees show partial overlap, suggesting that these activity patterns are somewhat independent.

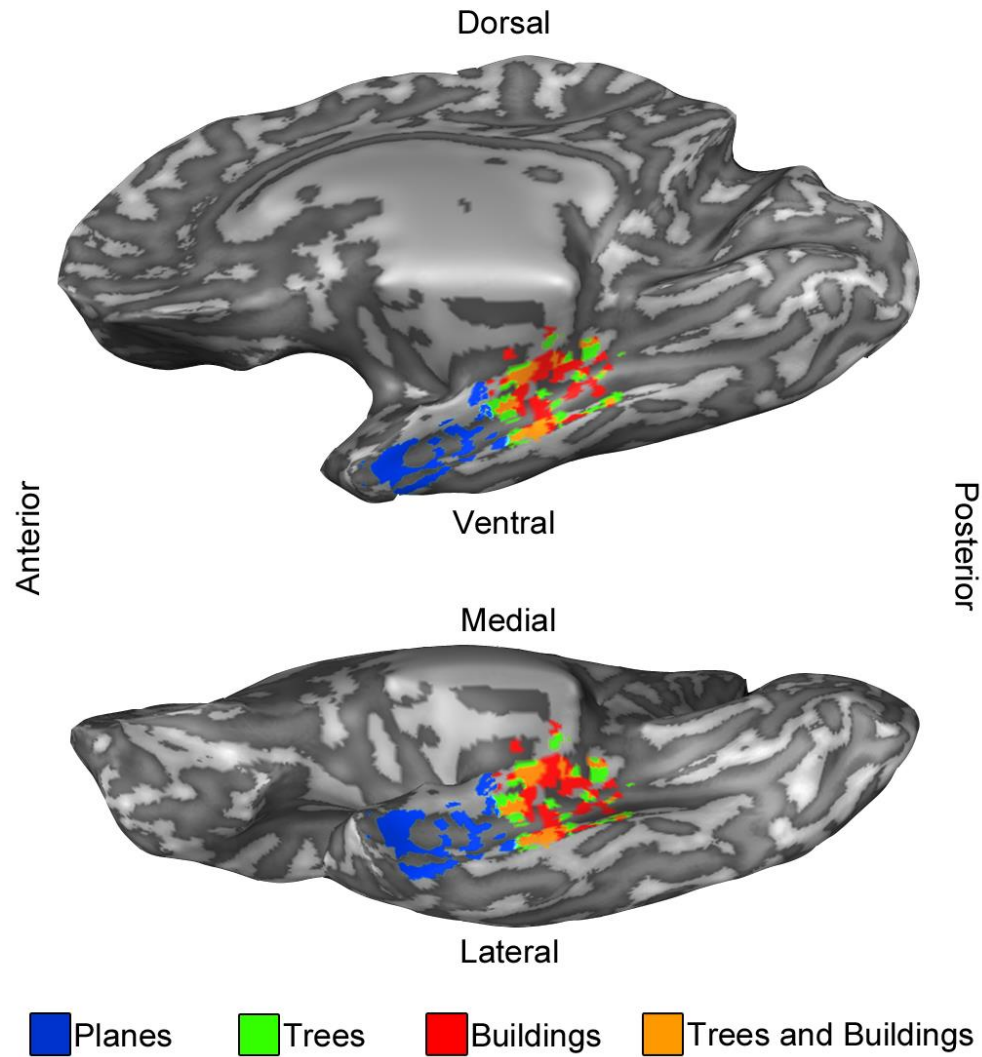


Figure 3.5 Spatial distribution of voxels with diagnostic relevance for familiarity-based decoding in a representative participant. For illustrative purposes, the data presented were obtained from one fully cross-validated iteration of the classification analysis. Only those voxels that appear consistently across iterations (i.e., included in at least one cross-validated train-test classification in a minimum 6 out of 10 trial sampling iterations) are depicted.

To address the issue of independence more formally, we conducted a cross-classification analysis using activity patterns associated with familiar and novel buildings and trees in right PhC. If classification in PhC is predicated on a memory signal that is common to buildings and trees, these analyses should reveal that the pattern of activity that distinguishes between familiar and novel trials from one stimulus category should also accurately discriminate for the other, and vice versa. Again, these analyses were conducted using the item-sampling procedure described previously, which matched trial numbers across both stimulus class and recognition responses. Critically, cross-classification was at chance in right PhC when the linear decision boundary optimized during SVM training for discrimination of familiar and novel buildings was used to classify familiar and novel trees ($M = .52$; $p > .11$ uncorrected). The complementary analysis, which established a decision boundary for trees and applied it to buildings, also yielded classifier accuracy that did not differ from chance ($M = .49$, $p > .32$). These data suggest that the distributed patterns of voxels that contribute to classification of familiar versus novel buildings and trees in PhC show evidence of functional independence.

In a final step, we also performed cross-classification analyses in the PrC/PhC gradient ROIs that yielded above chance classification for more than one stimulus category (i.e., planes and trees in PhC1, and trees and buildings in PhC2 and PhC3). As no additional feature selection was performed on data from these segmented ROIs, activity patterns associated with different stimulus categories within the same ROI are distributed over voxels that are entirely overlapping. Despite this spatial correspondence between voxels, our results suggest that the patterns of activity related to item recognition within each gradient ROI differ between categories as cross-classification was unsuccessful for each pertinent analysis (planes and trees in PhC1, $M = .49$, $p > .27$; trees and buildings in PhC2, $M = .52$, $p > .16$, and trees and buildings in PhC3, $M = .50$, $p > .46$).

3.4 Discussion

In the current study, we examined distributed patterns of activity in the MTL associated with the perceived familiarity of buildings, trees, and planes. Our primary goal was to examine whether the distributed patterns of activation pertaining to item recognition differed between PrC and PhC for objects that are typically fixed in location (i.e.,

buildings and trees) and those that are not (i.e., planes), while holding real-world size constant across categories. Moreover, we also sought to determine whether familiarity signals within each structure were dissociable in a category-specific manner. Our classification results revealed item recognition signals for planes in right PrC, but not for trees and buildings. By contrast, we observed familiarity signals for trees and buildings in right PhC, but not planes. Importantly, we found significant correlations between behavioural recognition performance and classifier accuracy for planes in right PrC and buildings in right PhC. Results from our cross-classification analyses suggest that the distributed patterns of activation in PhC that carry information pertinent to item recognition decisions for trees and buildings are distinct from one another. When considered together, this pattern of results suggests that fixedness in location in the environment is one object property that leads to differential item-recognition effects between structures. At a more fine-grained level, these data also point to category-specific patterns of item recognition signals in PhC.

The evidence revealed in the current study converges with findings from our previous research (Martin et al., 2013) in suggesting that representations in both PrC and PhC can be brought to bear on item recognition decisions. To the extent that the recognition memory judgments of interest (i.e., familiar vs. novel) were not confounded by unreported recovery of contextual detail, these findings argue against the notion that a distinction between items and contexts can fully characterize functional specialization with respect to recognition memory in PrC and PhC (Eichenbaum et al., 2007; Diana et al., 2007; Ranganath, 2010; Montaldi and Mayes, 2010). What, then, determines whether item recognition signals are carried by either PrC or PhC? One potential explanation is that stimulus category may be a critical determinant as extant fMRI research has revealed that visual stimuli are indeed represented in a categorical manner in MTL cortex (Diana et al., 2008; Litman et al., 2009; Liang et al., 2013; Huffman and Stark, 2014), and the ventral visual pathway more broadly (Haxby et al., 2001; Kriegeskorte et al., 2008; for review, see Grill-Spector and Weiner, 2014). However, our results, together with those from our previous research (Martin et al., 2013), provide initial evidence suggesting that reference to stimulus category alone may be insufficient to account for the difference in response profiles exhibited by these structures. Rather, specific object properties may

constitute a more fundamental distinction that determines whether item representations in PrC or PhC carry information pertaining to the prior occurrence of a given stimulus in the context of a recognition memory task. Importantly, however, these object properties may be continuous rather than dichotomous dimensions. That we observed above chance decoding of item recognition decisions for planes in both PrC and the anterior most extent of PhC in our ROI gradient analysis, and in both structures for chairs in our previous research (Martin et al., 2013), provides support for this proposal.

What specific object properties determine the relative contributions of PrC and PhC to item recognition? Previous fMRI research that has examined the representation of visual information in the absence of mnemonic demands has revealed preferential responses for objects with large real-world size, as compared to small real-world size, in medial aspects of ventral temporal cortex that include PhC (Cate et al., 2011; Konkle and Oliva, 2012). Other research has indicated that objects that are fixed in location, a feature that is correlated with object size, also tend to evoke differential responses in PhC (Mullally et al., 2011; Troiani et al., 2012). While the stimulus dimensions of fixedness and size are often correlated, being fixed in location critically defines the extent to which a given object can be characterized as a landmark with potential navigational relevance. Here, we have sought to evaluate the relative importance of landmark suitability in relation to item recognition signals carried by PrC and PhC using categorized objects that were equated in perceived real-world size. Our results indicate that PhC carries item recognition signals for objects that have potential navigational relevance, rather than all large objects. Specifically, the familiarity of buildings and trees was associated with distinct fMRI BOLD responses in PhC, but not PrC. Conversely, PrC carried item recognition signals for planes, which are large but have limited navigational relevance. How can this pattern of results be squared with previous fMRI research that has revealed differential PhC responses to large objects (Konkle and Oliva, 2012)? One possibility is that such differential responses are driven primarily by large objects that are also fixed in location. Alternatively, PhC may indeed process large objects independently of fixedness and the difference between item recognition signals for fixed and mobile objects may reflect the top-down abstraction of semantic information regarding these properties. Notably, information pertaining to object fixedness may not necessarily be an inherent property of

an object's perceptual features (see Bastin et al., 2013, for related proposals). Ultimately, further empirical research is required to evaluate these alternative explanations as the current study was not specifically designed to assess the potential role of semantic or other top-down processes in relation to item recognition signals in PrC and PhC.

While we interpret our results as evidence suggesting that the potential navigational relevance of a given object critically determines whether PhC carries information pertaining to familiarity-based item recognition, we do not wish to claim that familiarity-based item recognition alone can support successful navigation based on landmark recognition. To successfully serve as a navigational cue, an object must not only be recognized as one that has been previously encountered, but the associative information related to direction or bearing must also be recovered in a task-dependent manner. That is to say, recognizing a particular building does not confer a navigational advantage on its own accord. However, given that our participants had no pre-experimental exposure to the building and tree stimuli employed in the current study, either within the context of an active navigation task or otherwise, it appears impossible that the effects we observed in PhC are related to the representation of such navigationally relevant contextual information. What our data do suggest is that objects such as buildings and trees, which have potential navigational relevance by virtue of being fixed in location, are represented in PhC. Perhaps more importantly, however, that we could successfully decode familiarity-based item recognition judgments from patterns of activity related to such objects indicates that PhC represents them in a manner that carries information relevant for familiarity-based discrimination between target items and perceptually similar lures.

Findings from a number of neuropsychological investigations in patients with lesions that include aspects of PhC also point to a possible role in item recognition. Specifically, lesions that include PhC and more posterior lingual gyrus have been linked to landmark agnosia (e.g., Landis et al., 1986; Takahashi and Kawamura, 2002; cf Epstein et al., 2001). Landmark agnosia refers to the inappropriate selection and utilization of landmarks for the purpose of orienting in both novel and previously encountered environments. Although lesion location, extent, and descriptions of behavioural outcomes have varied across case studies, patients with landmark agnosia typically have both

perceptual and mnemonic impairments related to landmarks that are often observed despite a preserved ability to represent spatial information, reproduce maps, and describe routes (see Aguirre and D'Esposito, 1999, for review). As a whole, evidence from such patients is largely consistent with our MVPA results in suggesting that aspects of PhC play a critical role in landmark recognition.

Beyond linking the functional differences between PrC and PhC to specific stimulus properties, the current study also revealed category-specific item recognition signals within PhC. Specifically, results from our cross-classification analyses suggest that familiarity signals in PhC that pertain to buildings are distinct from those pertaining to trees. This observation is consistent with our previous research which has revealed distinct patterns of activation associated with the decoding of familiar and novel faces and chairs from distributed activity in PrC, and buildings and chairs from patterns of activation in PhC (Martin et al., 2013). This pattern of distributed category-specific item-recognition signals in MTL cortex mirrors the distributed category-specific effects that have been reported in more posterior ventral temporal cortex in non-mnemonic task contexts (Haxby et al., 2001; Kriegeskorte et al., 2008; for review, see Grill-Spector and Weiner, 2014; cf. Spiridon and Kanwisher, 2002). Given that familiarity-based item recognition is by definition based on a stimulus itself, rather than associative detail, we suggest that categorical representations in MTL cortex may provide a substrate upon which information pertaining to prior occurrence is coded. This explanation is generally in line with the proposal that MTL structures support category-specific representations that can be brought to bear on both mnemonic and perceptual discriminations, although on this account PhC is not thought to represent scene stimuli rather than objects (Murray and Bussey, 1999; Bussey and Saksida, 2007; Graham et al., 2010).

In summary, our findings indicate that item-recognition memory is supported by distributed representations in both PrC and PhC, suggesting that a distinction between item information and contextual detail cannot fully characterize the functional contributions of these structures to recognition memory. Importantly, based on the stimuli employed we found that landmark suitability may be a critical factor that determines

whether item recognition signals are coded in either PrC or PhC. Moreover, our results reveal category-specific item recognition signals within each structure.

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Chapter 4

4 Distributed Category-Specific Recognition Memory Signals in Human Perirhinal Cortex

4.1 Introduction

Humans have a remarkable capacity to discriminate between previously encountered and novel stimuli, an ability that is typically referred to as recognition memory or recognition of prior occurrence. A large body of research in humans, non-human primates, and rodents converge in suggesting that perirhinal cortex (PrC), a structure in the medial temporal lobe (MTL) that is intimately connected with the ventral visual pathway for object identification, plays a critical role in recognition memory (Brown and Aggleton, 2001; Eichenbaum et al., 2007; Murray et al., 2007; Squire et al., 2007). In humans, PrC has been implicated in recognition memory for many different stimulus classes, including objects, faces, and words (see Diana et al., 2007; Kim 2013). A noticeable but less consistent body of research also suggests that recognition of prior occurrence does not require the integrity of the hippocampus, and can proceed normally in the absence of recollection of contextual detail about specific past stimulus encounters (see Montaldi and Mayes, 2010; Ranganath, 2010; Squire et al., 2010; Yonelinas et al., 2010, for review and discussion). Such acontextual item-based recognition has been linked to phenomenological feelings of familiarity. While numerous neuroimaging studies have focused on dissociations between perirhinal and hippocampal contributions to recognition memory, the precise nature of PrC computations and representations that support item-based recognition still remains poorly understood. Important outstanding questions concern how differential signals for familiar versus novel items are reflected in the fMRI BOLD response, whether such signals are spatially distributed within PrC, and whether they show specificity for different object categories.

Electrophysiological evidence from a number of studies in rodents and in non-human primates suggests that the mechanism by which PrC could code for recognition of prior

occurrence is a decrease in neuronal firing rate (i.e., repetition suppression; Zhu et al., 1995; Desimone, 1996; Ringo, 1996; Xiang and Brown, 1998; Aggleton et al., 2012; c.f. Hölscher et al., 2003). It has been reported that as many as 25% of PrC neurons in macaque monkeys show response decrements for familiar as compared to novel objects in the context of delayed-matching to sample, delayed non-matching to sample, or continuous recognition-memory tasks (Brown et al., 1987; Sobotka and Ringo, 1996; Xiang and Brown, 1998). It should be noted, however, that not all studies with electrophysiological recordings have revealed response reductions in PrC in association with the repeated occurrence of objects. For example, Thome et al. (2012) did not observe any reduction in PrC firing rates in association with stimulus repetition in a passive viewing experiment, a finding that has been interpreted to suggest that such signals could be task dependent (Brown et al., 2012). Alternatively, this finding is open to the interpretation that item-based recognition may not be coded exclusively by a reduction in local firing rates but may involve distributed coding over populations of neurons in PrC (Thome et al., 2012; Burke et al., 2014).

Evidence obtained with fMRI in healthy humans has also linked item-based recognition to differential responses in PrC for previously studied as compared to novel items at the time of retrieval (see Diana, et al., 2007; Kim, 2013, for review). Notably, several studies have demonstrated a negative relationship between confidence in the perceived ‘oldness’ of test items, which is often assumed to track item-memory strength, and the BOLD response in PrC (e.g., Daselaar et al., 2006a, 2006b; Montaldi et al., 2006; Wang et al., 2014; see also Gonsalves et al., 2005). Given that this decrease in response for previously encountered items parallels the pattern of repetition suppression in electrophysiological recordings, it has attracted considerable attention in the literature. However, there are numerous challenges associated with mapping repetition effects in single-cell recordings onto fMRI BOLD signals (see Henson and Rugg, 2003; Grill-Spector et al., 2006; Gotts et al., 2012, for discussion). In fact, there is evidence to suggest that BOLD activity is more closely related to local-field potentials detected with multi-unit recordings than to neuronal spiking (Logothetis et al., 2001; Logothetis, 2008). Against this background, it is perhaps not surprising that some fMRI studies have also revealed a relative increase in BOLD signal for familiar as compared to novel items in PrC (e.g., Kafkas and Montaldi,

2012), with one investigation even reporting increases and decreases in distinct PrC clusters in the same study (Yassa and Stark, 2008). Such findings point to the possibility that item-based recognition memory signals are reflected in patterns of decreases and increases in the fMRI BOLD response that are spatially distributed across PrC.

Most studies on the role of PrC in recognition memory have examined the neural correlates of item recognition with univariate statistical analyses that probe for clusters of contiguous voxels with homogeneous response profiles (e.g., Daselaar et al., 2006a) or by averaging activity across all voxels in anatomically defined regions of interest (e.g., Wang et al., 2014). Multi-voxel pattern analyses (MVPA) of fMRI data, by contrast, can detect information carried in activity patterns distributed over multiple voxels even when these voxels are not part of a contiguous cluster, and, critically, even when they show a heterogeneous directional response to an experimental manipulation (for review, see Norman et al., 2006; Rissman and Wagner, 2012; Tong and Pratte, 2012).

We recently conducted an MVPA-based fMRI study, aiming to reveal distributed patterns of BOLD activity in MTL structures that may distinguish between subjectively familiar and novel items (Martin et al., 2013). We reasoned that it might be possible to decode the perceived mnemonic status of an item from patterns of PrC activity if patterns of activity for familiar items are generally more similar to each other than to patterns associated with items considered as novel, and vice versa (see also Rissman et al., 2010). We scanned participants while they made recognition-memory judgments for visual stimuli from several different object categories (faces, chairs, and buildings). Using a linear support vector machine (SVM) in separate training sessions for items from each stimulus category, we were able to successfully decode the perceived familiarity of individual faces and chairs (but not buildings) from distributed activity patterns in right PrC. As the MVPA approach employed was blind to the direction of effects it may indeed have revealed information distributed across voxels with a heterogeneous response profile. Based on the analyses reported, however, we cannot rule out that the classifier detected subtle differences in the mean response (in one direction) across all voxels that comprised the pattern (see Coutanche, 2013 for discussion).

The present report describes a series of new analyses conducted on the dataset reported by Martin et al. (2013) that test a number of new questions about how PrC codes for prior occurrence. Our primary goal was to determine whether patterns of activity in PrC that allow for the classification of the perceived familiarity of faces do indeed consist of voxels with heterogeneous response profiles in terms of direction of effects, and, if so, whether classification could still be successful if patterns were restricted to include only voxels with changes in one direction. To obtain further leverage on the issue, we also investigated whether classification accuracy for any such voxel patterns is correlated with behavioural performance across participants.

A second goal of the current investigation was to determine whether voxels in patterns of PrC activity that carry information about the familiarity of faces show specificity in their response for this particular stimulus category. Inasmuch as item-based recognition memory signals are, by their definition, based on the stimuli rather than any contextual information about a prior stimulus encounter, the nature of the pertinent object category may play an important role in their neural organization (see Graham et al., 2010; Cowell et al., 2010; Martin et al., 2012, for further discussion). Prior fMRI research that has examined category specific responses for visually presented stimuli in non-mnemonic tasks has revealed two types of effects in more posterior occipito-temporal regions. First, studies based on univariate analyses have revealed clusters of contiguous voxels in the ventral visual pathway that show maximal responses for exemplars from a specific visual category. Such clusters are often referred to as category-selective regions and have been reported for several ecologically relevant categories, including faces, body parts, words, and places (see Op de Beeck et al., 2008, for review). Second, MVPA-based studies have revealed patterns of activity distributed across voxels in wider swaths of posterior ventral temporal cortex that show category-specific responses even when clusters with preferential responses are excluded, and even for categories that are not associated with any contiguous clusters in univariate analyses (see Grill-Spector and Weiner, 2014; Haxby et al., 2014, for review). For example, the latter types of studies have revealed the presence of informational content relevant for face identity in distributed patterns of activity in ventral visual pathway regions that go beyond the classic lateral occipital and posterior fusiform- ‘face areas’ previously identified in univariate analyses (Haxby et al.,

2001; Kriegeskorte et al., 2008; Nestor et al., 2011). At present, it remains unknown whether patterns of recognition-memory signals for faces in PrC show a similar functional organization. This issue is of particular interest given that a category-specific region with a preferential response for faces has recently also been identified in the anterior collateral sulcus of PrC, a region sometimes referred to as the anterior temporal face patch (ATFP; Rajimehr et al., 2009; Nestor et al., 2011; Nasr and Tootell, 2012; O'Neil et al., 2013, 2014; Collins and Olson, 2014).

In the present study, we examined whether voxels with diagnostic relevance for decoding recognition memory judgments for faces in PrC show category specificity when probed with an independent functional localizer of the type that has been used to identify face-specific responses in the ventral visual pathway in many prior studies under passive-viewing conditions. Moreover, we investigated whether these voxels are restricted to the ATFP or are more widely distributed in PrC. We pursued this issue within the context of our broader goals to characterize the nature of item-based recognition-memory signals in human PrC, which, as discussed, also aimed to address whether pertinent information is reflected in distributed patterns of voxels with heterogeneous directional response profiles.

4.2 Materials and Methods

4.2.1 Participants

Nineteen right-handed individuals participated in the study (21-30 years of age, mean age = 25.2 years; 12 females). All participants were screened for the absence of a history of neurological disorders. Data from one participant were excluded from all analyses due to excessive head movement during scanning. Participants received financial compensation for their participation and provided informed consent according to procedures approved by the University of Western Ontario Health Sciences Research Ethics Board.

4.2.2 Stimuli and Behavioural Procedure

Stimuli were grayscale images depicting exemplars from three different object categories (i.e., faces, chairs, and buildings), though the current study focuses specifically on

patterns of BOLD activity related to the familiarity of face trials. Each target object was presented in isolation on a homogeneous, white background. The size of each image was bounded at 375 x 250 pixels, with at least one dimension corresponding to these limits. For the purpose of counterbalancing, images from each stimulus category were divided into three sets of 40 objects, two of which (i.e., 80 objects) served as items presented prior to scanning during a study session, and as corresponding targets in the scanned recognition-memory test stage. The remaining 40 items served as novel lures in the recognition task. Assignment of item sets to either target or lure lists was counterbalanced across participants.

The experimental task consisted of two discrete stages: an encoding session and a subsequently scanned recognition memory test. The initial encoding session was separated into six blocked sequences that were counterbalanced across participants. Each block consisted of 40 trials corresponding to one target list. Stimuli were presented for 3000ms with a 2000ms fixation ISI, and participants were asked to rate the relative attractiveness of each face, comfort of each chair, or value of each building using a five-point scale.

Participants subsequently completed a scanned recognition memory test consisting of 80 previously studied targets and 40 lures from each category, for a total of 360 trials distributed over eight functional runs of equal length and composition. Of these trials, 120 corresponded to presentation of face stimuli (i.e., 80 studied and 40 novel lures). Stimuli were presented for 2500 ms, with a jittered fixation-baseline separating trials (jitter sequence was optimized using the OptSeq2 algorithm; <http://surfer.nmr.mgh.harvard.edu/optseq/>). While in the scanner, participants viewed the stimulus display through a mirror at a distance that yielded an approximate object size of 18 x 13° visual angle. For their recognition judgments, participants were instructed to provide a rating of perceived familiarity on a scale between one (least familiar) and four (most familiar), with a fifth response option corresponding to recollection. Critically, they were asked to respond with a fast and intuitive assessment of their perceived item familiarity and to avoid attempting to recollect contextual details from the encoding stage of the experiment (see Dobbins and Han, 2006; Montaldi et al., 2006; Quamme et al.,

2010; Martin et al., 2013, for further discussion). Recollection of contextual details was defined as any situation that involved conscious awareness of information about the past item encounter that was independent of perceptual details of the stimulus itself, such as internal thoughts and associations that were formed during the initial item encounter.

4.2.3 Functional Localizer Tasks

Subsequent to the experimental task, each participant completed two independent functional localizer scans (which were not considered in our initial report, Martin et al., 2013). The localizer task followed a protocol that has previously been used in several other studies from our lab (e.g., Ganel et al., 2006; O'Neil et al., 2009, 2013; Cate et al., 2011) and is similar to that used in many other studies in the visual cognition literature more broadly. It involved presentation of grayscale faces, common objects, and places (scene landscapes and buildings with naturally occurring background) under passive viewing instructions. Importantly, stimuli employed in the localizer task were independent of those comprising the experimental recognition memory task. Stimuli from each category were presented in a blocked manner with alternating blocks of scrambled images corresponding to each stimulus category.

4.2.4 fMRI Acquisition Protocol

All MRI data were acquired on a Siemens TIM Trio 3-Tesla scanner with a high-resolution fMRI protocol optimized for MTL examination. Functional MRI volumes were collected using a T2*-weighted single-shot gradient-echo-planar acquisition sequence [TR = 2500 ms, TE = 26 ms, slice thickness = 2 mm, in-plane resolution = 2 X 2 mm, FOV = 220 mm X 220 mm, flip angle = 90°]. Each functional volume included 37 contiguous slices collected in an interleaved manner. For each experimental run (8 per participant), 176 volumes were collected. Each localizer scan (2 per participant) consisted of 150 functional volumes. To optimize MR signal in the anterior temporal lobes, a transverse orientation was chosen with the effort to include the entire temporal lobes and as much visual cortex as possible. This slice selection resulted in full coverage of the ventral aspects of occipital and full coverage of the entire temporal lobes in all participants, with exclusion of the most dorsal aspects of frontal and parietal cortices, as

well as occipital cortex in some participants. A saturation band was applied during functional runs in order to minimize artifacts related to eye-movements and the sinus cavity. T1-weighted anatomical images were obtained using an ADNI MPRAGE sequence [192 slices, TR = 2300 ms, TE = 4.25 ms, 1 mm isotropic voxels, FOV = 240 X 256 mm, flip angle = 9°].

4.2.5 fMRI Data Pre-processing

fMRI data were pre-processed in native space using BrainVoyager QX version 2.3 (Brain Innovation). Functional images were slice-scan time corrected, 3-D motion corrected with reference to the functional volume taken just prior to the anatomical scan, and high-pass filtered using a linear trend and a Fourier basis set of 2 cycles/run. Images were then co-registered with the anatomical image and aligned with the AC-PC plane. For the purpose of MVPA, experimental data were minimally smoothed using a three-dimensional Gaussian kernel with a full-width at half maximum of 3 mm. Functional data from the localizer experiment were smoothed using a three-dimensional Gaussian kernel with a full-width at half maximum of 8 mm. Functional data were convolved using a standard double gamma hemodynamic response function (Friston, 1998). Participant-specific GLMs of these data allowed for extraction of trial-specific beta estimates in all voxels of interest. Beta estimates derived from a modeled HRF were chosen as target measure for the MVPA (i.e., as classifier input) because they are particularly well suited to account for overlap in the hemodynamic response in fast-event related designs (Misaki et al., 2010). Changes in mean intensity across runs were modeled by including them as predictor of no interest in the participant-specific GLMs.

4.2.6 Identification of the Anterior Temporal Face Patch in Functional Localizer Scans

This region of interest was defined functionally, for individual participants, in the right hemisphere, using data from the localizer scans. A general linear model was specified for each localizer run with faces, places, and objects as predictors. Scrambled images served as the baseline condition. Participants' ATFPs were derived from the contrast [faces > places], which corresponded to a subject-specific fixed-effects contrast image. ROIs were

defined based on activation maps that were statistically thresholded using a whole-volume, uncorrected p -value $< .05$, and anatomical criteria that related to PrC boundaries (Pruessner et al., 2002).

4.2.7 Anatomical Definition of PrC for MVPA of Recognition Signals in Experimental Task

To conduct MVPA, an anatomically defined ROI for PrC in the right hemisphere was created in native MRI space with manual tracing separately for each participant. For this purpose, we used an established protocol that specifies anatomical landmarks for demarcation of PrC from surrounding cortical structures in the MTL (Pruessner et al., 2000, 2002).

4.2.8 MVPA of fMRI Data

For the purpose of classification, data were collapsed across response options such that the ‘familiar’ class of face trials corresponded to hits and false alarms at the two highest levels of familiarity (i.e., response options 3 and 4) and the ‘novel’ class of face trials comprised hits and false alarms at the two lowest levels of familiarity (i.e., response options 1 and 2). To eliminate potential classifier bias related to unequal trial numbers we employed a pseudo-random sampling procedure that equated the number of trials between the ‘familiar’ and ‘novel’ classes. This procedure was repeated over 10 iterations to ensure that all trials for a given participant were included in the classification analysis at least one time. Accordingly, 10 separate instances of the classification analysis (i.e., cross-validated classifier training and testing) were completed and inferential statistical analyses were performed on classifier accuracy averaged over these 10 iterations. Across participants, the average number of trials included for the classification of faces at each familiarity level (i.e., ‘familiar’ versus ‘novel’) was 39.8.

Pattern classification analyses were conducted using the Princeton MVPA toolbox (<http://www.pni.princeton.edu/mvpa>) and custom MATLAB code (The MathWorks, Natick, MA). As a first step, we performed feature selection in order to minimize the influence of noise in the functional data. The feature selection procedure employed here allowed for multivariate classification of perceived familiarity of faces based on activity

within a subset of PrC voxels that were not necessarily clustered in any systematic manner and showed either homogeneous or heterogeneous response profiles. Specifically, feature selection was based on voxel-wise measures of discriminability (i.e., *t*-tests between ‘familiar’ and ‘novel’). When contrasted with multivariate feature selection procedures, such as a multivariate searchlight which considers weighted combinations of voxel responses for class separation, the primary advantage of the current approach pertains to increased sensitivity for detection of cognitive states coded in activity patterns comprised of spatially distributed voxels. Accordingly, this approach is sensitive to meaningful patterns that are distributed beyond the spatial scale of a searchlight.

Feature selection was performed in each participant separately by choosing the subset of voxels in right PrC that appeared most informative for classification based on an initial univariate statistical analysis (see Norman et al., 2006 for discussion). Specifically, a *t*-test was conducted between beta values for ‘familiar’ and ‘novel’ trials in all voxels in right PrC for each cross-validation separately. All voxels were subsequently rank ordered according to their obtained *t*-statistic and those corresponding to the top 10% of that ranking were selected as features included for SVM classification (see below for additional detail regarding directional and non-directional feature selection procedures). For all familiar-novel classifications this analysis was also performed separately for each of the 10 iterations of item sampling. This feature selection procedure yielded an average of 55.1 functional voxels (2x2x2 mm) in right PrC across participants.

A linear support vector machine (SVM; libSVM, <http://www.csie.ntu.edu.tw/~cjlin/libsvm>) was used for classification of beta values with a linear kernel function and a constant cost parameter of $C = 1$. For each cross-validated classification analysis, the SVM was trained on all but two face trials; those trials not included in the training data set (i.e., one ‘familiar’ and one ‘novel’ trial) subsequently served as test trials for assessment of classifier performance. This train and test procedure was completed in a fully cross-validated manner such that every trial served as the test stimulus for classification. For each trial in the test set, the classifier returned a probability estimate that indicated the likelihood that the activity pattern corresponded to

either the ‘familiar’ or ‘novel’ class that was used for SVM training purposes. Probability estimates were then binarized in a winner takes all manner; classification was either correct (i.e., when the ‘true’ experimental condition was assigned the highest probability) or incorrect. Averaged across all 10 iterations, classifier accuracy for the perceived familiarity of faces reflects the percentage of test trials that were classified correctly in this binary manner. To obtain inferential statistics, we examined whether average classification performance was above chance (i.e., 0.5). For this purpose, we employed a single sample *t*-test to test against a population mean of chance level.

4.3 Results

As indicated in our initial report (Martin et al., 2013), MVPA based analyses of right PrC activity allowed us to successfully decode the perceived familiarity or novelty of individual faces with a mean classifier accuracy of 57% (Bonferroni corrected $p < .001$), and 14/18 participants showing activity patterns that could be classified with numerical above chance performance.

4.3.1 Direction of Signal Change in PrC Activity Patterns that Allow for Decoding of Recognition Memory Decisions for Faces

Successful decoding of recognition memory decisions, as summarized, above indicates greater within- than between-class similarity in PrC activity patterns for subjectively familiar as compared to novel trials. To characterize precisely how these class differences are reflected in BOLD activity we first examined the extent to which voxels with diagnostic relevance for classification showed the same or a varied response with respect to familiarity in terms of direction. Decoding results from our previous investigation (Martin et al., 2013) were obtained following a commonly used non-directional feature selection procedure that was based on initial voxel-wise measures of experimental effects in a GLM derived test statistic (i.e., *t*-values for contrast between familiar and novel). Specifically, voxels were rank ordered according to the absolute value of their obtained *t*-statistic, and the top 10% of voxels were selected for the purpose of SVM training and classification. In this manner, voxels in which activity decreased with familiarity, as well as others in which activity increased with familiarity could be included in feature

selection. However, it is also possible that all selected voxels responded to familiarity in a similar manner, resulting in successful decoding based on SVM leveraging of a spatially distributed mean difference. To evaluate this possibility we calculated mean beta values for subjectively familiar and novel trials based on activity in voxels that survived feature selection in the majority of classification analysis iterations (i.e., included in at least one cross-validated train-test classification in a minimum of 6 out of 10 trial sampling iterations). Mean beta values, collapsed across participants, are presented in Fig 1. At the group level, no significant difference was observed between beta values that corresponded to ‘familiar’ and ‘novel’ trials ($t_{17} = 0.21, p = .83$). Of the voxels included, only 46% showed a numerical decrease in activation for ‘familiar’ trials, indicating that both response directions were strongly represented in the selected voxel populations. At the single subject level, only 5 of 18 participants had a significant mean difference ($p < .05$) between both types of trials; moreover, only two of these five participants showed a decrease (familiar < novel) in beta values when averaged across the selected PrC voxels. Although these mean differences between classes were clearly limited and not consistent across participants, we also sought to determine whether classification would still be successful after demeaning familiar and novel beta values. Specifically, in this analysis, beta values across all voxels that survived feature selection were z -scored for each trial and participant separately; this ensures that mean differences are exactly zero. Critically, we found that classifier performance remained above chance in this scenario ($M = 56\%$, $t_{17} = 5.04, p < .001$). Decoding results obtained with and without z -scored beta values are presented in Fig. 2 for comparison. These results suggest that successful decoding of recognition memory decisions does not rely on the presence of a mean difference. By extension it suggests that feature selection that is blind to direction yields classification about recognition decisions based on patterns of voxels that have heterogeneous response profiles.

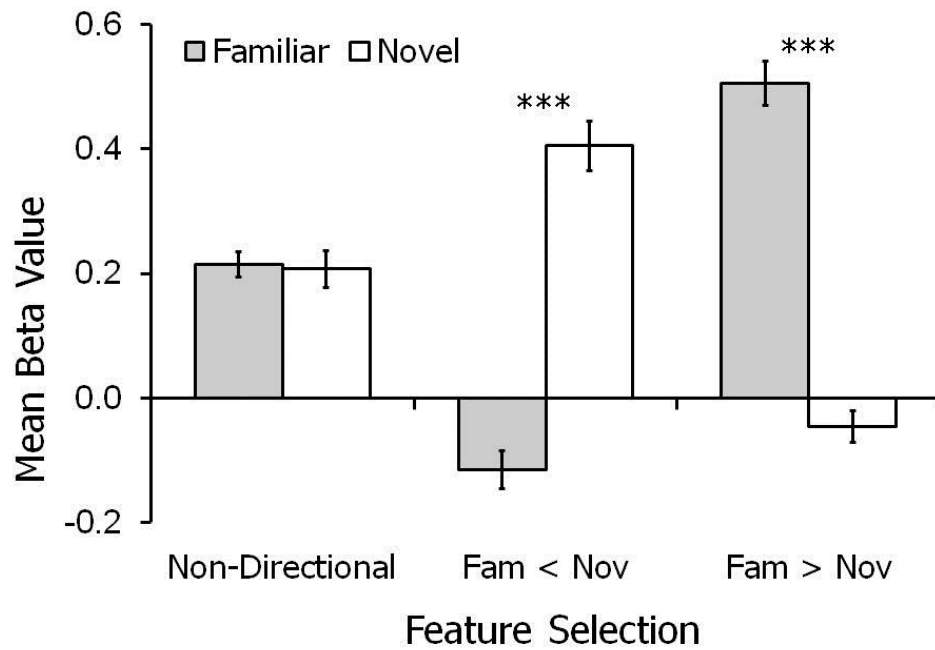


Figure 4.1 Mean Beta values in right PrC for familiar and novel trials. Mean Beta values were calculated across participants based on voxels that were reliably selected for classification following non-directional and both directional feature selection procedures. For this purpose, reliable voxels were those that survived feature selection in at least 6 out of 10 analysis iterations. All error bars indicate the SEM calculated across participants. *** $p < .001$.

4.3.2 Decoding of Recognition Memory Decisions from PrC Activity Patterns when Direction of Signal Change is Constrained

We next sought to determine whether successful classification of recognition decisions necessitates consideration of voxels with heterogeneous response profiles. We addressed this question using MVPA based on a feature selection approach that allowed for inclusion of voxels with a change in signal in only one direction. Towards this end, we ran two separate analyses with feature selection constrained to be based on voxels with decreases or increases in signal, respectively. Voxels were rank ordered according to raw, rather than absolute, t -values and those corresponding to the top or bottom 10% of these rankings were selected for the two separate MVPAs. Thus, in the first set, all voxels showed a decrease in response for familiar as compared to novel trials, while voxels in the second set showed the opposite response profile.

Mean beta values for voxels that survived this directionally constrained feature selection are presented in Figure 4.1 collapsed across participants. Not surprisingly, directionally constrained feature selection resulted in a significant mean differences in beta values across the selected voxels for subjectively familiar versus novel trials (familiar < novel $t_{17} = 11.58, p < .001$; familiar > novel $t_{17} = 14.97, p < .001$); these differences were also consistently present at the single subject level ($n = 18$, all p 's < .001). Noticeably, directionally constrained feature selection still resulted in classifier accuracy that was significantly greater than chance for both types of analyses (see Figure 4.2; familiar < novel $M = 63\%, t_{17} = 11.67, p < .001$; familiar > novel $M = 63\%, t_{17} = 10.32, p < .001$). These results suggest that information pertaining to item recognition decisions can also be successfully decoded from patterns of voxels with a homogeneous response profile and a significant mean difference in response between familiar and novel trials, regardless of whether this difference reflects a decrease or an increase.

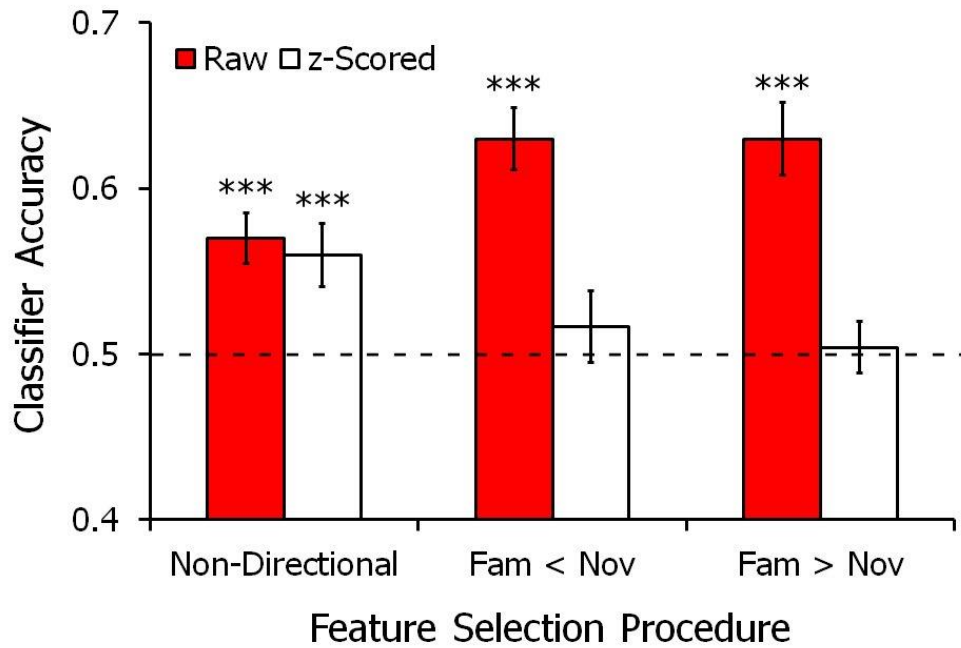


Figure 4.2 Decoding accuracy for perceived familiar versus novel trials from raw and z-scored patterns of activation across feature selection approaches. z-scoring was performed on Beta values across all voxels for each trial and participant separately to ensure that familiar and novel trials were equated at the level of mean activation. Dashed line indicates chance level for classification. All error bars indicate the SEM calculated across participants. *** $p < .001$.

4.3.3 Relationship between Classifier Accuracy for PrC Activity Patterns and Behavioural Recognition Memory Performance

Taken together the results of the analyses presented thus far suggest that recognition decisions can be successfully decoded from distributed activity patterns in PrC when there is no mean difference in response across the voxels comprising the patterns, but also when there is a difference in mean following directionally constrained feature selection. Is it possible to determine which of these different patterns in PrC is most relevant for successful behaviour? Note that all analyses presented involve decoding of recognition decisions without taking their accuracy, on a trial-by-trial basis, into account. This approach was chosen so as to maximize the number of trials available for training of the classifier. To get leverage in answering questions about behavioural performance, however, one can also examine the relationship between classifier performance and behavioural accuracy on a subject-by-subject basis (i.e., by focusing on inter-individual differences). Accordingly, we assessed this relationship for each of the three feature selection procedures previously described. To obtain an estimate of behavioural performance, we calculated familiarity-based discrimination between targets and lures using a measure derived from signal-detection theory (d'). The results of these correlation analyses are plotted in Figure 4.3. Critically, we found a significant positive correlation ($r = .47, p < .05$) between familiarity-based discrimination and classifier performance for voxel patterns in PrC using the unconstrained feature-selection procedure that allowed for the inclusion of voxels with decreases or increases in their response. In other words, those participants in whom decoding of recognition decisions from patterns of PrC activity patterns was more successful tended to perform better in familiarity-based discrimination of faces. By contrast, classifier accuracy and behavioural performance were not significantly correlated when feature selection was constrained to include only voxels with changes in signal in one direction (for voxels showing familiar < novel: $r = .16, p = .27$; for voxels showing familiar > novel: $r = .11, p = .33$). These data suggest that, although successful decoding of recognition-memory decisions from activity patterns in PrC can be obtained in multiple ways, only decoding based on patterns that consist of voxels with increases and decreases in signal shows a relationship to memory performance.

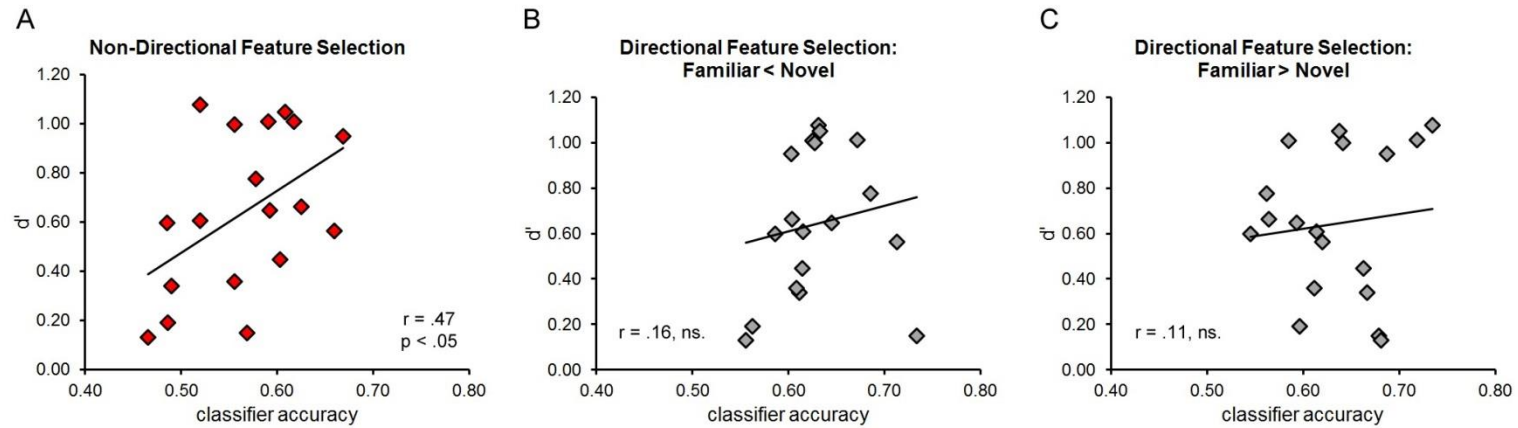


Figure 4.3 Pearson correlations between decoding accuracy and familiarity-based behavioural discrimination (d') across participants. *A*, Correlation obtained following non-directional feature selection. *B*, Correlation obtained following directional feature selection of voxels that showed activity reductions for familiar relative to novel trials. *C*, Correlation obtained following directional feature selection of voxels that showed increased activity for familiar relative to novel trials.

4.3.4 Spatial Distribution of PrC Voxels That Allow for Decoding of Recognition Memory Decisions for Faces

A second goal of the present study was to characterize the relationship between recognition-memory signals for faces in PrC and the ATFP, as defined with an independent functional localizer that employed a passive viewing paradigm. Toward this end, we first assessed the extent to which voxels with diagnostic relevance for the classification of recognition-memory decision for faces in PrC overlapped with the ATFP. For this purpose, we concentrated on the MVPA approach with a feature-selection procedure that allowed for inclusion of voxels with either direction of signal change. Diagnostic voxel distributions are depicted in Figure 4.4 with voxel-wise SVM weights projected onto the cortical surface of each of the 13 participants for whom we could identify the ATFPs with our functional localizer. Of the right PrC voxels that were selected in the majority of iterations for successful classification of recognition decisions, 17.7% (averaged across participants; range = 10.4 – 25.3%) overlapped with the ATFP. In other words, the large majority of voxels that were part of the patterns that allowed for successful decoding of recognition-memory decisions for faces were located outside of the ATFP, even when the latter was defined at the individual subject level. To determine whether the relatively small proportion of voxels within the ATFP are critical for decoding recognition decisions, we also conducted an MVPA excluding PrC voxels that were part of the contiguous clusters that defined the ATFP in these 13 participants. Critically, this analysis still revealed above chance classifier performance ($M = 57\%$, $t_{12} = 2.29$, $p < .05$). Taken together, these results suggest that voxels carrying information pertinent to recognition-memory decisions for faces are spatially distributed in PrC, and clearly extend beyond the ATFP.

Familiarity Voxel Patterns and Anterior Temporal Face Patch

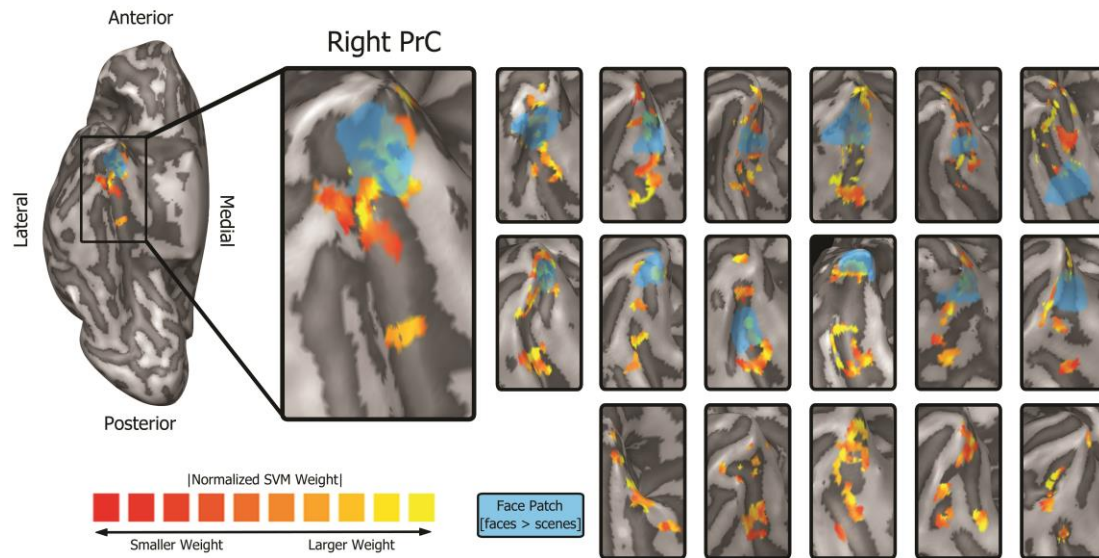


Figure 4.4 Spatial distribution of voxels with diagnostic relevance for decoding of item-recognition decisions in each participant. For illustrative purposes, the data presented for each participant were obtained from one representative, fully cross-validated iteration of the classification analysis. Only those voxels that appear consistently across iterations (i.e., included in at least one cross-validated train-test classification in a minimum 6 out of 10 trial sampling iterations) are depicted. Hot colors denote voxels with diagnostic relevance for classification of face familiarity and correspond to absolute values of normalized SVM weights averaged across cross-validations. SVM voxel weights reflect the relative contribution of each voxel in defining the decision boundary used for classification. Cool color patches correspond to the anterior temporal face patch in those participants for whom one could be identified based on independent functional localizer data [faces > scenes, whole-volume voxel-wise $p < .05$].

4.3.5 Category Specificity of Responses in PrC Voxel Patterns That Allow for Decoding of Recognition Memory Decisions for Faces

Does the limited overlap between voxels with diagnostic relevance for the decoding of recognition memory decisions for faces and the ATFP indicate that these spatially distributed voxels do not have any tuning or response selectivity for face stimuli? MVPA-based research on representations of faces (and other stimulus classes) in more posterior temporal lobe regions in non-mnemonic tasks suggests that even voxels outside of classic category-selective regions can show tuning for specific object categories (e.g., Haxby et al., 2001). Against this background, we assessed whether PrC voxels that form the distributed patterns allowing for classification of recognition decisions for faces, even though largely located outside of the ATFP, might still show a preferential response to face stimuli when probed with an independent functional localizer. Specifically, we examined localizer activity in voxels that were consistently included in feature selection in at least 6 of our 10 classification iterations for decoding of recognition memory decisions, excluding voxels that showed overlap with the ATFP in those participants for whom we were able to identify such clusters. A histogram of mean difference scores (averaged across blocks) for faces as compared to common objects, and faces as compared to scenes, are shown in Figure 4.5. Notably, the distribution is visually skewed towards positive values, hinting at predominant preferential tuning for faces in these voxel populations. Statistically, the mean difference score was indeed different from zero in both comparisons with other stimulus categories (faces > objects, $M = .12$, $t_{17} = 2.31$, $p < .05$; faces > places, $M = .16$, $t_{17} = 3.09$, $p < .01$). These data suggest that, although spatially more widely distributed than the ATFP, the voxels in patterns of PrC activity that allow for decoding of recognition-memory decisions for faces still show a modest tuning preference for faces under passive-viewing conditions in a classic functional-localizer paradigm.

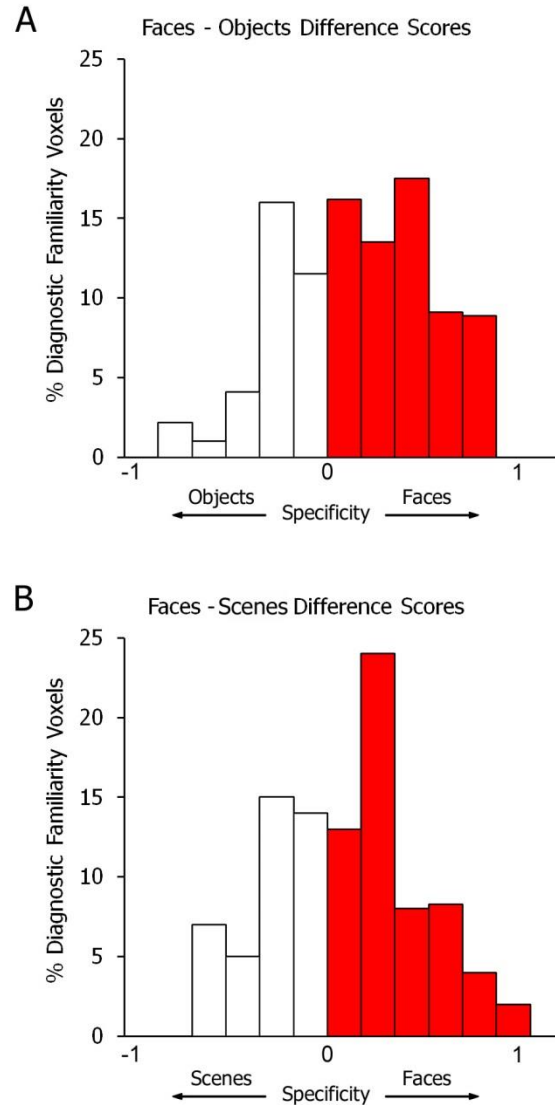


Figure 4.5 Distributions of category preference revealed with functional localizer data in right PrC voxels with diagnostic relevance for decoding of face familiarity. Histograms depict the proportion of voxels that show a preference for either *A*, faces (red bars) or objects (open bars), and *B*, faces (red bars) or scenes (open bars). Difference scores were calculated based on activity from the functional localizer scans in voxels with diagnostic relevance for decoding of recognition decisions for each participant separately. All difference scores were calculated after exclusion of voxels that overlapped with anterior temporal face patches. These values were then collapsed across participants and plotted as a proportion of the total number of voxels.

4.4 Discussion

We used fMRI-based MVPA to characterize the patterns of activity in right PrC that allow for successful decoding of item-based recognition-memory decisions for faces. We observed that, when no constraints for the direction of signal change in relation to familiarity were imposed, patterns that allowed for successful classification did indeed include voxels with decreases as well as voxels with increases in signal. Moreover, classification did not rely on any mean difference in activity across the voxels in the pattern in this situation. While we also found above chance classification when analyses were constrained to include only voxels with signal changes in one direction (and a corresponding mean difference), decoding accuracy across participants was related to behavioural accuracy of recognition decisions only when patterns of voxels with heterogeneous response profiles were considered. A second set of analyses revealed that the patterns of activity in right PrC that allow for decoding of recognition-memory decisions for faces are comprised of voxels that show category specificity in their response when probed with an independent functional localizer. We also found that these voxels are spatially distributed in PrC, and extend beyond the ATRP region that has previously been associated with face processing in univariate analyses.

Extant fMRI evidence obtained with univariate statistical analyses has typically linked the outcome of item-based recognition-memory decisions (i.e., familiar vs new) to mean activity differences in clusters of contiguous PrC voxels with the same direction of signal change. Such effects have often been associated with relative decreases in activity for old as compared to novel stimuli at the time of retrieval (Henson et al., 2003; Daselaar et al., 2006a, 2006b; Montaldi et al., 2006; Danckert et al., 2007; Wang et al., 2014), a finding that has attracted considerable attention due to its parallels in neurophysiological recordings in PrC. However, some fMRI studies have also reported relative increases in activity (e.g., Kafkas and Montaldi, 2012), or both types of effects for different clusters in the same study (Yassa and Stark, 2008). At present, the factors that drive the direction of signal change remain poorly understood (see Yassa and Stark, 2008, for discussion). Further, as discussed previously, the parallels in the direction of signal change across fMRI and neurophysiological recordings are not straightforward in terms of interpretation

(see Henson and Rugg, 2003; Grill-Spector et al., 2006; Logothetis, 2008; Gotts et al., 2012, for discussion). In light of this background, analytical approaches that do not require a priori directional predictions, such as MVPA, offer a clear advantage for probing the role of PrC in memory processing. They may reveal functional properties that would not be observed if the focus of enquiry were restricted to clusters of voxels with a homogenous response profile, or even to patterns of non-contiguous voxels with such a profile. Indeed, while above chance classification of recognition decisions could still be observed in the current study when feature selection was constrained to include PrC voxels with signal changes in one direction, classification accuracy was related to behavioural accuracy of item-based recognition-memory decisions only when patterns of activity included PrC voxels with decreases as well as voxels with increases in response. Put another way, these analyses revealed a relationship of PrC activity to inter-individual differences in memory performance only when predictions were unconstrained in terms of direction for signal change.

That we obtained above chance classification in the absence of significant mean activation differences between subjectively familiar and novel trials suggests that there is a systematic change in activity patterns across PrC voxels that is common across all trials within one class (i.e., familiar trials), which distinguishes it from activity patterns in the other class (i.e., novel trials). To the extent that these within-class similarities and between-class differences are reflected in patterns comprised of voxels with heterogeneous response profiles in terms of direction, these data support the idea that item-based recognition memory signals in PrC are distributed in nature, a suggestion that has recently also been raised in the neurophysiological literature (Thome et al., 2012; Burke et al., 2014). It is worth noting, however, that this interpretation does not automatically allow for the inference that the information content carried by pertinent patterns in PrC is multidimensional (Davis et al., 2014). A multidimensional code is typically defined with respect to multiple psychological, stimulus, or behavioural dimensions that are reflected in neural response patterns. Establishing the presence of such a coding schema requires a targeted experimental design and further probing of the distributed response patterns that allow for decoding of recognition memory decisions.

While the present study was not designed to determine the number of dimensions that are reflected in PrC recognition-memory signals, it does provide a starting point for asking related questions. A promising first step to address this issue is to examine whether distributed item-recognition signals in PrC show specificity for different stimulus categories. The results from the current study suggest that this is indeed the case. PrC voxels comprising patterns that allowed for decoding of recognition decisions for faces responded preferentially to faces as compared to common objects or scenes when probed with an independent functional localizer. Notably, we found that information diagnostic for the classification of familiar versus novel faces is coded in activity patterns that are spatially distributed and extend beyond a region of right PrC that has previously been shown to demonstrate preferential response to faces in univariate analyses, i.e., the ATFP. In fact, our analyses revealed successful decoding from activity patterns in right PrC even after exclusion of voxels comprising the ATFP from feature selection for the classifier.

Previous research has also revealed category specificity in distributed PrC response patterns. For example, Liang et al. (2013) used MVPA in the context of a target detection task and found that distributed patterns of BOLD activity in PrC honoured differences between faces, scenes, words, and sounds, with face representations being significantly different from all other types of stimulus categories examined (see also Diana et al., 2008; Huffman and Stark, 2014). The present study extends this prior research by revealing category specificity in memory signals in PrC at retrieval that are related to participants' recognition memory responses. That memory signals in PrC show such category-specificity in their organization is also supported by findings that we summarized in our initial report on this study (Martin et al., 2013). Specifically, these earlier analyses revealed only limited spatial overlap between patterns of activity in right PrC that allowed for classification of recognition memory decisions for faces and those that allowed for classification of recognition memory decisions for chairs. Moreover, we found that classification was unsuccessful when the linear classifier that had been trained for classification of familiar versus novel faces was used to decode the familiarity of chairs.

Considered together, the results from the current analyses suggest specificity in PrC response patterns for recognition-memory decisions at two levels. First, such patterns have specificity at the level of stimulus category. Second, they have specificity that relates to the perceived memory status of items within a category. While the successful classification of perceived memory status in our study implies that activity patterns in PrC generalize, at least in part, across different exemplars of familiar faces and across different exemplars of novel faces, respectively, this regularity does not imply that the specificity required for exemplar recognition is not retained in PrC response patterns. Indeed, previous fMRI research has successfully employed MVPA to decode the identity of specific exemplars, i.e., facial identities, from activity patterns in PrC and in neighboring anterior temporal regions, when participants were required to identify a small set of repeatedly presented individuals (Nestor et al., 2011; Anzellotti et al., 2013; Anzellotti and Caramazza, 2014; Kriegeskorte et al., 2007). Moreover, fMRI research has also revealed object specific response patterns in PrC for other stimulus categories in non-mnemonic tasks (Clarke and Tyler, 2014). An important goal for future research is to characterize distributed response patterns in PrC for specific exemplars of faces and objects as they change from being perceived as novel to being familiar.

4.5 References

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Chapter 5

5 General Discussion

5.1 Summary of Goals and Findings

George Mandler (1980) first invoked the example of the ‘butcher on the bus’ to illustrate how familiarity and recollection support the recognition of prior occurrence:

Consider seeing a man on a bus whom you are sure that you have seen before; you “know” him in that sense. Such a recognition is usually followed by a search process asking, in effect, where could I know him from? Who is he? The search process generates likely contexts (Do I know him from work; is he a movie star, a TV commentator, the milkman?). Eventually the search may end with the insight, that’s the butcher from the supermarket! (p. 252-3)

However, in addition to capturing the critical distinction between familiarity-based item recognition and the recollection of contextual details, his example also speaks to the stimulus specific nature of familiarity-based recognition. When encountered in an atypical context, it is the butcher who is familiar, not the bus more generally, the scene outside the window, or other passengers; an impression of familiarity typically pertains to a specific item (i.e., person or object), rather than the entire immediate environment more generally. Accordingly, based on this simple observation we may infer that there is indeed a relationship between familiarity-based recognition and stimulus content. Moreover, previous neuropsychological and fMRI research has revealed that visually presented stimuli are represented in the ventral visual stream in a manner that preserves categorical differences between stimuli (see Op de Beeck et al., 2008; Grill-Spector and Weiner, 2014, for review). However, extent studies that have examined the neural correlates of recognition memory have primarily employed words as stimuli (Diana et al., 2007; Kim, 2013) with the objective of determining the extent to which familiarity-based

item recognition can be dissociated from recollection based on recovery of contextual information. Accordingly, there has been little empirical consideration of potential differences between memory signals for items from different stimulus categories. Against this background, the overarching goals of my thesis were to systematically examine and characterize item recognition signals for different stimulus categories. Specifically, the studies presented here sought to identify how and where the information underlying such representations are coded in the MTL and to incorporate these findings into a theoretical framework concerning the representation of objects in visual processing regions more broadly. Towards this end, I have employed MVPA of fMRI data to decode item-based recognition decisions from activity patterns in anatomically defined MTL structures in the context of experimental tasks that use categorized stimuli as memoranda.

In Chapter 2, I presented results from an experiment that sought to evaluate the claim that PrC carries item information in recognition decisions whereas PhC carries representations of context information, as purported by the BIC model of MTL organization. Results from this experiment revealed item recognition signals in both PrC and PhC, despite the absence of retrieval of contextual detail concerning the initial stimulus encounters on the analyzed trials. In right PrC, I found patterns of activity that distinguished familiar from novel faces. In right PhC, by contrast, I observed such patterns for buildings. Familiarity signals for chairs were present in both structures, but shared little overlap on a more fine-grained scale with the patterns observed for faces and buildings. Importantly, these results suggest that PrC and PhC make category-specific contributions to familiarity-based item recognition. By implication, PhC does not only represent episodic context in recognition-memory decisions and the involvement of PrC in representing item familiarity is not ubiquitous.

The rationale and questions addressed in Chapter 3 were directly motivated by results reported in Chapter 2. Here, I conducted a second fMRI study that examined the specific stimulus properties that might determine whether item recognition signals are present in PhC, rather than PrC, with a focus on landmark suitability as indexed by object fixedness. While landmark suitability is likely not the only stimulus property that critically drives differential signals in PhC, it was selected as a starting point in addressing this question

in light of recent fMRI evidence linking both large size and/or fixedness in location to object representations in PhC (Mullally and Maguire, 2011; Konkle and Oliva, 2012; Troiani et al., 2012). The results from this study revealed a dissociation between PrC and PhC with item recognition signals related to non-landmark objects (i.e., planes) coded in PrC and landmarks (i.e., buildings and trees) in PhC. Importantly, patterns of item recognition signals in PhC that pertained to buildings were distinct from those pertaining to trees in the same structure. These results suggest that landmark suitability is a critical stimulus factor that determines whether item recognition signals will be obtained in PrC or PhC. Moreover, they buttress results from Chapter 2 suggesting that item recognition signals within each of these structures have a category-specific organization.

In Chapter 4, I returned to issues concerning recognition-memory for faces, aiming to characterize the manner in which PrC codes familiarity signals and to explore the issue of category-specificity with independent functional localizer data. While previous univariate fMRI research has suggested that item recognition is often associated with activity decreases in PrC for familiar as compared to novel items at the time of retrieval (e.g., Daselaar et al., 2006, Wang et al., 2014), I provide evidence obtained with MVPA indicating that such signals can be distributed across voxels with directionally heterogeneous response profiles; in other words, some voxels showed activity decrements with familiarity while others showed increments. Importantly, decoding accuracy obtained from these distributed patterns with a linear classifier was correlated with behavioural recognition accuracy across participants. Lastly, these data also revealed that the voxels comprising patterns in which item recognition are coded respond preferentially to faces when compared to either man-made objects or scenes under passive viewing conditions.

5.2 Implications for Current Theories of MTL Contributions to Recognition Memory

The results presented in the current thesis support a number of tenets central to each of the models reviewed in Chapter 1. However, they also raise important theoretical questions related to how well each can accommodate category-specific item recognition effects in PrC and PhC. Ultimately, the extent to which predictions derived from each

model are consistent with the results I have reported varies across models and specific aspects of the data. Here, I will place my results into the context of each of these models, noting support and challenges associated with each. Importantly, as the studies that I have reported in my thesis focused specifically on item recognition, my results do not speak to predictions concerning the recollection of contextual detail made by any of the models reviewed.

As previously noted, dual-process models purport that MTL contributions to recognition memory are fractionated in a process-based manner; PrC is thought to support familiarity-based recognition whereas recollection is associated with hippocampal processing (Aggleton and Brown, 1999). Evidence from Chapters 2 and 3 linking activity patterns that carry information about the familiarity of faces, chairs, and planes to PrC is consistent with this proposal. However, the observation of familiarity signals for buildings, chairs, and trees in PhC argues against the notion that PrC is the only MTL region that codes for familiarity-based item recognition. Moreover, the category-specific effects reported in Chapters 2, 3, and 4 cast doubts on the notion that process-based differences fully capture functional specialization in the MTL.

Recall that the BIC model and CRAFT are both guided by neuroanatomical research that has revealed differential connectivity between MTL structures and the ventral and dorsal visual processing pathways (Eichenbaum et al., 2007; Diana et al., 2007; Montaldi and Mayes, 2010; Ranganath et al., 2010). Specifically, it is assumed that differential connectivity in the MTL confers privileged access to representations pertaining to items and contexts in PrC and PhC, respectively. The BIC model suggests that item representations in PrC and context representations in PhC can both support familiarity-based recognition as well as the associative processing related to recollection. CRAFT diverges at this level as it suggests PrC and PhC are limited to supporting item and context familiarity, respectively. Evidence presented in Chapters 2, 3, and 4 indicating that PrC carries information about the familiarity of faces, chairs, and planes is consistent with predictions from both the BIC model and CRAFT. However, demonstrating that item recognition signals for landmarks, including buildings, trees, and possibly chairs, are carried by PhC, even under conditions in which items are presented in isolation without

any background, is largely inconsistent with both models. Moreover, in their adherence to a distinction that makes reference to items versus contexts, neither model can readily account for the category-specific effects obtained both across and within PrC and PhC in Chapters 2 and 3. At the very least, this pattern of results suggests that a distinction between items and contexts does not fully characterize differences in functional specialization between PrC and PhC.

Lastly, on the representational account recognition memory and perceptual discriminations are considered to be supported by common representations in the MTL that are engaged in a task dependent manner (Murray and Bussey, 1999; Bussey and Saksida, 2007; Graham et al., 2010). Given the importance of this link between memory and perception, proponents of this account maintain that stimulus category, rather than process-based differences or the distinction between items and contexts, determine the relative contributions of different MTL structures to discriminations between complex stimuli with high feature overlap. Specifically, it has been proposed that PrC supports object representations that can support familiarity-based recognition as well as recollection. By contrast, the HC is thought to support representations for scene stimuli in such processes. Ultimately, my results do not address predictions regarding scenes as the stimuli employed in the recognition-memory experiments were limited to objects presented in isolation, as depicted in Figures 2.1 and 3.1. The representational account's emphasis on stimulus representations is generally consistent with my results suggesting that item recognition signals are represented in a category specific manner. Notably, in Chapters 2, 3, and 4 I demonstrate that item recognition signals related to objects that show preferential responses in PrC (i.e., faces) and PhC (i.e., buildings) in non-mnemonic task contexts are also coded in these structures. However, the category-specific effects that I obtained across different object categories in PrC and PhC suggest that the representational account is underspecified.

To conclude, although each of the models reviewed predict different aspects of the findings that comprise my thesis, no single theoretical position can fully account for the entire pattern of results. Accordingly, a novel model that synthesizes and incorporates features of the BIC model, CRAFT, the representational account, and current proposals

regarding the organizational structure of information coding in the ventral visual stream more broadly may provide a more comprehensive account of the current results and findings in the literature at large.

5.3 Hierarchical Model of MTL Contributions to Recognition Memory

A comprehensive model of MTL contributions to recognition memory that can account for extant neuropsychological and fMRI evidence and accommodate the results presented in the current thesis is currently lacking. Given the seeming importance of categorical information in the ventral visual stream together with its high degree of connectivity with the MTL, a framework for the development of such a model should be consistent with the organizational structure of representations pertaining to visually presented stimuli in the ventral temporal cortex. Results from a number of studies suggest that VTC codes categorical information in distributed and overlapping representations (e.g., Haxby et al., 2001; Kriegeskorte et al., 2008). Importantly, similar conclusions can be drawn from findings revealed using MVPA to decode categorical information from PrC and PhC (e.g., Diana et al., 2008; Liang et al., 2013; Huffman and Stark, 2014). The ability to decode category membership from such representations is predicated on greater similarity in distributed responses for stimuli from the same category than for distributed responses from a different category (i.e., representations generalize across stimuli from the same category). The work that I have presented here extends this general framework by revealing that patterns of activity in PrC and PhC that differentiate familiar from novel recognition responses generalize across stimuli from the same category, but not to other categories (i.e., inability to cross-classify in Chapters 2 and 3). For example, at one level, distributed PrC responses corresponding to faces are more similar to one another than they are to those corresponding to stimuli from different categories (e.g., chairs). At another level, the distributed responses corresponding to familiar faces are also more comparable to one another than they are to those corresponding to faces judged to be novel (see Grill-Spector and Weiner, 2014, for related proposals regarding VTC).

Against this background, I am proposing a hierarchical model of MTL functioning which suggests that category-specific information in PrC and PhC is reflected in highly

integrated object representations that can be brought to bear on both mnemonic and perceptual discriminations in a task dependent manner. On this account, information pertaining to the prior occurrence of an object is nested within these distributed category-specific representations in both PrC and PhC. In this regard, the proposed model can accommodate the category-specific item recognition effects obtained in PrC and PhC in Chapters 2, 3, and 4 of this thesis. Moreover, depending on task demands, these item representations can support either familiarity-based item recognition or associative recollection of item-based contextual detail. Lastly, one of the central tenets of the proposed model is that, familiarity-based item recognition effects differ between PrC and PhC in a manner that is related to specific stimulus properties. The findings presented in Chapter 4 suggest that the extent to which objects are fixed in location constitutes one pertinent dimension (see section 5.4 for further elaboration), though others may be identified through future research. With respect to the HC, this account adopts the functional role specified by the BIC model. Namely, the HC serves to bind item and context information into discrete episodic representations.

Within the framework outlined, it is perhaps not immediately clear how findings implicating PhC in item recognition can be reconciled with the well-established literature indicating that this structure supports contextual representations that are not easily conceptualized as objects or items. For example, it has been proposed that PhC can represent spatial, cognitive, emotional, and semantic context (Bar and Aminoff, 2003; Diana et al., 2007; Ranganath, 2010; Aminoff et al., 2013). Importantly, evidence from two recent lines of research indicates that PhC may in fact represent objects and contexts in functionally distinct manners. Specifically, Bastin et al. (2013) have revealed important latency differences related to the processing of object and scene stimuli in aspects of PhC (additional details provided in section 5.4). Further, functional connectivity analyses have revealed that PhC is broadly connected to two non-overlapping visual networks. The first includes retrosplenial cortex and regions of the dorsal visual stream and the second includes object processing regions situated in the ventral visual stream, such as lateral occipital complex (Baldassano et al., 2013). Critically, these findings can bridge the apparent gap between representations related to items and those pertaining to more abstract contextual information.

5.4 Role of Top-Down Semantic Abstraction

Results from previous fMRI research suggest that representations of visually presented stimuli are organized at a large-scale in a medial to lateral manner in VTC (see Grill-Spector and Weiner, 2014, for review). This medial to lateral division has been mapped onto distinctions pertaining to the real-world size of objects (large versus small; Konkle and Oliva, 2012), eccentricity biases (peripheral versus foveal; Hasson et al., 2002), and object animacy (inanimate and animate; Haxby et al., 2011). While such studies typically do not include functional maps extending as far anterior as PrC, they do include PhC. For the purpose of the current discussion, studies that have linked PhC to differential representation of objects with large real-world size or objects that tend to be processed in peripheral vision (e.g., buildings) are of particular interest. Although PhC ostensibly represents information pertaining to large objects, the results I present in Chapter 3 suggest that the mere presence of such size does not necessarily translate to corresponding item recognition signals being coded in this region. Specifically, I revealed familiarity signals in PhC for buildings and trees, but not planes, despite the fact that stimuli comprising these categories were matched with respect to perceived real-world size. I interpret this pattern of results as evidence suggesting that, although PhC may process visually presented objects with large real-world size, such representations are only brought to bear on familiarity-based item recognition decisions when the objects are also suitable landmarks with potential navigational relevance. This interpretation is in line with fMRI research that has revealed differential responses in PhC to objects that are large and fixed in location even in the absence of mnemonic demands (Mullally et al., 2011; Troiani et al., 2012).

Importantly, the critical difference between large objects that are either fixed in location or not may not necessarily be gleaned from information related to object form as reflected in perceptual details. For example, there are no inherent perceptual properties in a static image of a plane that indicate such objects are not necessarily fixed in location. Rather, the relative mobility of an object, a stimulus property related to landmark suitability, may correspond to abstract semantic or conceptual knowledge regarding its function.

Interestingly, top-down processing has recently been proposed to account for differential

object responses in aspects of PhC. Bastin et al. (2013) examined local field potentials obtained with intracranial EEG recordings in neurosurgical patients with intractable temporal lobe epilepsy. Specifically, the authors examined the time course of responses associated with scene, building, and non-building object stimuli. Their results revealed that aspects of PhC differentiate between scene and non-scene objects as early as ~80 ms after stimulus onset, whereas differential responses to buildings and non-building objects did not emerge until ~170 ms after stimulus onset. This pattern of results was interpreted as evidence suggesting that there are two information processing stages in PhC. The first is an early stage that distinguishes scenes from non-scenes on the basis of bottom-up perceptual information of geometric elements that are unique to scenes, such as spatial layout or visual summary statistics. The second stage occurs at longer latencies and serves to distinguish navigationally relevant objects from other objects that are not suitable landmarks on the basis of top-down semantic processing.

Although speculative, it may be this latter top-down feedback stage that determines the extent to which familiarity-based item recognition signals are obtained in PhC versus PrC. Given that PrC receives inputs from PhC, object representations initially processed in more medial aspects of VTC based on their large real-world size or a peripheral eccentricity bias may subsequently be fed forward to PrC for mnemonic processing after top-down semantic processes deem large objects, such as planes, to have limited navigational relevance. That I obtained item recognition signals for planes in PrC is consistent with this notion. Interestingly, evidence of familiarity signals for chairs in both PrC and PhC suggests that the object properties that determine whether item recognition signals are coded in PrC or PhC may be continuous rather than dichotomous dimensions. Accordingly, the familiarity of some objects may be coded in both structures when they satisfy both inclusion and exclusion criteria for consideration as landmarks.

5.5 Characterizing the Distributed Nature of Item Recognition Signals in PrC

Results reported in Chapter 4 suggest that familiarity-based item recognition signals related to faces are coded in a distributed manner in right PrC. Specifically, obtaining above chance classification in the absence of significant mean activation differences

between familiar and novel trials indicates that there is a systematic profile of activation across voxels that is common within, but not between, recognition decisions. Moreover, these within-class similarities and between-class differences were carried by patterns of directionally heterogeneous activity, further pointing to a distributed signal. At another level, examination of the relationship between the ATFP (i.e., a face selective patch in PrC) and the patterns of activation that allowed for classification of item recognition decisions for faces revealed that these signals are spatially distributed within PrC.

Demonstrating that item recognition decisions could be decoded from directionally heterogeneous activity patterns in the absence of mean activity differences cannot be interpreted as evidence to suggest that the informational content underlying such signals is multidimensional (Davis et al., 2014). A multidimensional code refers to information that is distributed across voxels that carry different types of information related to multiple psychological states; informational content not present in any single voxel can emerge as a latent dimension when responses across multiple voxels are considered at a pattern level. By contrast, when activity within all voxels tracks a single psychological state, though to varying degrees, information is coded as a single dimension. Davis et al. (2014) have convincingly demonstrated that MVPA is indeed sensitive to informational content reflected in either a multidimensional or unidimensional code. Notably, the directionally heterogeneous item-recognition signals revealed using MVPA in Chapter 4 can potentially be interpreted as reflecting varying degrees of responses along a single dimension of familiarity. Alternatively, this pattern may reflect a multidimensional code with response increases and decreases reflecting non-identical information (i.e., different cognitive processes or stimulus properties) represented across voxels. Indeed, it has been suggested that familiarity signals may be multiply determined with interactions between episodic, semantic, and perceptual memory systems contributing to recognition decisions (Henson and Gagnepain, 2010). For example, familiarity-based recognition judgments have been linked to implicit memory signals such as conceptual fluency purportedly generated by a semantic memory system that has been suggested to interact with episodic memory signals (Voss and Paller, 2009; Voss and Federmeier, 2011). If familiarity signals are related to multiple, interactive mnemonic sources they may ultimately be

coded in a multidimensional manner. However, further research is required to systematically adjudicate between these possibilities.

While I favour an interpretation of directionally heterogeneous item recognition signals in PrC that makes reference to distributed coding, there is at least one alternative interpretation of this finding that warrants further consideration. Given that the majority of extant fMRI and neurophysiological evidence suggests that it is a reduction in neural responses that denotes recognition of prior occurrence, it is plausible that the incremental responses in the directionally heterogeneous patterns of activation may reflect correlated, but functionally unrelated processing. Specifically, PrC likely represents and transforms information that is entirely unrelated to item recognition. As one example, results from recent fMRI research points to a role of PrC in the coding of semantic information related to visually presented objects (e.g., Bruffaerts et al., 2013; Clarke and Tyler, 2014). This type of processing need not carry information related to specific prior stimulus encounters. Moreover, it may be reflected in increased BOLD responses that in some way correlate with the signal of interest (i.e., item recognition). If this is indeed the case, then it is possible that, through the process of selecting features for the purpose of classification based on responses that discriminate between item recognition decisions, these correlated signals could masquerade as item recognition signals. While, demonstrating that the accuracy of decoding item recognition decisions from directionally heterogeneous patterns of activation is correlated with behavioural recognition performance argues against this alternative interpretation, the analyses and results that I have presented cannot unequivocally rule it out.

5.6 Future Research Directions

Results obtained from the research presented in Chapter 3 indicate that relative mobility is an object property that critically determines whether familiarity-based item recognition signals are coded in PrC or PhC. As noted, this finding is in line with previous proposals suggesting that PhC represents scenes as well as landmark objects with potential navigational relevance. However, relative mobility may be only one stimulus property that has implications for the dissociation between PrC and PhC. It is also possible that the apparent importance of relative mobility may be a reflection of the specific stimulus

categories selected as memoranda. Additional research is required to systematically evaluate the possibility that other stimulus dimensions may play equally important roles in this regard. As a starting point, future research should assess distinctions that have been linked to the medial to lateral large scale organization of information coded in ventral temporal cortex. For example, living objects tend to evoke differential responses in medial aspects of VTC, including PhC, as compared to non-living objects, which are processed in more lateral regions.

A second matter that requires further research concerns the identification of the experimental conditions under which distributed item recognition signals emerge in PrC. While previous univariate analyses of fMRI data have primarily linked familiarity-based item recognition to mean activity differences obtained in clustered PrC voxels, comparable analyses conducted using a group level GLM with the data reported in Chapter 4 failed to reveal any such effects. Rather, results obtained using MVPA indicate that item-recognition signals can also be reflected in distributed activation patterns. It should be noted that I do not wish to refute results obtained in previous fMRI studies that have employed univariate statistical analyses to reveal familiarity signals coded in blobs with mean activity differences. Indeed, numerous studies have found such effects (e.g., Ranganath et al., 2004; Gonsalves et al., 2005; Daselaar et al., 2006; Montaldi et al., 2006; Wang et al., 2014). Rather, I emphasize that under some circumstances item recognition signals can be reflected in activity patterns that differ from those coded in contiguous voxels with homogeneous response profiles. Nevertheless, this discrepancy raises important questions concerning the experimental conditions and/or manipulations that evoke these different signals.

One speculative explanation that can account for these apparent coding schemes makes reference to potential differences related to perceptual and semantic processing. The stimuli used in the experiment from Chapter 4 were categorized (i.e., faces) and differed primarily at the level of subtle perceptual details that may be difficult to verbalize or elaborate upon at either the time of encoding or retrieval. By contrast, the large majority of studies that have linked mean activity differences in PrC to item recognition have employed words as stimuli (see Diana et al., 2007, for review; cf Montaldi and Mayes,

2006). Importantly, item information represented in PrC may be coded in a fundamentally different manner when stimuli are processed at a perceptual level as compared to those that include a much richer semantic analysis. Notably, recent fMRI research has indicated that PrC may indeed play an important role in conceptual processing, in addition to its well documented role in perceptual processing (Bruffaerts et al., 2013; Clarke and Tyler, 2014). Whether item-recognition signals are reflected in directionally heterogeneous, distributed patterns of activation may be related to the extent to which successful task performance is predicated upon perceptual, rather than semantic, processing. Ultimately, further research is required to systematically evaluate this possibility.

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Appendices

Appendix A: Documentation of ethics approval



Research Ethics

Use of Human Participants - Initial Ethics Approval Notice

Principal Investigator: Prof. Stefan Kohler
 File Number: 104545
 Review Level: Delegated
 Protocol Title: Familiarity-Based Object Recognition
 Department & Institution: Social Science Psychology, Western University
 Sponsor: Canadian Institutes of Health Research

Ethics Approval Date: October 31, 2013 Expiry Date: April 30, 2014

Documents Reviewed & Approved & Documents Received for Information:

Document Name	Comments	Version Date
Western University Protocol		2013/10/16
Recruitment Items	Revised SONA Sign-up Description (Received Oct.25/13)	
Other	Debriefing Sheet (Received Oct.31/13)	
Letter of Information & Consent	Revised LOI and Consent	2013/10/25

This is to notify you that The University of Western Ontario Research Ethics Board for Non-Medical Research Involving Human Subjects (NMREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the applicable laws and regulations of Ontario has granted approval to the above named research study on the approval date noted above.

This approval shall remain valid until the expiry date noted above assuming timely and acceptable responses to the NMREB's periodic requests for surveillance and monitoring information.

Members of the NMREB who are named as investigators in research studies, or declare a conflict of interest, do not participate in discussions related to, nor vote on, such studies when they are presented to the NMREB.

The Chair of the NMREB is Dr. Riley Hinson. The NMREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000941.

[Redacted Signature]

Signature

Ethics Officer to Contact for Further Information

Grace Kelly	Wikki Tran	Erika Basile
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Curriculum Vitae

EDUCATION

- 2009 – Current Ph.D. Candidate (Behavioural and Cognitive Neuroscience)
Western University, Canada
Advisor: Dr. Stefan Köhler
Title: Category-specific item recognition and the medial temporal lobe
- 2007 – 2009 M.Sc. (Behavioural and Cognitive Neuroscience)
Western University, Canada
Advisor: Dr. Stefan Köhler
Title: Déjà vu and recognition memory in temporal lobe epilepsy
- 2002 – 2006 Honours B.A. Psychology
University of Windsor, Canada
Graduated with Great Distinction
Advisor: Dr. Lori Buchanan
Title: Lateralized orthographic and phonological language processing

PEER-REVIEWED PUBLICATIONS

Martin, C.B., Fiacconi, C.M., & Köhler, S. (in press). *Déjà vu: A window into understanding the cognitive neuroscience of familiarity*. In Duarte, A., Barense, M., & Addis, D.R. (Eds.), *Handbook on the Cognitive Neuroscience of Memory*. Wiley-Blackwell.

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SUBMITTED MANUSCRIPTS

Martin, C.B., Cowell, R.A., Gribble, P.L., Wright, J., & Köhler, S. Distributed category-specific recognition memory signals in perirhinal cortex.

Bowles, B., Duke, D.S., **Martin, C.B.**, Rosenbaum, S.R., McRae, K., & Köhler, S. Human perirhinal cortex supports frequency judgments as well as judgments of cumulative lifetime familiarity.

MANUSCRIPTS IN PREPARATION

Martin, C.B., & **Köhler, S.** Parahippocampal and perirhinal cortex differentially support item recognition memory for objects with and without navigational relevance.

SELECT CONFERENCE ABSTRACTS

Martin, C.B., Köhler, S. (2015). Category-specific patterns of recognition memory signals in perirhinal and parahippocampal cortex. Cognitive Neuroscience Society, San Francisco, CA, USA.

Martin, C.B., Cowell, R.A., Gribble, P.L., Köhler, S. (2014). Are Familiarity-Based Memory Representations in Human Perirhinal Cortex Distributed? Society for Neuroscience, Washington, D.C., USA.

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