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Functional specialisation of the medial temporal lobe and hippocampus: the representational approach

Jeremy Gardette

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THÈSE

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Spécialisation fonctionnelle du lobe temporal interne et de l'hippocampe : approche représentationnelle

Functional specialisation of the medial temporal lobe and hippocampus: the representational approach

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A mes grand-parents,

JT, AT, SG, et JMG

Abstract

The medial temporal lobe (MTL) is a set of interconnected structures located on the medial face of the temporal lobe, which include the hippocampus and perirhinal cortex. Numerous results have challenged the view that these regions constitute a module exclusively dedicated to declarative memory. A different type of models thus emerged, built around the notion of *representation*. Further, an approach termed representational-hierarchical (RH) proposes to decompose cognitive processes into representations and operations. In this view, the representation is the key factor determining the engagement of a given MTL region in a cognitive process, independently of the operation. The present thesis aimed to assess the predictions of the RH model, and to investigate how its principles of functional organisation interact with (1) the long-axis of the hippocampus, and (2) hemispheric lateralisation.

We first investigated, in two behavioural studies (N=66 and N=76), how the process of *recollection* can be broken down into a representation and an operation, using a partial-cue image reconstruction paradigm. Our results showed that it is possible to isolate pattern-completion of scenes and objects, but that additional cognitive mechanisms can be confounded depending on task instructions. In a subsequent fMRI study (N=51), we replicated the previously-reported result that the hippocampus is specifically engaged in pattern-completion of scenes; whereas the perirhinal cortex was more recruited by object processing. We also extended it to additional operations (i.e., visual-discrimination and familiarity-based memory), thereby supporting the RH view of the MTL: the preferential engagement of the hippocampus and perirhinal cortex in scene and single object representations, respectively, is independent of the operation. In addition, our results revealed that the specialisation of the hippocampus was not equivalent in its posterior and anterior segments, which rather supports a specialisation of the hippocampus long-axis depending on the *resolution* of the representation processed. This constitutes an extension of the RH principles within the hippocampus. Finally, we assessed the hemispheric lateralisation of representational specialisation as operationalised through perceptual manipulations. To this end, we tested patients who underwent left or right MTL surgery for drug-resistant epilepsy in a visual-discrimination task. Perceptual-complexity dependant impairments were found in case of right, but not left, MTL damage. Taken together, our findings are in favour of the RH view of the MTL; they also highlight the diversity of features that characterise a given representation, thereby opening new questions for future research.

Keywords: Medial temporal lobe, memory, representations, fMRI, visual perception

Résumé

Le lobe temporal médian (MTL) est un ensemble de structures interconnectées situé sur la face médiale du lobe temporal, dont font partie l'hippocampe et le cortex perirhinal. De nombreux résultats ont remis en cause la vision proposant que ces régions constituent un module exclusivement dédié à la mémoire déclarative. Des modèles différents ont ainsi émergé, construits autour de la notion de *représentation*. De plus, une approche nommée représentationnelle-hiérarchique (RH) propose de décomposer les processus cognitifs en représentations et opérations. D'après ce modèle, la représentation est le facteur déterminant l'engagement d'une structure donnée du MTL dans un processus cognitif, indépendamment de l'opération. Le but de cette thèse était de tester les prédictions du modèle RH ; et d'explorer comment ses principes d'organisation fonctionnelle interagissent avec (1) l'axe long de l'hippocampe, et (2) la latéralisation hémisphérique.

Nous avons d'abord exploré, dans deux études comportementales (N=66 et N=76), la façon dont le processus de *remémoration* peut être décomposé en une représentation et une opération au moyen d'un paradigme de reconstruction d'images à partir d'indices partiels. Nos résultats ont montré qu'il est possible d'isoler le pattern-completion de scènes et d'objets, mais que d'autres mécanismes cognitifs peuvent être confondus selon les instructions utilisées. Dans une étude en IRMf (N=51), nous avons ensuite répliqué le résultat montrant que l'hippocampe est spécifiquement engagé dans le pattern-completion de scènes, tandis que le cortex perirhinal était plus recruté par le traitement des objets. Nous avons également généralisé ce résultat à d'autres opérations (i.e., discrimination visuelle et familiarité), soutenant ainsi l'approche RH du MTL : l'engagement préférentiel de l'hippocampe et du cortex perirhinal pour les représentations de scènes et d'objets décontextualisés, respectivement, est indépendant de l'opération. De plus, nos résultats ont révélé que la spécialisation de l'hippocampe n'était pas équivalente entre ses segments postérieur et antérieur, ce qui soutient plutôt une spécialisation de l'axe long de l'hippocampe selon la *résolution* de la représentation traitée. Cela constitue une extension des principes du modèle RH au sein de l'hippocampe. Nous avons enfin cherché à déterminer si la spécialisation représentationnelle opérationnalisée via la manipulation de facteurs perceptifs présente une latéralisation hémisphérique. Pour cela, nous avons testé dans une tâche de discrimination visuelle des patients ayant bénéficié d'une chirurgie du MTL gauche ou droit dans le cadre d'une épilepsie pharmaco-résistante. Nous avons observé des déficits dépendant de la complexité perceptive du matériel en cas de lésion du MTL droit mais pas du MTL gauche. Dans l'ensemble, nos résultats sont en faveur de l'approche RH du MTL ; ils soulignent également la diversité des éléments qui caractérisent une représentation donnée, ouvrant ainsi des pistes pour de futures recherches.

Mots clefs : Lobe temporal médian, mémoire, représentations, IRMf, perception visuelle

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Contents

| | |
|--|-----------|
| Abstract | 2 |
| Résumé | 4 |
| Acknowledgements | 5 |
| Foreword | 10 |
| Preamble | 12 |
| 1. What is the medial temporal lobe?..... | 12 |
| 2. What is the amnesic syndrome? | 14 |
| Chapter I – The multiple-memory systems: A neuropsychological approach to medial temporal functions | 15 |
| 1. Working/short-term memory versus long-term memory | 15 |
| Evidence in favour of a dissociation..... | 15 |
| Is working memory always preserved in amnesia? | 16 |
| 1. Non-declarative versus declarative memory | 17 |
| Evidence for a dissociation..... | 17 |
| Are all kinds of priming preserved in amnesia? | 19 |
| 2. Semantic versus episodic memory..... | 20 |
| Can episodic and semantic memory be dissociated in memory-impaired patients?..... | 20 |
| The modular view of memory systems | 23 |
| An alternative view: The unitary vision of declarative memory | 23 |
| 3. Recognition versus recall memory | 25 |
| Evidence for a dissociation..... | 25 |
| Can the Multiple-memory systems view account for recognition and recall memory? . | 26 |
| Synthesis..... | 27 |
| Chapter II – The MTL beyond systems: Process-based and content-based models on MTL functions | 28 |
| 1. Measuring recollection and familiarity in recognition memory | 28 |
| Recognition memory | 28 |
| Subjective experience and the remember/know paradigm | 29 |
| Objective measure of recollection via source memory | 29 |
| Confidence ratings and the ROC paradigm | 30 |
| 2. The dual-process view of MTL regions and recognition | 31 |
| Neuropsychological evidence for a dual-process model | 31 |
| The dual-process model of the MTL and recognition memory | 31 |
| 3. Recognition: between memory processes and memory content..... | 33 |

| | |
|--|-----------|
| Inconsistent results from recognition memory | 33 |
| The domain-dissociation and the emergence of content-based models | 34 |
| 4. Towards content-based models of the MTL | 35 |
| Main framework of the content-based models | 35 |
| The binding item and context model | 36 |
| Stepping away from the modular view of the MTL | 37 |
| Synthesis..... | 37 |
| Chapter III - The MTL beyond memory: the high-resolution binding and scene construction theories..... | 38 |
| 1. From associative memory to high-resolution binding | 38 |
| Principles of the High-resolution binding model | 38 |
| Experimental evidence in favour of the HRB | 39 |
| The HRB predictions beyond the memory domain..... | 40 |
| Beyond the HRB model | 40 |
| 2. From space representation to scene construction | 41 |
| The MTL and space representation..... | 41 |
| The Scene Construction Theory | 42 |
| Evidence in favour of the SCT..... | 43 |
| The Boundary Extension effect | 44 |
| The HRB and SCT: opposed but complementary? | 45 |
| Synthesis..... | 46 |
| Chapter IV – The representational-hierarchical view: An integrative model? | 47 |
| 1. The representational-hierarchical approach | 47 |
| The perceptual-mnemonic feature conjunction model..... | 47 |
| From non-human primates to humans | 48 |
| The representational-hierarchical model | 49 |
| 2. Representations, operations, and dimensionality | 50 |
| Breaking down cognitive processes | 50 |
| Representational dimensionality | 51 |
| Predictions of the RH view | 52 |
| 3. The patch protocol to investigate pattern-completion-like memory while manipulating representational dimensionality | 53 |
| Isolating pattern-completion from representational dimensionality? | 53 |
| The patch-cue protocol as a solution | 54 |
| Methodological questions raised by the patch-cue protocol | 55 |
| Theoretical questions raised by the patch-cue protocol | 55 |

| | |
|--|-----------|
| Synthesis..... | 55 |
| Chapter V: The anterior-posterior axis of the hippocampus and hemispheric specialisation | 57 |
| 1. The RH model and the anterior-posterior axis of the hippocampus | 57 |
| Dividing the hippocampus into long-axis segments | 57 |
| The hippocampus long-axis specialisation: reunifying the SCT and HRB models? | 58 |
| The broad-to-sharp model of the hippocampus as an extension of the RH view | 59 |
| Locating recollection in the long-axis of the hippocampus | 60 |
| 2. The RH model and hemispheric specialisation | 60 |
| Material-dependant memory impairments in case of unilateral MTL damage | 61 |
| Extending the lateralisation to the RH specialisation of the MTL..... | 61 |
| Synthesis..... | 62 |
| Thesis objectives..... | 63 |
| Materials: General | 66 |
| 1. Classes of stimuli | 66 |
| 2. Manipulations in the Matching task | 67 |
| 3. Recognition task and visual patches | 69 |
| Chapter VI – Characterising the patch-cue protocol: what is reconstruction? | 71 |
| 1. Study 1: Reconstruction versus recollection: Remember/know investigation of the patch-cue paradigm | 73 |
| Introduction..... | 73 |
| Methods | 74 |
| Results | 77 |
| Discussion | 79 |
| 2. Study 2: Comparable contribution of memory representations to scenes and objects reconstruction? | 80 |
| Introduction..... | 80 |
| Methods | 81 |
| Results | 84 |
| Discussion | 86 |
| Synthesis..... | 87 |
| Chapter VII: Hippocampal and perirhinal engagement in memory and visual perception: the role of representational content (Study 3)..... | 88 |
| Introduction..... | 90 |
| Methods | 92 |
| Results | 100 |

| | |
|--|------------|
| Summary of the main results | 108 |
| Discussion | 108 |
| Synthesis..... | 113 |
| Chapter VIII – Representational specialisation and hemispheric lateralisation | 114 |
| 1. Lateralisation of fMRI activations from Study 3..... | 116 |
| Regions of interest (ROIs) and analyses | 116 |
| Results | 116 |
| Discussion..... | 121 |
| 2. Visual discrimination in case of unilateral MTL damage: Study 4..... | 123 |
| Introduction..... | 123 |
| Methods | 124 |
| Results | 128 |
| Discussion..... | 130 |
| Synthesis..... | 132 |
| Chapter IX – General discussion | 133 |
| 1. Summary of thesis objectives and main results..... | 134 |
| 2. Recollection, reconstruction, and the patch-cue paradigm | 134 |
| Dissociating the operation from the representation | 134 |
| Where is recollection in the hippocampus? | 135 |
| 3. The MTL processes representations across operations..... | 137 |
| Representational specialisation of the hippocampus and PRC across operations..... | 137 |
| Where is familiarity in the MTL? | 139 |
| 4. Future perspectives: different kinds of dimensionality along two brain axes? | 140 |
| Broad and sharp scene representations in the hippocampus long-axis..... | 140 |
| Different kinds of high-dimensional representations | 142 |
| 5. Conclusion | 144 |
| Appendices | 146 |
| Appendices A: Studies 1 & 2 supplementary material | 147 |
| Appendices B: Study 3 supplementary material..... | 150 |
| Appendices C: Neuropsychological tests used in Studies 3 and 4..... | 164 |
| References..... | 171 |

Foreword

The complex relation between the human brain and behaviour has inspired decades of cognitive neuroscience research. Among the different areas of the brain, the medial temporal lobe (MTL) has been the focus of numerous studies over the past 50 years (figure 0.1). Advances in this field were driven by two main factors. The first is the rise of neuropsychology, or the study of patients with brain lesions, of which the behaviour is examined in order to link specific brain regions with certain aspects of cognition. In the case of the MTL, a clinical profile termed *amnesic syndrome* was identified, and allowed to ascribe a role in memory processing to this part of the brain. The second is the development of neuroimaging techniques. Functional magnetic resonance imaging (fMRI) is non-invasive and allows to measure the activity of regions located deep in the brain; it is therefore particularly suitable for investigating the MTL.

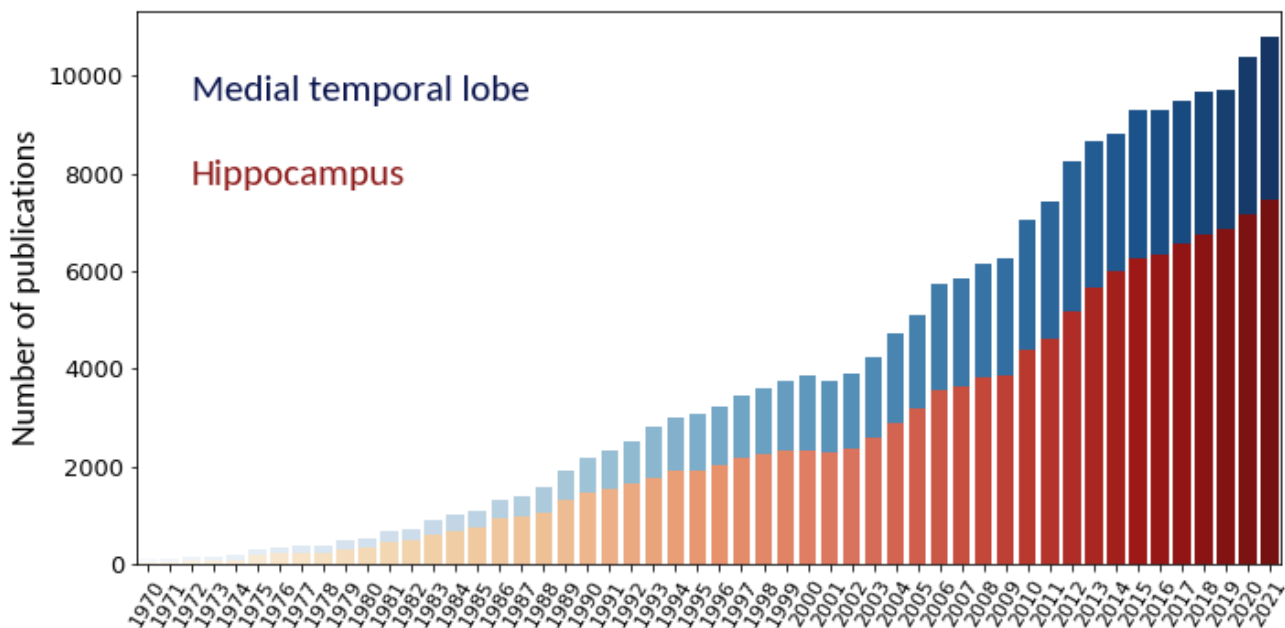


Figure 0.1. Evolution of publications per year from 1970 to 2021 or research related to the medial temporal lobe in general (in blue) and to the hippocampus specifically (in red) in PubMed (<https://pubmed.ncbi.nlm.nih.gov>). Detailed queries: Medial temporal lobe - (((("medial temporal"[Title/Abstract]) OR (parahippocampal[Title/Abstract])) OR (perirhinal[Title/Abstract])) OR (hippocamp*[Title/Abstract]); Hippocampus - ("hippocamp*" [Title/Abstract]). Search carried out in October 2022.

Research on this question has been marked by several milestones, and the neurocognitive models of the MTL evolved consequently. One major evolution was to step away from thinking these regions as a unitary anatomic-functional module. The functional specialisation of the different MTL subregions consequently gained growing interest. Among those, the hippocampus is a key structure and is extensively studied (figure 0.1). Understanding the functions of the MTL therefore implies to understand the specific functions of its different subregions. Accordingly, the models of the MTL shifted from a unitary view to

a more distributed account of its functional organisation. Several theoretical conceptions succeeded one another, built around the principles of memory systems, memory processes, memory content, and finally memory representations.

This thesis is in line with the representational conception. Instead of constituting a functional unit in the service of memory exclusively, MTL regions would be specialised in processing certain types of representations, irrespective of the cognitive domain. This shift led to new questions and hypotheses, and despite a long-lasting and thorough investigation, the functions associated with the MTL remain debated. The experimental work presented in this thesis aimed at furthering our understanding of the role played by these regions in memory and non-memory processing.

In five theoretical chapters, we will present how the models of MTL functional organisation evolved. First of all, we will start by introducing the anatomical regions that constitute the focus of this work, as well as the widely-documented profile termed *amnesic syndrome*. Following this preamble, a first chapter describes how the study of patients with amnesia led to the development of structural models. Subsequently, the process and content-based conceptions of the MTL that emerged from recognition memory research are exposed. Chapter three is dedicated to the high-resolution and scene construction views of the hippocampus, which extend beyond the domain of memory. In the fourth chapter, the representational-hierarchical model of the MTL is introduced, together with its recent developments and the questions they raised. Finally, we will present how this conception can be confronted with two axes of brain organisation: the long-axis of the hippocampus, and hemispheric specialisation.

Preamble

1. What is the medial temporal lobe?

The temporal lobe is delineated by the lateral sulcus, which splits it from the frontal and parietal lobes, and a straight line drawn from the parieto-occipital sulcus to the pre-occipital notch that marks the border between the temporal and occipital lobes (Kiernan, 2012). The MTL, located in the medial part of the temporal lobe, includes the hippocampal formation, the amygdala, and the parahippocampal gyrus (PHG; Van Hoesen, 1995; figure 0.2).

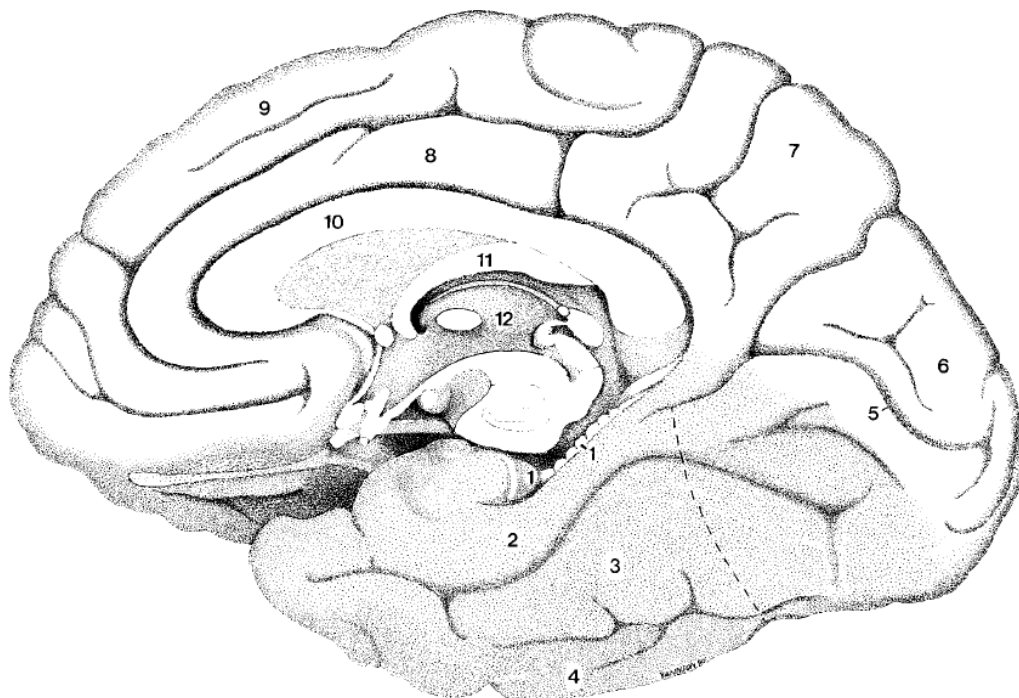


Figure 0.2. From Duvernoy, 2005: Dissection displaying the medial part of the right hemisphere. 1: hippocampus; 2: parahippocampal gyrus; 3: fusiform gyrus; 4: inferior temporal gyrus; 5: calcarine sulcus; 6: occipital lobe; 7: parietal lobe; 8: cingulate gyrus; 9: frontal lobe; 10: corpus callosum; 11: fornix.

The term hippocampal formation refers to the hippocampus, the dentate gyrus, the subiculum, and associated white matter (Kiernan, 2012; Van Hoesen, 1995). The hippocampus is a coiled gyrus, of which the shape does resemble a seahorse. In the long axis (anterior-posterior), three sections of the hippocampus are generally distinguished: the head, the body, and the tail (Hayman et al., 1998). The head of the hippocampus includes a curved medial projection that is part of the uncus, the anterior part of the PHG that bends over it (figure 0.3.A; Kiernan, 2012; Zeidman & Maguire, 2016). Based on cellular and functional properties, several internal subfields were identified: CA1, CA2, CA3 (CA stands for cornu ammonis, or Ammon's horn) and the subicular complex (figure 0.3.A). The subicular complex is a transitional area between the hippocampus and adjacent cortex (Kiernan, 2012), and is composed of the prosubiculum, the subiculum, the presubiculum, and the parasubiculum (Ding & Van Hoesen, 2015). The dentate gyrus (DG) is a thin and concave strip wrapped around

segment CA4 (Duvernoy, 2005). Although the subfields organisation is broadly similar along the entire hippocampus, the proportions of each subfield representation vary in its long axis: CA1 and subiculum are more represented in the anterior part of the hippocampus whereas CA2, CA3 and the DG are more present posteriorly (Malykhin et al., 2010; Poppenk et al., 2013; Zeidman & Maguire, 2016).

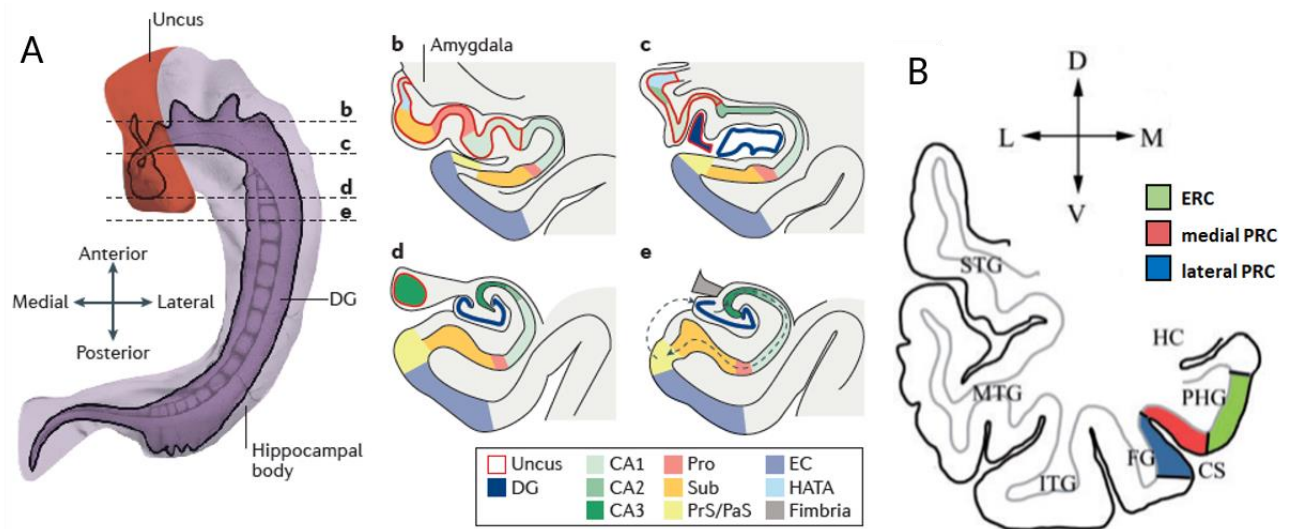


Figure 0.3. A: From Zeidman & Maguire (2016), internal organisation of the hippocampus and position of the uncus. B: Adapted from Kivisaari et al. (2012), temporal lobe from a coronal slice. DG: Dentate gyrus; CA: cornu ammonis; Pro: Prosubiculum; Sub: Subiculum; PrS/PaS: Pre/Parasubiculum; HATA: hippocampus-amygdala transitional area. D: dorsal; V: ventral; L: lateral; M: medial; EC/ERC: Entorhinal cortex; PRC: Perirhinal cortex; STG: superior temporal gyrus; MTG: middle temporal gyrus; ITG: inferior temporal gyrus; FG: fusiform gyrus; CS: collateral sulcus; PHG: parahippocampal gyrus; HC: hippocampus.

The cortex adjacent to the hippocampal formation is part of the PHG, which extends from the tip of the calcarine fissure (i.e., the lingual part of the occipital lobe) to the amygdalar complex (Van Hoesen, 1995). The collateral sulcus borders laterally the PHG; and laterally to the collateral sulcus is the fusiform gyrus (figure 0.3.B). The entorhinal cortex (ERC) is the largest cortical area of the PHG (Brodmann area, BA28). The ERC is present along the entire length of the PHG, and is directly adjacent to the presubiculum and parasubiculum subfields of the hippocampal formation (Insausti et al., 1998). The ERC is bordered laterally by the perirhinal cortex (PRC; BA35), which is located on the medial bank of the collateral sulcus, close to the rhinal sulcus (i.e., the anterior end of the collateral sulcus; Insausti et al., 1998; Kiernan, 2012). Laterally to the PRC lies the entorhinal cortex (BA36). In the neuroimaging and neuropsychology literature, the *perirhinal* region usually encompasses both areas 35 and 36 (Ding & Hoesen, 2010). Area 35 of the PRC houses a region termed *transentorhinal area* because of its unusual cytoarchitectonic properties, and is considered a transitional area between the PRC and ERC (K. I. Taylor & Probst, 2008). The parahippocampal cortex (PHC) is posterior to the PRC and is composed of sub-regions TH (i.e., medial PHC) and TF (i.e., lateral PHC; Lavenex & Amaral, 2000). Finally, the amygdalar body, or amygdala, is a nuclear complex located anteriorly to, and partly overlapping, the head of the hippocampus (Kiernan, 2012). It

has been divided into the basolateral, the centromedial, and the cortical, groups of nuclei (Weiss et al., 2021). The hippocampus and amygdala are largely interconnected, and the transitional region between them is call the hippocampus-amygdala-transitional-area.

2. What is the amnesic syndrome?

Patients with MTL lesions have been documented since the beginning of the twentieth century, and were already linked to memory disorders (Von Bechterew, 1900). Those lesions can arise from varied aetiologies such as herpes simplex encephalitis, traumatic head injury, lobectomy (often due to drug-resistant epilepsy), anoxia, ischemia, or neuroprogressive diseases. The MTL is not the only brain region of which the dysfunction leads to memory impairments (e.g., prefrontal or diencephalic regions), but amnesia has more generally been associated with MTL degradations (Allen, 2018). As MTL regions are the focus of this work, we will use the label “amnesia” to refer to the classical pattern of memory impairments that results from MTL damage. Brenda Milner and colleagues later studied in depth the famous case of patient H.M., permitting significant advances in the neuropsychology of memory (Milner, 1972; Milner et al., 1968). The damage from which suffered H.M. included the bilateral hippocampi and parahippocampal gyri, and were due to neurosurgery for epilepsy (see Annese et al., 2014). The clinical profile associated with lesions of the MTL typically encompasses difficulties to recognise people, names, or places, to remember events, to learn new material, or to estimate one’s own age. In contrast, intellectual, linguistic, perceptual, and social abilities are intact (Milner et al., 1968). Thus this profile is sometimes termed “*pure*” *amnesic syndrome*. Importantly, the memory disorders found in the amnesic syndrome affect the learning of new information, that is, information one encounters subsequently to the lesion, called *anterograde memory* (Spiers, Maguire, et al., 2001a; figure 0.4). In comparison, *retrograde memory* refers to the ability to retrieve information that was encountered prior to the lesion. Retrograde memory is usually intact in patients with MTL lesions, except for events that happened shortly before the lesion, a pattern referred to as Ribot’s law (Allen, 2018). Such amnesic syndrome is therefore termed *anterograde amnesia*.

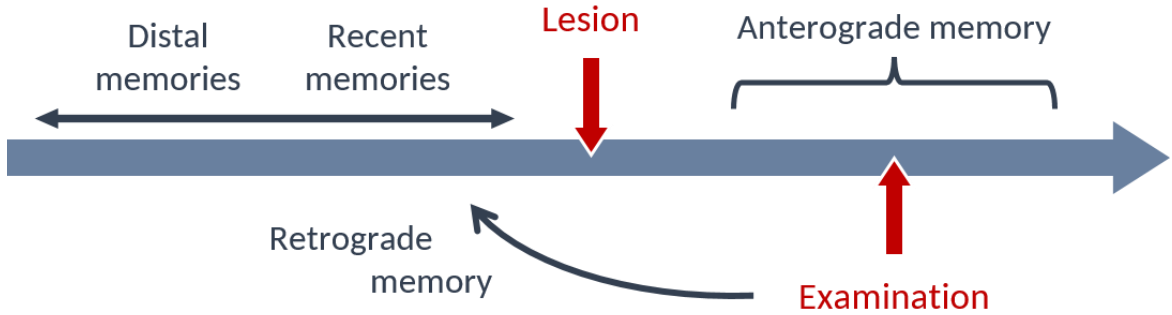


Figure 0.4. Schematic representation of retrograde versus anterograde memory as function of time of examination.

Chapter I – The multiple-memory systems: A neuropsychological approach to medial temporal functions

In this first chapter we will introduce the neuropsychological approach of the medial temporal lobe (MTL). This approach is based on the study of patients presenting MTL lesions. Since the observation that such damages are associated with memory disorders, this area has been known as the “medial temporal lobe memory system” (Squire & Zola-Morgan, 1991; Tulving & Craik, 2000). The study of amnesic patients has further allowed to fractionate memory into distinct systems (Allen, 2018), resulting in the multiple-memory systems view, and stepping aside from the former unitary view of human memory (e.g., Underwood, 1964).

1. Working/short-term memory versus long-term memory

Evidence in favour of a dissociation

One of the main observations stemming from work on amnesic patients is that their memory impairment crucially depends on the delay between learning and test. As described by Milner (1972), H.M. was able to retain a 3-digits number for as long as 15 minutes by continuous rehearsal. However, when distracted, he would forget the number even though he had repeated it for several minutes. This observation suggests the existence of two distinct memory systems differentiated by task delay. Various experimental procedures have been used to investigate this distinction in amnesic patients.

The most widely used procedure is the *digit span* task, in which subjects are orally presented with series of digits of varying length, and instructed to repeat each series aloud. The length of the series increases to N+1 digits once the subject correctly repeated one or more of three N-digits series, starting with 5 digits. When the subject fails in correctly repeating any of the three series of length N, N-1 is considered the subject's *digit holding span* (or *digit span*). H.M. and four other patients presenting amnesia from varied aetiologies demonstrated normal performances on this task with a mean span of 7, whereas that of control subjects was 8.3 digits (Drachman & Arbit, 1966).

In a different version of the task, subjects were continuously presented with a series one-digit longer than their digit span until they were able to correctly repeat that series. The number of trials needed to correctly repeat a series was considered the criterion for the series' length (with a maximum of 25 trials). When a subject met the criterion, the series' length increased by one digit, up to 20 digits. The maximum number of digits a subject was able to

correctly repeat within 25 or less trials is considered their *digit storage capacity*. In contrast with the previous task, the same four patients exhibited markedly reduced digit storage capacities. Whereas all control subjects reached a storage capacity span of 20 digits, the patients' mean storage capacity was 8.6 digits (Drachman & Arbit, 1966). This dissociation supports the existence of two distinct memory systems. The first, underlying the short-term holding of a limited set of information and preserved in amnesia, is termed short-term memory or working memory (WM; Baddeley, 1992; Baddeley & Hitch, 1974). In contrast, long-term memory (LTM) is involved in learning larger sets of information through repetitions over longer time periods, and is impaired in amnesia.

Evidence for this dissociation also comes from free-recall tasks, in which subjects are presented with a list of words, and instructed to recall them in any order. In this task, healthy participants traditionally show an increased rate of recall for the items presented at the end of the list in comparison to the rest of the words. This pattern is termed the *recency effect*. This effect is believed to rely on WM since it is unaffected by manipulations that modulate overall retention performances, which would depend on LTM (Glanzer & Cunitz, 1966). Baddeley and Warrington (1970) demonstrated that the recency effect was intact in patients with amnesia, whereas overall memory performance was markedly impoverished as compared to control subjects (figure 1.1).

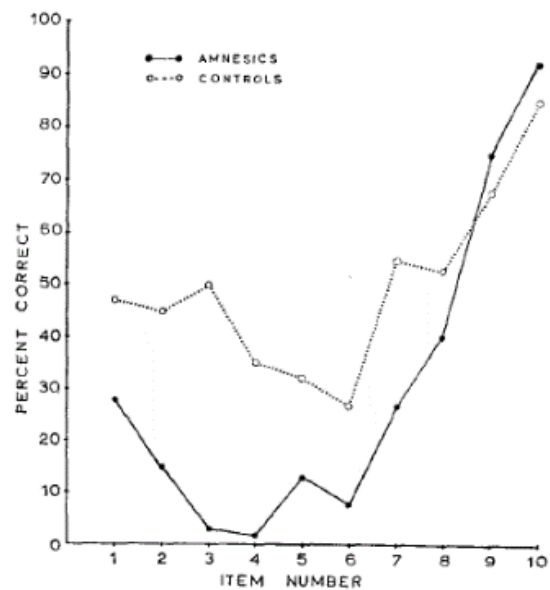


Figure 1.1. From Baddeley & Warrington (1970): Percentage of recall in the free recall task as function of item presentation order for amnesic patients and controls.

The demonstration that lesions to the MTL affect LTM independently of WM has been supported by various neuropsychological descriptions (reviews in Spiers et al., 2001a; Squire et al., 1993). The reversed profile has been described in patient K.F. by Shallice & Warrington (1969). This patient had a left parieto-occipital lesion acquired at the age of 28. In spite of normal LTM performances, K.F. showed considerable impairments on all WM tasks (Shallice & Warrington, 1970). These complementary patterns demonstrated that LTM and WM can be impaired independently. It was thus concluded that the MTL would support the generation of long-lasting memory traces (Squire, 1992).

Is working memory always preserved in amnesia?

Although numerous evidence strengthened the WM/LTM dissociation, some studies reported that not all WM capacities are intact in amnesic patients. Warrington and Taylor (1973) investigated faces and surnames span capacities of amnesics and control subjects,

using a short-term recognition task. Participants were first presented with item sets of varying length. Immediately after, they were presented with larger sets of items among which 1/3 were the learned items and 2/3 were lures, and were instructed to find the items they had seen before. Whereas amnesic patients and control subjects had similar span capacities for surnames, the patients were impaired for face recognition when the set was larger than one. In a second version of the task, the length of the stimuli sets was fixed to 3, but the delay was manipulated: no delay versus 30-seconds delay. Again, whereas delay slightly reduced the performances of both the amnesics and controls in a similar way for surnames, the amnesics were markedly impaired for faces, even with no delay (Warrington & Taylor, 1973). Similar observations were made using the delayed matching-to-sample task. In this task, a stimulus is first presented, and is presented again, mixed with lures; and the participants must choose the target item. Sidman and colleagues (1968; see also Milner, 1972) applied this task to H.M. with either verbal (i.e., trigrams) or non-verbal (i.e., ellipses) stimuli. To estimate the effect of delay on H.M.'s performances, they used an *adjusting-delay* procedure: the delay increases when the subject succeeds a trial and decreases when they fail, starting with no delay. Whereas H.M. was able to retain trigrams up to 40 seconds, he was impaired beyond 5 seconds for ellipses (although his performance was normal with no delay, ensuring that this impairment was not due to his visual-discrimination abilities). It was further reported that amnesic patients had impaired visual WM for faces, colours, and spatial locations (Olson, Moore, et al., 2006). Based on these observations, it was proposed that WM would be involved in the retention of non-verbal material for about 15-30 seconds, delay after which LTM would take over, whereas the retention of verbal material could be supported by WM for longer delays (i.e., up to 60 seconds), likely through rehearsal (O'keefe & Nadel, 1978).

A critical result came from Olson and colleagues, who tested WM for spatial locations, single objects, and location-object conjunctions (Olson, Page, et al., 2006). They reported that whereas their performances were intact for locations and objects alone, amnesic patients were markedly impaired for location-object conjunctions, for delays as short as 4 seconds. Consistently, amnesics were also impaired when tested on associations between objects and scene images (Hannula et al., 2006). Therefore, in addition to its role in LTM, the MTL seems to be involved in WM when conjunctions between elements are required.

2. Non-declarative versus declarative memory

Evidence for a dissociation

A neuropsychological double-dissociation has permitted to distinguish WM from LTM, and to demonstrate that the MTL is mainly involved in LTM. However, it appears that not all LTM capacities are impacted by amnesia. Milner and colleagues trained H.M. to trace a line around the outline of a drawing while the only visual feedback he had was through a mirror, and recorded the number of errors he made for each trial. H.M. showed a normal decrease in error rate as function of trial repetition (i.e., close to that of control participants), and achieved a

rate neighbouring zero on the third day of training (Milner, 1972). Critically, he was not aware that he had been practicing this task. It was further demonstrated that H.M. was able to learn various motor skills through repetition, although he had no explicit recall of it (Corkin, 1968). Based on these results, it was assumed that the memory system for motor skills and abilities learning, termed *procedural memory*, does not rely on MTL regions.

Another task used to elicit preserved LTM capacities in amnesic patients is Gollin's incomplete drawings task (Gollin, 1960). The material comprises 5 sets of 20 drawings depicting objects and animals. The five sets are differentiated by their degree of completeness (or degradation), which makes them more or less difficult to identify. Participants are first presented with the five sets successively, from the most incomplete to the most complete. For each image they are instructed to try identifying the drawing as quickly as possible. One hour later the whole test is repeated (with no forewarning of it) and the number of errors made as function of the difficulty of the set is measured. Normal subjects show a decrease in the error rate between test and retest for a given difficulty; in other words, identification is made easier by repetition. Although their error rate was higher than that of controls, H.M. (Milner et al., 1968) and other amnesic patients (Warrington & Weiskrantz, 1968) showed a normal decrease in error rate at retest. Like for procedural learning, the patients had no explicit recall of performing the same task before. These observations suggest that *implicit priming* is preserved in amnesia, in contrast with *explicit* memory. Priming paradigms consist in modifying the subject's behaviour, in particular increasing the chance to identify or to produce an item, by exposing them to the test material prior to the test phase (e.g., Rosenbaum et al., 2005). Importantly, no explicit instruction is needed to elicit priming effects. For instance, Graf and colleagues (1984) first presented controls and amnesic patients with a list of words, and used four different test methods: free recall, cued recall, recognition, and word completion. In contrast with all other conditions, in the word-completion condition participants were not instructed to retrieve the words presented before, but only to complete trigrams with whatever word came to their mind. Patients were impaired in all conditions except the latter, demonstrating that when they were not oriented towards memory retrieval, a priming effect occurred. Some researchers proposed that these effects, considered *perceptual priming*, would rely on a perceptual representation system (PRS), which would store the perceptual shape of stimuli, without their concept or meaning (Schacter, 1992; Tulving & Schacter, 1990). Perceptual priming and the putative PRS implicitly facilitate the perception of an already-encountered stimulus through processing *fluency*, without conscious access to the exposition episode being required.

In contrast with perceptual priming, *conceptual priming* consists in enhancing the access to a concept by prior "activation" of this concept. For instance, Graf and colleagues (1985) reported that the likelihood of using a word to complete a trigram presented visually was enhanced both by prior visual and auditory priming of that word. Whereas amnesic patients were impaired in an additional free-recall condition, they showed the same conceptual priming effects as control subjects. This result suggests that priming can occur even though

the prime and the test cue share no perceptual common feature, including in amnesic patients. In a second experiment, participants were primed with exemplars of conceptual categories (e.g., *football* and *rugby* for the category *sport*), and were then asked to produce the first eight exemplars that came to their mind for each category. Importantly, test cues only consisted in the category labels, thus ensuring no perceptual overlap between primes and test cues. Amnesic patients showed a similar priming effect as control subjects, confirming that conceptual priming is also preserved in amnesia (Graf et al., 1985). The study of priming thus highlighted the divergence between direct (explicit) and indirect (implicit) evaluations of memory, revealing additional LTM preservations in amnesia.

It has thus been demonstrated that procedural memory and priming are preserved in amnesia, leading to a distinction between the *declarative* and *non-declarative* memory systems. Declarative memory is the system for explicit content such as general knowledge, facts, and events, which can easily be put into words (often referred to as “knowing what”). Non-declarative memory encompasses procedural memory (or “know how”) and implicit memory phenomena such as priming, conditioning, and habituation, that are more difficult to express verbally (Squire, 1992; Squire & Zola-Morgan, 1991). These advances led researchers to conclude that MTL lesions specifically impair long-term declarative memory (Schacter, 1987).

Are all kinds of priming preserved in amnesia?

The preservation of non-declarative memory in presence of MTL lesions is supported by numerous studies. Not all types of implicit memory, however, are intact in amnesia. In line with the series of experiments by Graf and colleagues presented above, Gabrieli, Cohen, and Corkin (1988) investigated the learning of new conceptual information (i.e., new word definitions) in H.M., but reported no evidence for any learning, neither when measured directly nor indirectly. In another study, participants were instructed to find a target letter among distractors displayed in a particular spatial layout (Chun & Phelps, 1999). Crucially, some layouts were repeated across the experiment (i.e., the old trials) whereas other were not (i.e., new trials). While the response time of control subjects decreased for old trials, amnesic patients did not benefit from repetition. In other words, they had no priming effect for spatial configurations as compared to the controls. Comparable observations were made in natural scene processing. Ryan and colleagues used eye-tracking to examine how the visual exploration of scene images is modulated by image repetition as an indicator of implicit memory (2000). They first demonstrated that image repetition modified the visual exploration behaviour of both control and amnesic subjects, suggesting that priming for visual scenes is preserved in amnesia. Yet, in another condition the layout of the scene elements was manipulated. The authors reported higher proportions of eye fixations in the region that had been manipulated, only when the manipulation was not noticed by control participants (i.e., the effect was implicit). As compared to control subjects, what was termed the *configuration priming effect* was absent in amnesics. Taken together, these results support that while simple

perceptual priming is intact, priming for configuration, layout, or associative material, is impaired in amnesia.

The identification of preserved LTM capacities in amnesia allowed researchers to sharpen the memory functions associated with medial temporal regions from LTM to explicit LTM. However, it appeared that some implicit memory effects do depend on the MTL. Therefore, the correspondence between declarative and explicit memory on the one hand, and non-declarative and implicit memory on the other hand, has been discussed. In particular, it was proposed that declarative memory, rather than the system for explicit memory, would be the system for relational memory (Cohen et al., 1999; Cohen & Eichenbaum, 1993). This account is consistent with the proposal that the MTL is also involved in WM under certain circumstances, that is, when the task involves relations/conjunctions between elements.

3. *Semantic versus episodic memory*

The MTL is thus particularly involved in declarative memory. Further research suggested that two main declarative-memory systems can be distinguished: episodic and semantic memory. Tulving was the first to conceptualise the distinction between these systems (e.g., 1972, 1985). According to his conception, episodic memory is the system for personally-experienced, spatially- and temporally-contextualised events (or *episodes*). Semantic memory is the system for all information and general knowledge about the world and oneself. Importantly, unlike episodic memory, semantic memory is fundamentally decontextualised (Tulving, 1972). Accordingly, episodic and semantic retrievals are distinguishable. Whereas the retrieval of an episodic memory is associated with the feeling of *remembering* the episode, accessing a semantic information comes with the sensation of *knowing* that information. Tulving further proposed that these two forms of retrieval are accompanied with different states of consciousness: namely auto-noetic consciousness for episodic memory (i.e., the feeling of oneself in the past) and noetic consciousness for semantic memory (i.e., the sense of knowing an information without the associated encoding context). The phenomenology of auto-noetic consciousness has been extensively studied, leading to the concept of mental time travel, or projecting oneself in the past or the future, which is the defining capacity of episodic memory (e.g., Corballis, 2019a, 2019b). Consistently, both remembering past events and imagining future events seem to be impaired in amnesia, supporting that mental time travel works in both directions (Klein et al., 2002).

Can episodic and semantic memory be dissociated in memory-impaired patients?

While episodic memory is strikingly impaired in amnesia, it is less clear whether semantic memory is preserved or impacted in this pathology. Whereas some authors claim that both semantic and episodic memory are impaired in amnesia (Knowlton & Squire, 1995; Squire, 1992), others assert that semantic memory and episodic memory can be altered independently (Tulving et al., 1991). Crucially, the profile of impairments associated with MTL damage is anterograde amnesia (see Preamble section; figure 0.4). When assessing various

memory systems in amnesic patients, researchers then need to focus on the learning of new information. Thus to reveal preservations of semantic memory when episodic memory is impaired, one must demonstrate the semantic nature of the newly-learned material, in order to rule out the possibility that remaining episodic memory capacities could explain the effect. One way of doing so is to show that patients can learn new concepts or word meanings, without being able to remember the encoding episode.

Various reports identified such patterns, in patients who consistently presented hippocampal lesions. Kitchener and colleagues documented the case of patient R.S., who had severe amnesia, but had been able to learn new information such as famous people, public events, and words (1998). Similarly, McKenna and Gerhand investigated the case of K.N., and described his ability to learn new semantic concepts while his episodic memory was at floor (2002). Shimamura and Squire tested amnesic patients on the learning of short meaningful sentences (1988). They demonstrated that when their performances were equalised to that of controls (by delaying the test for the latter), amnesics were not more impaired when presented with paraphrases instead of the original sentences. This suggests that they did learn new flexible knowledge, although impoverished in comparison to controls, and were not merely driven by the sentences' perceptual form. Tulving and colleagues extensively studied the case of K.C., a patient with scattered brain lesions including bilateral hippocampi who developed severe amnesia (for review Rosenbaum et al., 2005). Despite a strong episodic-memory impairment, K.C. was able to learn new computer-related words (Glisky et al., 1986b) and knowledge (Glisky et al., 1986a). However, it was argued that such learnings were "simple stimulus-response", possibly relying on implicit memory, not semantic learning (Rosenbaum et al., 2005). It was later demonstrated, however, that K.C. was able to access newly-learned words without any similarity in cueing, either through cross-modal cues (Tulving et al., 1991) or semantic definitions (Hayman et al., 1993) ; as well as new sentence puzzles (McAndrews et al., 1987). Additional experiments confirmed that amnesic patients were able to efficiently learn new words (Kovner et al., 1983; Mattis & Kovner, 1984). Critically, in all the studies reviewed, investigators invariably reported that patients had no episodic recall of the learning session. Taken together, these results suggest that new factual information can be learned when anterograde episodic memory is impaired, and point toward a specific role of the hippocampus in episodic memory. Yet, amnesic patients appear unable to elaborate on new semantic learnings, such as integrating them into pre-existing semantic knowledge and categories, or explicitly accessing their definition (see Westmacott & Moscovitch, 2001 for evidence in K.C.). Therefore, semantic learning in amnesia remains strongly impoverished as compared to that of normally-functioning subjects, suggesting that acquired amnesia does not offer a strict dissociation between anterograde episodic and semantic memory.

If the results from acquired amnesia did not permit to rigorously conclude that anterograde semantic memory can be preserved when episodic memory is impaired, the study of developmental amnesia provides strong arguments in favour of this dissociation. Wood and colleagues first reported the case of T.C., who contracted herpes simplex encephalitis at the age of 9, resulting in bilateral MTL damage (1989). Although she had profound episodic amnesia, T.C. exhibited anterograde semantic memory including language, vocabulary, reading and spelling, and arithmetic. A similar case was reported with patient C.C. who developed amnesia at 10 (Ostergaard, 1987). In contrast with T.C., although patient C.C. was able to progress at school, his scores in lexical decision, reading vocabulary, verbal fluency, and semantic categorisation were markedly impaired in comparison to control subjects. These reports, however, lacked precision in the description of the brain damage from which T.C. and C.C. suffered. The most striking evidence later came from Vargha-Khadem and colleagues (1997), who documented the cases of Beth, Jon, and Kate, who were subject to hippocampal damage at birth, at 4, and at 9, respectively. The three patients present profoundly-impaired episodic memory for both verbal and non-verbal materials (figure 1.2). However, they all three integrated in the education system, and developed normal (in regard to their IQ) performance in language (i.e., speech, reading, and spelling) and semantic processing (i.e., vocabulary, information, and comprehension subtests of the Wechsler Memory Scale; Wechsler, 1945). Finally, Martins and colleagues (2006) described two patients with developmental amnesia, R.H. and K.F. Even though the learning of K.F., who's episodic memory impairment was stronger than that of R.H., was slower, both were able to learn new semantic information. Overall, these results suggest that semantic memory can develop in absence of episodic memory.

The reverse pattern of impairment is found in *semantic dementia*, the temporal variant of fronto-temporal dementia (David et al., 2006; Desgranges et al., 2007; Hodges et al., 1992, 1994). This pathology is characterised by a progressive loss of semantic concepts, leading to anomia, impaired word comprehension, impoverished categorical exemplars generation and general knowledge. In contrast, episodic memory is generally reported as intact in these patients (De Renzi et al., 1987; Hodges et al., 1992, 1994; Pietrini et al., 1988; Sartori & Job, 1988; Warrington, 1975; Warrington & Shallice, 1984). Although neuroprogressive diseases present a high degree of inter-individual variability, the semantic impairment found in semantic dementia has been linked to anterior temporal regions atrophy, namely the PRC, temporopolar cortex, and anterior fusiform gyrus (Davies et al., 2004; Hodges & Patterson,

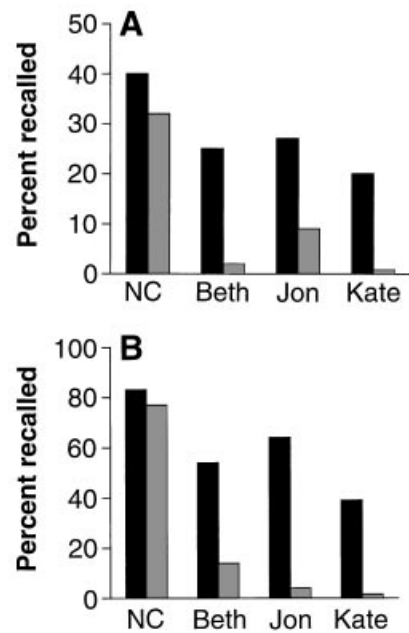


Figure 1.2. From Vargha-Khadem et al., (1997), memory scores of the 3 patients for A: the logical memory and B: the visual memory subtests of the Wechsler Memory Scale. NC: Normal controls; black bars: immediate; grey bars: delayed memory.

2007). Importantly, these regions were considered intact in Beth, Jon, and Kate, and could thus be responsible for their preserved semantic capacities (Vargha-Khadem et al., 1997). Although comparing a developmental disorder to a neuroprogressive disorder remains questionable, the complementary observations of developmental (in addition to acquired) amnesia and semantic dementia permitted to show that episodic and semantic memory can be impaired independently, depending on the MTL subregions damaged. Taken together, these results support the assumption that declarative memory can be split into two anatomofunctional systems within the MTL: a hippocampal-episodic system and an inferior-anterior semantic system.

The modular view of memory systems

In line with his conception of episodic and semantic memory, and with the arguments for a dissociation between them, Tulving proposed the serial, parallel, and independent (SPI) model (Tulving, 1995; figure 1.3). The model is termed SPI because it assumes that encoding is serial, storage is parallel, and retrieval is independent. Serial encoding means that for information to enter a given system, it requires the lower-level systems to be functional. Storage of information in the different memory systems would be done in parallel. Finally, independent retrieval refers to the possibility to retrieve information from one system irrespective of the functioning of the other systems (Tulving, 1995, also 1985a). Conceptually, the SPI model stems from the

neuropsychological approach of memory, and aligns with the structural and modular view of memory (as opposed to non-modular conceptions, e.g., Craik & Lockhart, 1972). Other structural models have been proposed, such as the multi-inputs model of Graham and colleagues (Graham et al., 2002), the hierarchical model of Mishkin (mainly stemming from non-human animal research; Mishkin et al., 1997), or the first version of the MNESIS model from Eustache and Desgranges (2008; for subsequent developments, see Eustache et al., 2016). The characteristic shared by these models is that memory is divided in multiple systems that rely on distinct brain regions. Among these systems, the episodic and semantic systems would both rely on MTL regions, and would be independent.

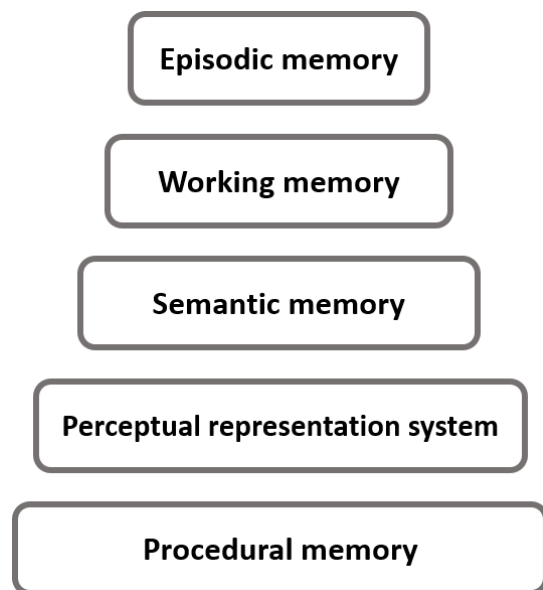


Figure 1.3. Adapted representation of the serial, parallel, and independent model from Tulving (1995).

An alternative view: The unitary vision of declarative memory

A different view of how MTL regions underlie declarative memory is the unitary vision of Squire (Squire, 1992; Squire et al., 1993). This model (figure 1.4), fundamentally structural,

presents an anatomo-functional taxonomy of memory systems (Squire & Zola, 1996). In this conception, the MTL forms a functional unit responsible for declarative memory, and any MTL lesion would impair episodic and semantic memory in similar ways. Squire and colleagues gave a different interpretation of the results from acquired and developmental amnesia studies (Squire & Zola, 1998). In addition to the weakness of the semantic learnings observed in adult amnesic patients, they argued that the effects demonstrated in the relevant studies (e.g., Tulving et al., 1991 with K.C.) were implicit, and thus do not fall into the definition of declarative memory. Furthermore, they reported the case of E.P., who presented very-severe amnesia, and showed no sign for semantic learning (Hamann & Squire, 1995; Squire & Knowlton, 1995). The authors concluded that when a patient has a “complete” impairment of episodic memory, semantic learning is impossible. Additionally, they argued that the documentation of school progress is not sufficient to ensure significant semantic memory development in patients with developmental amnesia, since it is unclear what amount of semantic learning should be achieved during a given school period. The authors assumed that remnants of episodic memory could be responsible for the semantic memory acquisitions demonstrated by the patients (Squire & Zola, 1998). Consequently, it would be the *size*, and not the *site*, of the MTL lesion, that would be critical in amnesia, and determine the severity of the impairment (Squire et al., 2004).

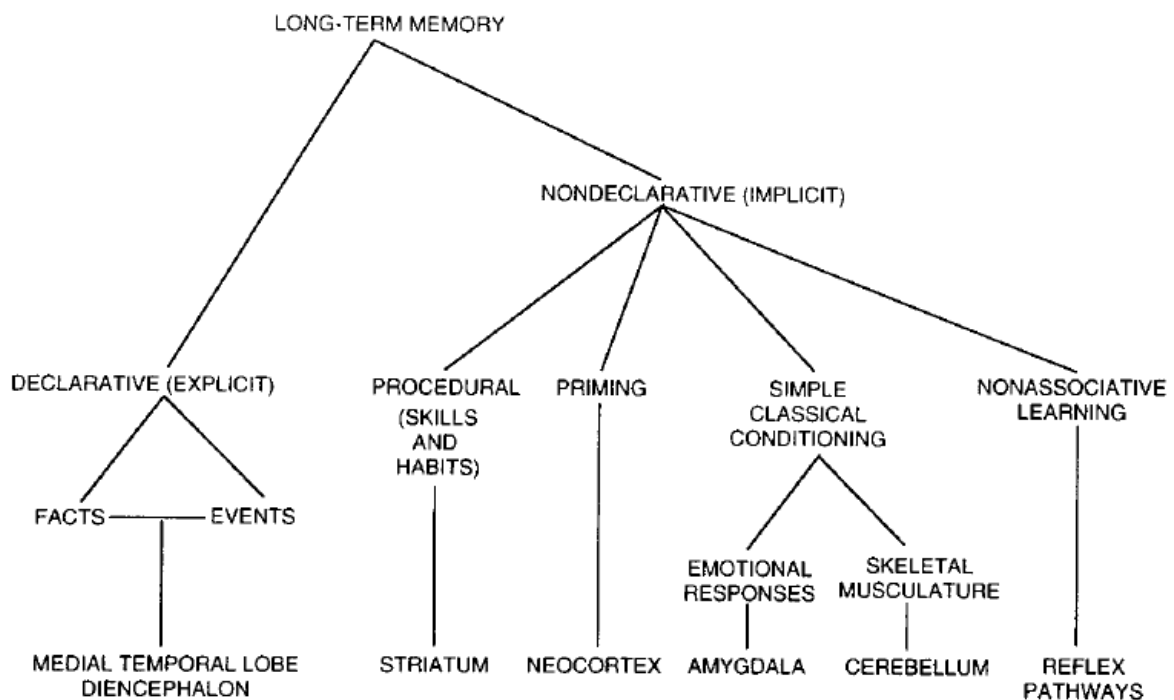


Figure 1.4. From Squire & Zola, 1996. The structural model of Squire, a taxonomy of memory systems. In this model the medial temporal lobe supports declarative memory (i.e., both episodic and semantic memory) in a unitary way.

4. Recognition versus recall memory

Evidence for a dissociation

In addition to the observation that the episodic and semantic components of declarative memory can be impaired separately, research also identified the importance of *how* memory is evaluated. Declarative memory is traditionally assessed through two major procedures : recognition and recall (e.g., Squire, 1992). Recall consists in asking participants to (freely or with cues) remember the material they have previously studied; whereas in recognition they are instructed to determine which, in a set of stimuli, have been presented before. Because both procedures evaluate memory for previously-presented items, it could be expected that amnesic patients would be equally impaired on the two tasks. Yet, experimental evidence suggests otherwise.

Hirsh and colleagues first reported disproportionate impairments of recall capacities as compared to recognition capacities in amnesic patients (1986, 1988). Aggleton and Shaw later reviewed 33 studies investigating recognition memory in amnesia, and reported that although recognition-memory deficits are frequently encountered in amnesia, they are not systematic. Importantly, they pointed out a particular profile of amnesia in which recognition memory is spared: isolated hippocampal lesions (Aggleton & Shaw, 1996). A series studies reported similar lesion and impairment profiles, with namely patients D.F. (Henke et al., 1999), Jon (Baddeley et al., 2001), Y.R. (A. R. Mayes et al., 2002), M.R. (Bastin et al., 2004), K.N. (Aggleton et al., 2005), and F.R.G. (Barbeau et al., 2005). Holdstock and colleagues identified the conditions under which Y.R. failed recognition tasks: when target and lure stimuli were perceptually similar, and when recognition was tested on object-location conjunctions (2002). This observation was confirmed in a group study in which patients with isolated hippocampal lesions were only impaired in recognition for objects associations, whereas patients with large MTL lesions were impaired in all recognition conditions (Turriziani et al., 2004).

Although some controversial results exist (Manns & Squire, 1999; Reed & Squire, 1997; see also Kopelman et al., 2007), the study of amnesic patients essentially indicates that the different subregions of the MTL do not play equivalent roles in declarative memory tasks: the hippocampus would be critical in recall memory whereas recognition memory would rely on extra-hippocampal regions. Yet, consistent with the conclusions drawn from the WM and priming research, it also appears that recognition memory for conjunctions is altered in patients with declarative memory impairments. Hence recognition of single items specifically is impaired in amnesia only when the lesions extend to extra-hippocampal regions. In line with this assumption, Barbeau and colleagues (2011) reported a double-dissociation between patients F.R.G. (described in Barbeau et al., 2005) and J.M.G. F.R.G. presents a circumscribed lesion of the hippocampus with intact anterior sub-hippocampal structures (i.e., including the PRC); whereas J.M.G presents the reverse profile: an isolated lesion of anterior sub-hippocampal regions with the hippocampus preserved (figure 1.5.A). These patterns of lesion concern the right hemisphere, the left MTL being completely destroyed in both patients, this

is why memory was investigated using visual material only. Critically, whereas F.R.G. was consistently impaired on all recall tasks but succeeded recognition tasks, the opposite pattern of impairment was observed for J.M.G. (figure 1.5.B). This study thus provides a double dissociation between recognition and recall memory within the MTL. Whereas recall would rely on the hippocampus, recognition memory for single items would involve the inferior-anterior extra-hippocampal part of the MTL.

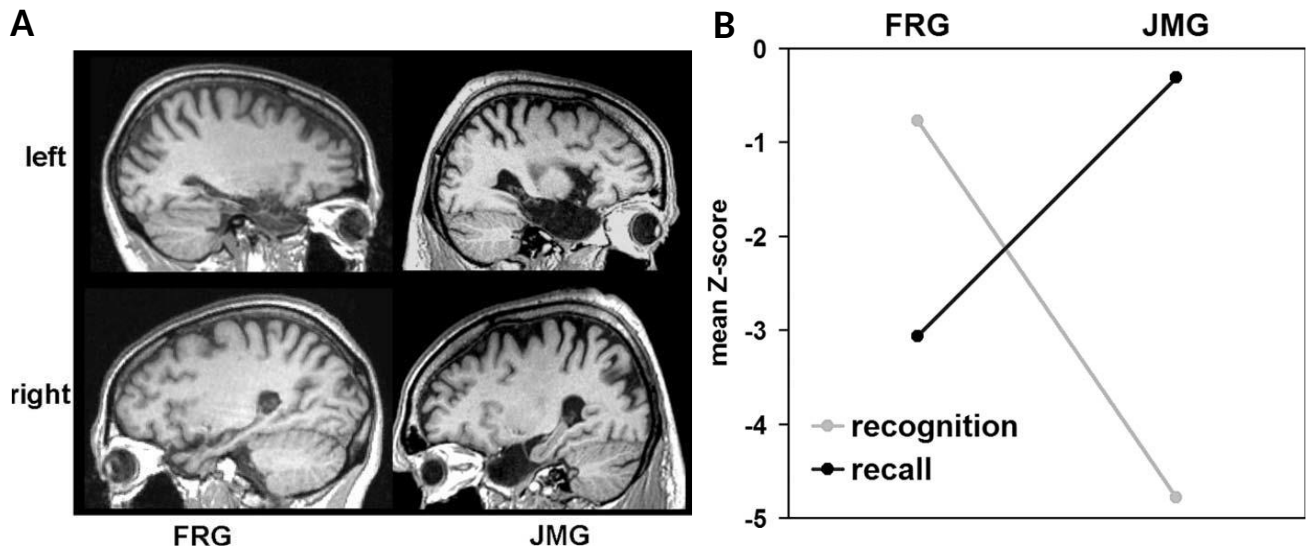


Figure 1.5. From Barbeau et al, 2011. A: anatomical scans of the left (top) and right (bottom) hemispheres in sagittal view of FRG (left) and JMG (right). B: mean z-scores of patients FRG and JMG on recognition and recall tasks.

Can the Multiple-memory systems view account for recognition and recall memory?

Research on amnesia provided arguments in favour of a dissociation between recall and recognition memory. Recall and recognition, however, are tasks, not cognitive entities. Thereby emerges the question of what forms (or systems) of memory are involved in these tasks. The observation of dissociable impairments for recognition and recall memory in amnesia argues against the intuitive idea that they equally rely on episodic memory. Recall tasks undoubtedly fall within the scope of episodic memory. Since no, or limited, clue is available to the subject, this task implies to remember information from the encoding period (Tulving, 1972). Therefore, patients with impaired episodic memory are most likely to fail recall tasks. The observation that patients suffering from hippocampal damage, and lack episodic memory, are particularly impaired in recall tasks argues in favour of this assumption. In contrast, in recognition tasks stimuli are available to the subjects to make memory judgments. It seems reasonable to assume that mental time travel could contribute to such judgments. However, it was demonstrated that recognition memory depends, at least partially, on extra-hippocampal structures (Barbeau et al., 2011). Therefore, recognition memory should rely, at least partially, on non-purely episodic memory processing. Perceptual fluency could fulfil this role, and the procedure of recognition memory resembles that of priming. Yet, recognition memory taps into declarative memory, not non-declarative/implicit

memory. The observation that impairments are found in recognition memory in case of hippocampal lesions depending on task manipulations also makes it challenging to map a specific memory system onto recognition memory. It was thus proposed that the contribution of the MTL to recognition paradigms could be divided into more than one *memory process*: recollection and familiarity (Eichenbaum et al., 2007).

Synthesis

Neuropsychological dissociations allowed researchers to identify and conceptualise multiple memory systems. Modular models have been proposed to explain the anatomofunctional organisation of memory and provided a basis to understand medial temporal functions. Among those memory systems, the MTL would support long-term explicit memory, or declarative memory. Inconsistencies exist, however: WM and perceptual priming do rely on the MTL, and recognition memory on the hippocampus, when they are tested with associative material such as conjunctions or layouts. In addition, the multiple-memory systems view cannot account for recall versus recognition results. These observations call for alternative accounts of the MTL, and in particular of its contribution to recognition memory.

Chapter II – The MTL beyond systems: Process-based and content-based models of MTL functions

Whereas recall memory appears to rely on the hippocampus and is undoubtedly the domain of episodic memory, the system-based taxonomy cannot explain the patterns of impairment found in recognition memory tasks. Therefore, it has been argued that more than one *memory process* contributes to recognition. This chapter first exposes the evidence supporting a dissociation between *recollection* and *familiarity* in the MTL, and the process-based account that emerged from it. Subsequently, models that explain recollection and familiarity in terms of *memory content* are presented together with experimental arguments in favour of this view.

1. Measuring recollection and familiarity in recognition memory

Recognition memory

In recognition paradigms, participants are presented with previously-encoded stimuli mixed with lures (i.e., distractors), and instructed to determine for each of them if it is old or new. Alternatively, sets of 2 or more stimuli can be presented at test, among which subjects are required to identify the *old* item. In normally-functioning subjects, a stimulus presented in a recognition task is perceived with a varying degree of familiarity; that is, it *feels* more or less *familiar* to the subject

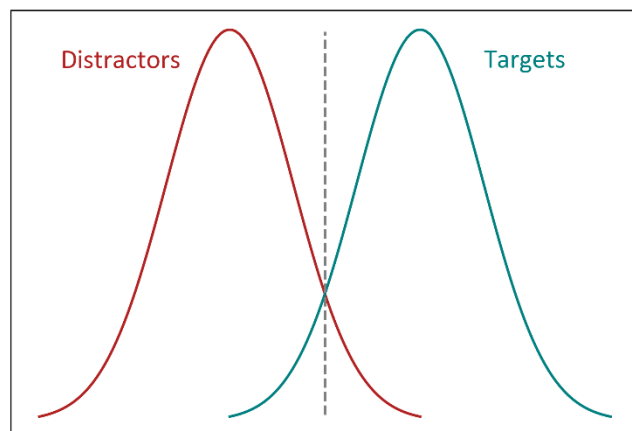


Figure 2.1. Probability of recognising old (cyan) and new (red) stimuli in a recognition task as function of the degree of familiarity. Theoretical example drawn from arbitrary data. Based on Besson et al. (2012).

(Egan, 1958; Atkinson & Juola, 1973). Accordingly, previously-presented stimuli are perceived with a higher degree of familiarity than lures, on average, and thus are more likely to be judged as old, or *recognised* (Mandler, 1980; figure 2.1). In this view, each subject uses an implicit criterion to decide whether or not a stimulus is familiar enough to be categorised as old (dotted line in figure 2.1). Considering that two response options (i.e., old and new) can be applied to stimuli of two kinds (i.e., targets and distractors), four types of events are described. The correct recognition of a target is termed *Hit*, whereas the false recognition of a distractor

is considered a *False Alarm* (FA). Finally, new responses correspond either to the *correct rejection* of a distractor or to the *omission* of a target.

Various attempts were made to model participants' responses in recognition tasks (e.g., Atkinson et al., 1974; Donaldson, 1996; Dunn, 2004). Whereas some authors claimed that two processes termed familiarity and recollection differentially contribute to recognition (e.g., Yonelinas, 1994; see also Wixted & Mickes, 2010), others favoured a single-process view (e.g., Slotnick & Dodson, 2005; Starns & Ratcliff, 2008). This contradiction has been the matter of a long-standing debate, which is not detailed here: in the rest of this chapter, we will assume the existence of two processes, and refer to this view as a *dual-process model* (Wixted, 2007). The process of *familiarity* is defined as the feeling that a stimulus has been encountered before, without necessarily remembering details from the encoding (Mandler, 1980; Yonelinas, 2002). In the context of recognition, this feeling is used as an indicator of prior exposure to the cue item. In contrast, *recollection* is the rich and detailed retrieval of a memory in its context (Yonelinas, 1999, 2002). In recognition tasks, recollection usually corresponds to the recall of information that was associated with the stimulus during encoding and is recalled at test, such as thoughts or contextual details (Montaldi & Mayes, 2010).

Subjective experience and the remember/know paradigm

Subjective experience can be used to dissociate familiarity and recollection. The *butcher in the bus* phenomenon is often cited as an example: it happens when meeting a person in an unusual context: while his/her face feels familiar, one cannot recall where/when this person was met before (Mandler, 1980). In other words, this phenomenon corresponds to familiarity without recollection. Several procedures have been designed to measure the respective contributions of familiarity and recollection to recognition memory. Among them, the *remember/know* (R/K) paradigm uses the subjective experience associated with recognition judgments (Gardiner et al., 1998; Rajaram, 1993; Tulving, 1989). For each item judged as old, participants are asked to indicate whether they specifically remember seeing the stimulus during encoding, or they simply know that have seen it. Accordingly, recognition in trials labelled as *remember* is believed to be supported by recollection, whereas *know* trials correspond to familiarity. An additional response option, *guess*, is frequently proposed to participants to avoid contaminating the other two response options in case of vague memory sensations.

Objective measure of recollection via source memory

Assessing memory for contextual information constitutes an objective measure of recollection memory. The class of paradigms based on this principle is termed *source memory* (Dudas et al., 2005; Yonelinas, 2002; see also Johnson et al., 1993). Each stimulus presented during encoding is associated with one or more contextual details among several possibilities. Those *source* details can be of several types, such as the position on the screen, background

colour, font type or size. Another possibility is to divide stimuli into several blocks presented sequentially. When an item is recognised at test, the participant is asked to recall the associated context. Accordingly, whereas stimulus recognition can be supported by familiarity alone, source memory requires the recall of contextual information from the encoding period, that is, recollection. It was argued, however, that source memory can be supported by associative familiarity if there are too few source options, since participants can simulate the association between the cue stimulus and each source option and choose between them on the basis of their degree of familiarity (J. R. Taylor & Henson, 2012). In the Process-dissociation procedure (PDP), items are also associated with contextual information at encoding (e.g., white versus grey backgrounds), but recognition is assessed under two conditions. In the *inclusion* condition, participants are asked to determine for each stimulus if it was presented or not during encoding, irrespective of the context. In the *exclusion* condition, in contrast, they are instructed to respond “yes” to the old items that were presented in a particular context (e.g., on a white background), and “no” to the other old stimuli (e.g., those presented on a grey background) in addition to the new stimuli. Whereas the inclusion condition can be resolved using familiarity only, the exclusion condition involves source memory and therefore taps into recollection (Bastin et al., 2004). The PDP paradigm is derived from Jacoby’s apparatus in which new stimuli were repeated across the recognition task (Jacoby, 1991; see also Jennings & Jacoby, 1997). This manipulation provokes familiarity for those repeated distractors, and forces the use of recollection to determine whether the stimulus was presented during encoding or only repeated during recognition.

Confidence ratings and the ROC paradigm

The Receiver-operating characteristics (ROC) differs from the procedures presented above in that it is based on confidence ratings (review in Yonelinas & Parks, 2007). Participants are asked to indicate how confident they are that the item is old or new. A six-points scale is generally used, ranging from *sure old* (1) to *sure new* (6). The proportions of each response given to targets and lures are then calculated. ROC curves correspond to the cumulative proportions of responses given to targets as function those proportions for lures. For instance, the third point has for abscissa the proportions of responses 1, 2, and 3 given to lures, and for ordinate those proportions for targets (figure 2.2). The diagonal line therefore represents a theoretical situation in which targets and lures are not separated on confidence judgments, or chance level (Yonelinas & Parks, 2007). In normally-functioning subjects, the area under the curve

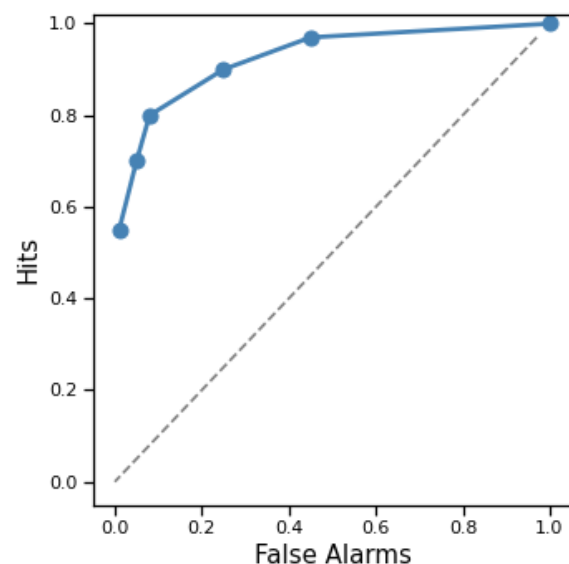


Figure 2.2. Example of ROC curve. Theoretical example drawn from arbitrary data.

(sometimes called “bowing”) represents memory sensitivity. Based on the assumption of two processes contributing to recognition, familiarity would contribute to this component of the ROC curve. In contrast, the first point represents the contribution of recollection, as it is drawn from the proportions of targets (usually high) and lures (usually low) items recognised with the highest degree of confidence. In the case of distractors with a high degree of familiarity, for instance foils very similar to targets, recollection may also lead to rejection, a phenomenon termed *recollection rejection* (Rotello et al., 2000).

2. The dual-process view of MTL regions and recognition

Neuropsychological evidence for a dual-process model

The demonstration of disproportionate impairments of recall memory as compared to recognition memory in presence of focal hippocampal lesions (Barbeau et al., 2011) suggested a partial independence between the brain circuits involved in these tasks. In line with a dual-process model, recall would rely on recollection, which is supported by the hippocampus. In contrast, recognition can be performed with familiarity only, and thus is (partially) spared in case of isolated hippocampal lesions. This view predicts that measuring the respective contributions of recollection and familiarity to recognition should reveal selective impairments depending on the MTL regions lesioned. Bastin et al. (2004) studied patient M.R. who presents with an isolated hippocampal lesion, using the PDP. Whereas M.R.’s performance equated that of controls in the inclusion condition, he made significantly more false alarms in the exclusion condition for repeated items, indicating a deficit in recollection (see also Verfaellie & Treadwell, 1993). Consistently, Yonelinas et al. (2002) reported that recollection was impaired following hippocampal damage, whereas larger MTL lesions impaired both recollection and familiarity using both the ROC and R/K procedures. Those results were later replicated in patients with lesions to the hippocampus (Aggleton et al., 2005; Holdstock et al., 2005; Turriziani et al., 2008; Yonelinas et al., 2004) and to the fornix and mammillary bodies (Vann et al., 2009). Düzel et al. (2001) also reported congruent results from electro-encephalography (EEG). The reverse pattern of results was reported by Bowles and colleagues (2007) in N.B., a patient with selective PRC damage. Using the ROC and RK procedures, they evidenced preserved recollection but impaired familiarity. In addition, the authors manipulated response deadline in a recognition task and showed that N.B. was impaired in the short deadline (i.e., 400 ms) but not in the long deadline condition (i.e., 2000 ms), suggesting that recognition in this patient was supported by recollection only.

The dual-process model of the MTL and recognition memory

Although some studies yielded controversial results (Gold et al., 2006; Manns et al., 2003; Manns & Squire, 1999; Reed & Squire, 1997), the study of patients with selective lesions either to the hippocampus or the PRC mainly supports a dual-process account of recognition memory (Eichenbaum et al., 2007). The main representative of this view is the Dual-Process

Theory proposed by Aggleton & Brown (1999). This model describes two main pathways involved in recognition. The first underpins recollection and involves the hippocampus, perirhinal, entorhinal, and parahippocampal cortices, as well as sub-cortical and frontal regions (figure 2.3 left). The second, underlying familiarity, does not depend on the hippocampus; but relies on the PRC (figure 2.3 right). Importantly, those pathways rely on partially separate, but interleaved structures (Aggleton & Brown, 2006). Although this model fits the data showing that recollection and familiarity can be impaired independently, it has been claimed that it could not explain all patterns of deficits found in patients. First, it was reported that patients with selective hippocampal lesions were impaired in recognition tasks when targets and foils were highly similar (Holdstock et al., 2002, 2005; Migo et al., 2009). Under such circumstances, targets and lures present overlapped familiarity distributions, and the criterion (or threshold) used to separate them becomes inefficient (Holdstock et al., 2002; figure 2.1). Therefore, the task cannot be performed using familiarity only. This pattern is predicted by the Complementary Learning Systems model (CLS; McClelland et al., 1995; Norman & O'Reilly, 2003). Like the dual-process theory, the CLS model stipulates that the hippocampus is crucial for recollection whereas the PRC performs familiarity; but adds a mechanistic modelling¹ of how those processes are computed, which explains the modulations of recognition performance by task manipulation (Holdstock et al., 2002). Another point made by Montaldi and Mayes (2010) is that recollection and familiarity differ regarding two aspects. One is that recollection involves the recall of elements not directly (or physically) present at test, whereas familiarity does not. The second aspect is *information*: while familiarity involves the cue stimulus only, recollection involves associative information in addition to the cue stimulus. In line with this observation, a body of research has investigated the effect of the information on which memory is tested as a manipulation of recognition paradigms, which we will refer to as *memory content*.

¹ The CLS is a neural-network based model. The field of neural-networks is beyond the scope of this thesis. The CLS is briefly presented here, however, as its predictions are relevant to the study of how MTL lesions impact recognition memory.

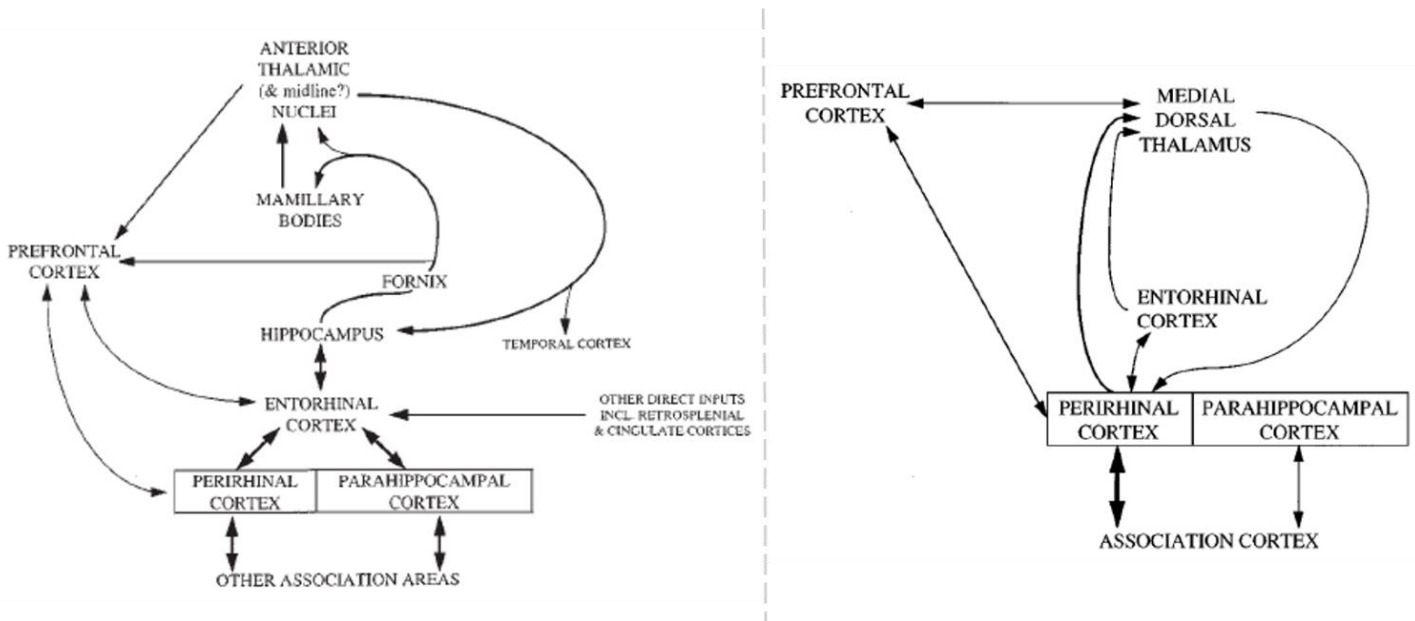


Figure 2.3. Dual-process model proposed by Aggleton & Brown (1999). Left: Hippocampus-dependant circuit underlying recollection, Right: Hippocampus-independent circuit underlying familiarity. A simplified version can be found in Barbeau et al. (2010).

3. Recognition: between memory processes and memory content

Inconsistent results from recognition memory

In addition to the situations in which recollection is required, research also demonstrated that hippocampal patients were impaired in recognition memory depending on the memory content assessed. Memory content was first modulated using different types of associative materials. The recombination procedure has often been used to study associative recognition. It consists in presenting paired stimuli in the study phase; some of which are presented in the same form at test whereas others are presented in a *recombined* form. Recombined pairs are formed from stimuli that were presented during the study phase, but in a different pair (figure 2.4). Since all test stimuli include items presented during encoding, foils differ from targets only in that their association has changed, thus recognition can only

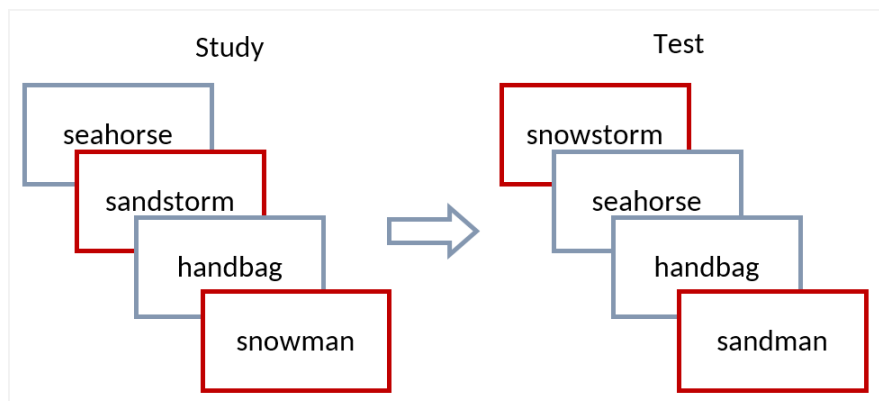


Figure 2.4. Recombination procedure illustrated in the intra-item condition. Grey boxes represent targets; red boxes represent lures. Adapted from Mayes et al. (2007).

be performed via memory for the associations. Associative recognition has been tested under three main conditions: (1) *intra-item* associations (e.g., words formed of 2 components that can be recombined, figure 11); *within-domain* associations (e.g., face-face or object-object pairs); and *between-domain* associations (e.g., face-word or object-locations pairs).

The case of Y.R., a woman who developed amnesia at the age of 48 following the administration of an opiate drug, has been extensively documented (e.g., Holdstock et al., 2000). Mayes and colleagues (2002) reported that while her recall memory was markedly impaired, her recognition memory was preserved and unmodulated by task manipulations such as the nature of the material (i.e., verbal vs. visual), amount of items and amount of foils per target, task delay, task difficulty, and task format (i.e., forced-choice vs. yes/no). In contrast, Y.R.'s recognition performance was impaired for object-location associations (Holdstock et al., 2002). This deficit extends to other between-domain associations: words and temporal positions, visual items and temporal order, animal pictures and profession names, faces and voices, faces and names, words and definitions, and pictures and sounds (A. R. Mayes et al., 2004). In contrast, Y.R. performed normally in recognition tasks for intra-item and within-domain associations (e.g., word-word or face-face). The same pattern was found in another patient with similar lesions (Holdstock et al., 2005). Those results suggest that the hippocampus supports recognition for associations between different kinds of information, specifically. One possible explanation is that recognising between-domains associations requires recollection; whereas familiarity is sufficient in the case of within-domain association, especially through unitisation (Yonelinas et al., 1999; further explanations in Montaldi & Mayes, 2010; and A. Mayes et al., 2007). However, by reviewing psychological, lesion, and neuroimaging results, Mayes and colleagues (2007) showed that familiarity can support recognition memory even for non-unitised associations. Evidence rather point toward a domain dichotomy, with the PRC processing unitised and non-unitised intra-item and within-domain associations, whereas the hippocampus is critical for associating any other kind of information such as between-domain, spatial, temporal, or other contextual information. This view specifies that the hippocampus uses a pattern-separating algorithm to bind information into highly distinct representations, which is particularly suited for recollective memory. The PRC, in contrast, uses a pattern-generalising algorithm that makes representations less distinct, and is more suited for familiarity memory.²

The domain-dissociation and the emergence of content-based models

The domain dissociation proposed by Mayes, Montaldi, and Migo, can be related to the observation of non-associative content-specific deficits in patients with MTL damage. Cipolotti and colleagues (2006) reported the case of V.C., a patient with specific hippocampal lesions. While his performance in recognition was normal for unknown faces, it was at floor for verbal and topographical materials. Crucially, the authors used the ROC procedure and found that

² The role of the hippocampus in pattern-separation was documented elsewhere (e.g., Zotow et al., 2020), and will be discussed in next chapters.

familiarity and recollection memory showed similar patterns of impairment/preservation depending on the material type. The same results were reported by Bird et al. (2007) in patient R.H., who presents an isolated lesion of the right hippocampus. R.H. has normal recollection and familiarity for faces, as well as verbal materials (likely supported by his intact left MTL), whereas his recollection and familiarity memory are both impaired for topographical material. Taylor and colleagues (2007) investigated 3 patients with lesions limited to the hippocampus and 3 patients with larger MTL lesions that included the PHC, ERC, and PRC. Hippocampal patients had impaired recognition for scene stimuli but not for faces, whereas MTL patients were impaired for both kinds of stimuli. More recently, Lacot et al. (2017) re-examined the case of J.M.G, a patient with large MTL lesions that spared the right hippocampus and a limited portion of the medial PHC, first documented by Barbeau and colleagues (2011). J.M.G performed normally in visual recall tasks, but was impaired in recognition tasks for single items, with similar impairments of familiarity and recollection. In contrast, both familiarity and recollection were normal when assessed using scene stimuli. These observations revealed that the patterns of impairment produced by MTL lesions map different kinds of memory content, which fed a different class of models, centred on memory *content*, and built around the concept of *binding*.

4. Towards content-based models of the MTL

Main framework of the content-based models

The class of models termed here content-based models is built on the hierarchical organisation of neocortical inputs to the MTL and between MTL subregions. The PRC receives its inputs from the ventral-visual stream (VVS or “what” pathway), and from lateral temporal and frontal cortices (Mishkin et al., 1983; Suzuki & Amaral, 1994, 2004). The PHC receives most of its inputs from regions that belong to the dorsal-visual stream (DVS or “where” pathway)

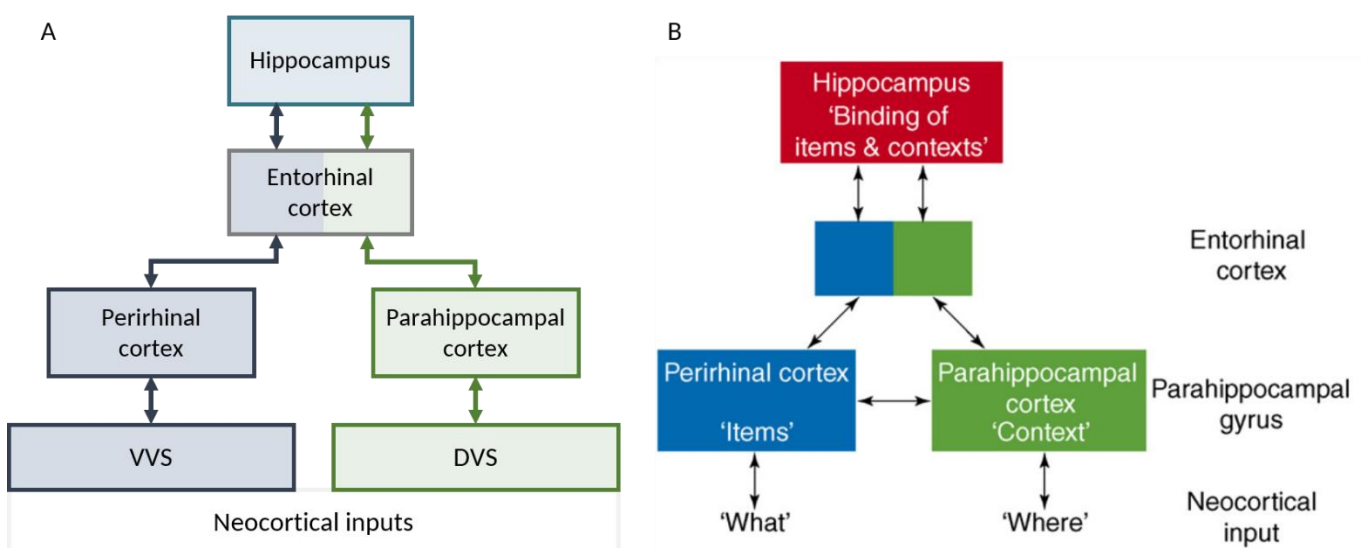


Figure 2.5. A: General framework of the MTL hierarchical organisation, adapted from Lavenex & Amaral, (2000) and Shimamura, (2010). B: Binding item and context model, Diana et al. (2007).

such as the retrosplenial, cingular, posterior parietal, and super temporal, cortices (Kobayashi & Amaral, 2003; Suzuki & Amaral, 1994). The PRC and PHC project onto the ERC, which in turn sends its output to the hippocampus (Lavenex & Amaral, 2000). This hierarchical organisation of MTL regions (figure 2.5.A) provides a general framework particularly suitable for models built around the concept of *binding*. Shimamura (2002) proposed the relational binding theory (RBT), and later the hierarchical RBT (hRBT; Shimamura & Wickens, 2009). The central notion of this account is hierarchical binding: memory representations are created at a given level of the hierarchy by binding together inputs from the lower levels, and are in turn bound with other information in the next level. Specifically, the PRC would bind together information stemming from the VVS, resulting unified item representations; whereas the PHC would gather inputs from the DVS to form context representations. Those representations would converge in the hippocampus, which binds them to create episodes. Thus, together with the principle of binding, emerged the idea that MTL regions are specialised according to the type of content they process (e.g., Ranganath, 2010).

The binding item and context model

The principles of hierarchical binding and content specialisation are shared by several other models. Among them is the Binding Item and Context model (BIC; Eichenbaum et al., 2007), which puts the emphasis on the associative role of the hippocampus. Diana, Yonelinas and Ranganath (2007) reviewed 40 fMRI studies of recognition memory to provide an overview of how the PRC, PHC, and hippocampus contribute to familiarity and recollection for single and associative contents. They reported that the hippocampus and PRC respond preferentially to recollection and familiarity, respectively. This pattern is coherent both with the dual-process theory and with content-based models (i.e., hRBT, BIC). In addition, the PHC presented a pattern similar to that of the hippocampus (i.e., frequently found activated during recollection, rarely for familiarity), which contrasted with that of the PRC. Finally, the hippocampus is strongly involved in associative memory, particularly between-domain, whereas the respective contributions of the PRC and PHC were comparable and weaker than that of the hippocampus. These observations match the BIC model predictions: the PHC would represent context information whereas the PRC would represent item information; and the hippocampus would bind the item and context information together (figure 2.5.B). Both the PHC and hippocampus are involved in recollection as the former supports contextual information, whereas the latter supports the association between item and context. Consistently, associative recognition memory relies particularly on the hippocampus, and recruits the PHC and PRC in a similar manner as they represent the information to be associated. Davachi et al. (2003) reported fMRI results particularly coherent with this account: activity in the hippocampus and PHC correlated with subsequent source memory but not with item memory, which rather correlated with PRC activity (consistent results were later reported in Staresina et al., 2011). Other models have been built on similar bases as the hRBT and BIC. For instance, the Convergence, Recollection, and Familiarity Theory (CRAFT) uses the

same hierarchical framework, but adds an algorithm-based differentiation between the hippocampus and MTL cortices derived from that of the CLS model (Montaldi & Mayes, 2010).

Stepping away from the modular view of the MTL

Overall, the content-based models offered an alternative to process-based models in explaining how the MTL supports episodic memory. Differences exist between these models (for a detailed overview of the shared and different predictions of BIC, CRAFT, and MUST models, see Montaldi & Mayes, 2010); yet they share common basic principles. Importantly, this view does not deny the existence of recollection and familiarity as memory processes, or their relevance in understanding human memory. Rather, they propose a different conceptualisation of how these processes emerge from MTL regions. The hippocampus would be specialised not in episodic recollection *per se*, but in item-context associations. The PRC and PHC, in contrast, would be specialised in representing items and contextual information, respectively. The recruitment of those regions is therefore modulated by task material; but also by task demand. For instance, the PRC alone may support recognition memory since standard recognition tests do not evaluate memory for contextual information. Another advance allowed by these models is to challenge the modular view according to which the MTL would constitute a memory system, segregated from other systems, such as a posterior visual-perception system (Shimamura, 2010). In other words, this led to reconsider the borders between MTL and extra-MTL cortical areas. In this regard, the concept of hierarchy applied to the internal organisation of the MTL also applies to its main inputs, namely the VVS and DVS. In particular, Bussey, Saksida, and Murray (2005), proposed regarding the VVS as a hierarchical continuum, which includes the PRC, rather than as a separate functional module in the service of perception.

Synthesis

Overpassing the multiple memory systems view, two memory processes were identified: familiarity and recollection. Paradigms such as the R/K, source memory, and the ROC procedure, allowed to measure the respective contributions of these two processes to recognition memory. From the observation of specific recollection and familiarity impairments in patients with hippocampus and PRC damage, respectively, emerged the dual-process theory. Further investigations of recognition memory revealed that in addition to the process engaged, task material also modulated the impairments found in patients with lesions to the hippocampus. These observations gave rise to an alternative framework of the MTL, built around the notions of *memory content* and *binding*. This class of models marked a break with the modular view of the MTL, and laid the foundations of the conception presented in the next chapter: representation-based models of the MTL.

Chapter III - The MTL beyond memory: the high-resolution binding and scene construction theories

The models described in the present chapter differ from the former in that they extend the functions associated with the MTL beyond the memory domain. As we will see, this view has been supported by studies that found impairments in patients with lesions to the MTL in tasks that do not require any memory operation. It also helps resolving the contradictory findings presented in chapter I that priming and WM are impaired in amnesia under certain circumstances. Two different and complementary perspectives that emerged from those results will be presented: the high-resolution binding and scene construction theories. Those models differ in regard to their interpretation of the diversity of cognitive domains that involve the MTL in general and the hippocampus particular.

1. From associative memory to high-resolution binding

Principles of the High-resolution binding model

Built on the idea that the hippocampus binds together item and context information in the service of episodic recollection (Eichenbaum et al., 2007), the high-resolution binding (HRB) model integrates evidence that this region is also critical to other cognitive domains (Yonelinas, 2013). The defining feature of the HRB model is that it explains this evidence through the lens of high-resolution (or *precision*). This is relevant, notably, in the context of episodic memory search, as the association between an item and contextual details needs to provide a unique-enough signature to allow recovering a specific memory among similar ones (Ekstrom & Yonelinas, 2020). This seems in adequacy with computational accounts according to which the hippocampus performs pattern-separation, thus being particularly suited for later highly-specific retrieval, or *pattern-completion* (McClelland et al., 1995; Norman & O'Reilly, 2003). Yonelinas (2013) empathised two main aspects of recollection, namely its associative character and its high-resolution, and claimed that those components may serve functions other than LTM. The author reviewed behavioural work in human and concluded that recollection- and familiarity-like processes can be pinpointed in WM tasks. In complex visual discrimination tasks, a state-, and a strength-based processes were identified (Aly & Yonelinas, 2012). Whereas state-based responses relied on local, low-level features, strength-based responses corresponded to global-feature match/mismatch between the images. Consistently, the HRB predicts that the hippocampus, by supporting high-resolution binding, would be critical to strength-, but not state-based perception.

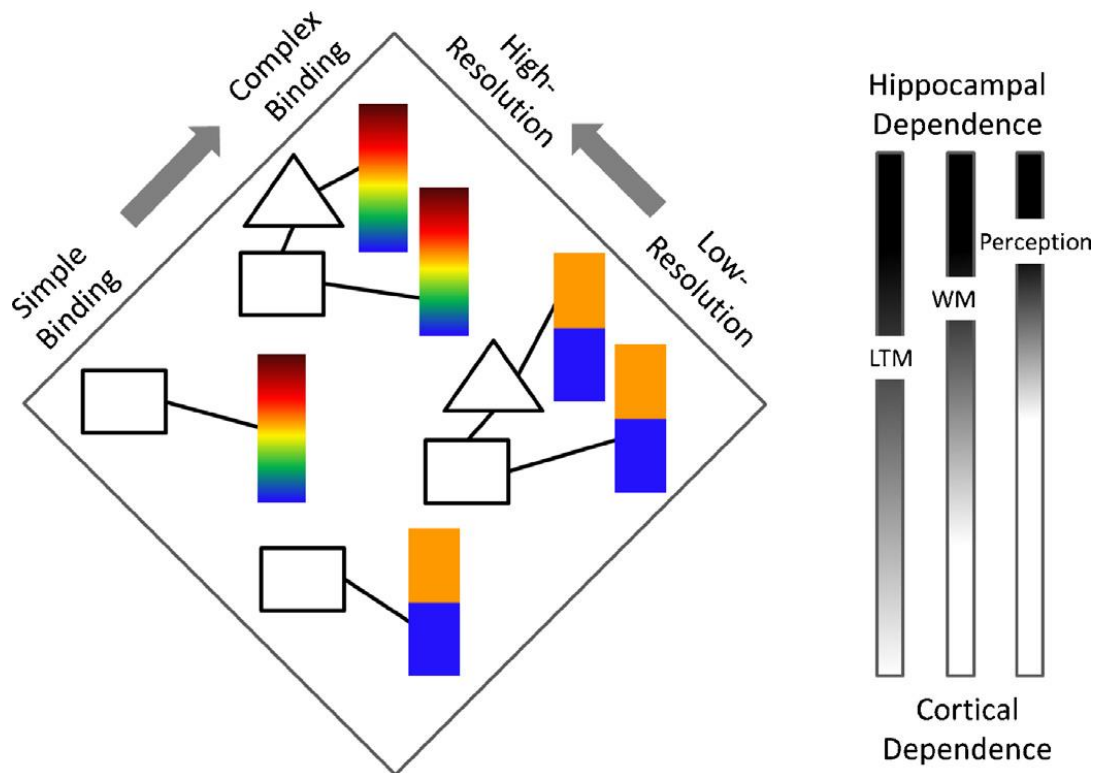


Figure 3.1. From Yonelinas (2013): the high-resolution binding model. The square on the left represents task demand according to two dimensions: the complexity of binding and the resolution of the representations. On the right is represented the degree to which a cognitive activity depends on the hippocampus versus on other cortical areas.

Experimental evidence in favour of the HRB

According to the HRB model, the extent to which a cognitive task relies on the hippocampus would depend both on the complexity of the binding between information that it requires and on the resolution of those information (figure 3.1). Critically, these characteristics have been manipulated in tasks that imply no long-term memory demand, thus allowing to test the model's predictions. As was presented in chapter I, although WM is generally preserved in amnesia, impairments were found under certain circumstances. The studies by Olson and colleagues, who reported that WM was impaired in hippocampal patients for object-location associations but preserved for both types of information when presented alone, particularly fits the HRB model (Olson, Moore, et al., 2006; Olson, Page, et al., 2006; see also more recently Jonin et al., 2019; Borders et al., 2022, 2017). Moreover, patients with the same profile were impaired in a task requiring to maintain colours in WM (Zhang & Yonelinas, 2012; for the original apparatus see Zhang & Luck, 2008). Crucially, the patients were not impaired in the general type of colour selected, but only in the precision of the colour (for further evidence on detail-generation impairments in amnesia, see Rosenbaum et al., 2009). Impairments in WM for scene-object associations (Hannula et al., 2006) and for topographical materials (Hartley et al., 2007) following hippocampal damage also support a role in WM for high-resolution associative stimuli. Controversial results were reported by Jeneson and colleagues: in two studies they showed that patients with selective lesions to the

hippocampus performed normally in an object-location associations memory task when the delay corresponded to WM, but were impaired at longer delays, presumably tapping LTM (Jeneson et al., 2010, 2012). In regard to the HRB model, it was claimed that the task used in those studies could be resolved without engaging the hippocampus due to the low resolution of the stimuli (Yonelinas, 2013). Finally, Hannula and Ranganath (2008) investigated MTL activity using a WM paradigm that required the association of several objects with spatial locations. The hippocampus responded preferentially to object-location match than mismatch trials, and preferentially to position mismatch than swap mismatch trials (i.e., an object was moved from one position to another vs. two objects were swapped, respectively).

The HRB predictions beyond the memory domain

Complex visual-discrimination impairments evidenced in patients with MTL lesions were also reviewed by Yonelinas (2013). Those deficits were found for scene stimuli in case of lesions to the hippocampus, and for scenes and single items such as faces and objects in case of larger MTL lesions that encompassed the PRC (Barens et al., 2005, 2007; A. C. H. Lee, Buckley, et al., 2005, 2006; A. C. H. Lee, Bussey, et al., 2005). Visual-discrimination impairments for complex associative objects resulting from damage to the hippocampus were also reported by Ware and colleagues (2011) and by Knutson and colleagues (2012; although the authors interpreted the results in a different way than Yonelinas, 2013). Using the procedure previously employed to dissociate state- from strength-based perception (Aly & Yonelinas, 2012), Aly, Ranganath, and Yonelinas (2013) identified specific impairment of strength-based perception in patients with hippocampal lesions. Furthermore, hippocampal activity measured through fMRI in control participants correlated with strength-based, but not state-based perception. Those data fit the HRB model in supporting that the hippocampus is critical to visual perception when high-resolution materials must be associated only, as compared to situations in which the task can be resolved using local perceptual features. Additional fMRI evidence came from Lee and Rudebeck (2010), who reported that increasing the spatial demand of a WM task (i.e., scene comparison vs. shape-layout associations comparison) enhanced activity in the hippocampus and PHC even when the WM demand was low. In contrast, no such effect was found when increasing the WM demand (i.e., n-1 back vs. n-2 back). Barens and colleagues (2010) further supported the role of the hippocampus in the visual discrimination of scenes; and showed that it was modulated by the manipulation of viewpoint, that is, whether the stimuli were presented from the same or different angles.

Beyond the HRB model

The HRB comes with several implications. It does not ascribe a role in LTM to the hippocampus; rather this region would be critical to any cognitive activity that requires the binding of high-resolution elements. In a complementary way, Olsen and colleagues (2012) proposed the Binding and Comparison model. According to this model, the hippocampus would support the binding of multiple disparate features, and the comparison of the

representations thus created with other representations stored in memory. If this view is compatible with the HRB model, other proposals are not. Notably, numerous studies on WM and perception have linked the hippocampus with the scene processing (for reviews see A. C. H. Lee et al., 2012; Graham et al., 2010). Scene stimuli were also used in the study by Aly and colleagues (2013) presented above. The authors argued that scenes are the optimal type of material to investigate strength- and state-based perception. Yet, Yonelinas (2013) also claimed that the contribution of the hippocampus to complex visual perception is not specific to scenes. Rather, scene images would fall into the scope of the hippocampus since they include numerous discrete and precise elements that one must bind together in order to create a coherent representation (and to support strength-based perception). In this regard, the HRB model contrasts with the view presented in the next section, in which the concept of spatial scene is central.

2. From space representation to scene construction

The MTL and space representation

If numerous studies have linked MTL regions with associative memory, the role of these regions in space processes has been extensively investigated as well (e.g., O'Keefe & Nadel, 1978). An exhaustive account of this literature is beyond the scope of this work (for further details, readers are referred to Moser et al., 2008), but a brief introduction of the main concepts is necessary. First, *place cells* elicit firing rate specific to the position of the individual in the environment (O'Keefe & Dostrovsky, 1971; for evidence in humans see Ekstrom et al., 2003). *Head direction cells*, in contrast, code for a specific direction, independently of the individual's position in the environment (Moser et al., 2008; Wiener & Taube, 2005). Cells that code for the boundaries of the environment have also been identified, and termed *boundary vector cells* (Barry et al., 2006) or *border cells* (Solstad et al., 2008). Place, head direction, and border cells have been found in the hippocampus, among other regions such as the ERC. Finally, *grid cells*, found in the ERC, represent the environment in the form of a matrix, and are thought to provide the hippocampus with spatial information (Fyhn et al., 2004, 2007). The identification of those spatial-selective cells fed the idea that the hippocampus serves as a cognitive map, first proposed by Tolman (1948) and continued by O'Keefe and Nadel (1978; see also Eichenbaum et al., 1999). Referred to as the Cognitive Map Theory, it assumes that spatial navigation relies on a malleable map of the environment, which is independent from the position of the individual. This notion, supported by the ability of rats to use shortcuts as well as strategy-based navigation, was opposed to the previously presumed simple stimulus-response behaviour in non-human animals (Tolman, 1948). Building on this idea, it was proposed that place cells would code the position where the animal thinks it is rather than its actual position in the environment. Bridging the animal and human literatures, the Boundary Vector Cell (BVC) model empathised the central role of border cells in representing the boundaries of the environment (Bird et al., 2012; Burgess et al., 2000). These hippocampus-dependent representations would be critical to any cognitive activity that requires to

represent a spatial scene, such as spatial navigation, episodic memory, but also mental imagery (Bird et al., 2010).

The Scene Construction Theory

Thus emerged the assumption that the hippocampus is specialised in representing spatial scene, which strongly influenced further research on MTL functions (Maguire & Mullally, 2013). It was previously demonstrated that episodic recollection and future thinking both rely on the hippocampus, in patients with amnesia (Klein et al., 2002; see chapter I) and in fMRI studies (Addis et al., 2007; Schacter & Addis, 2009). The shared feature of remembering the past and imagining the future was thought to be the projection of oneself (in the past and the future), or mental time travel (Tulving, 1985b). However, Hassabis and colleagues challenged this hypothesis with two concurrent studies. They used fMRI to investigate the common and distinct brain networks underlying the imagination of new scenes, recall of previously imaging scenes, and recall of episodic memories. As a conjunction

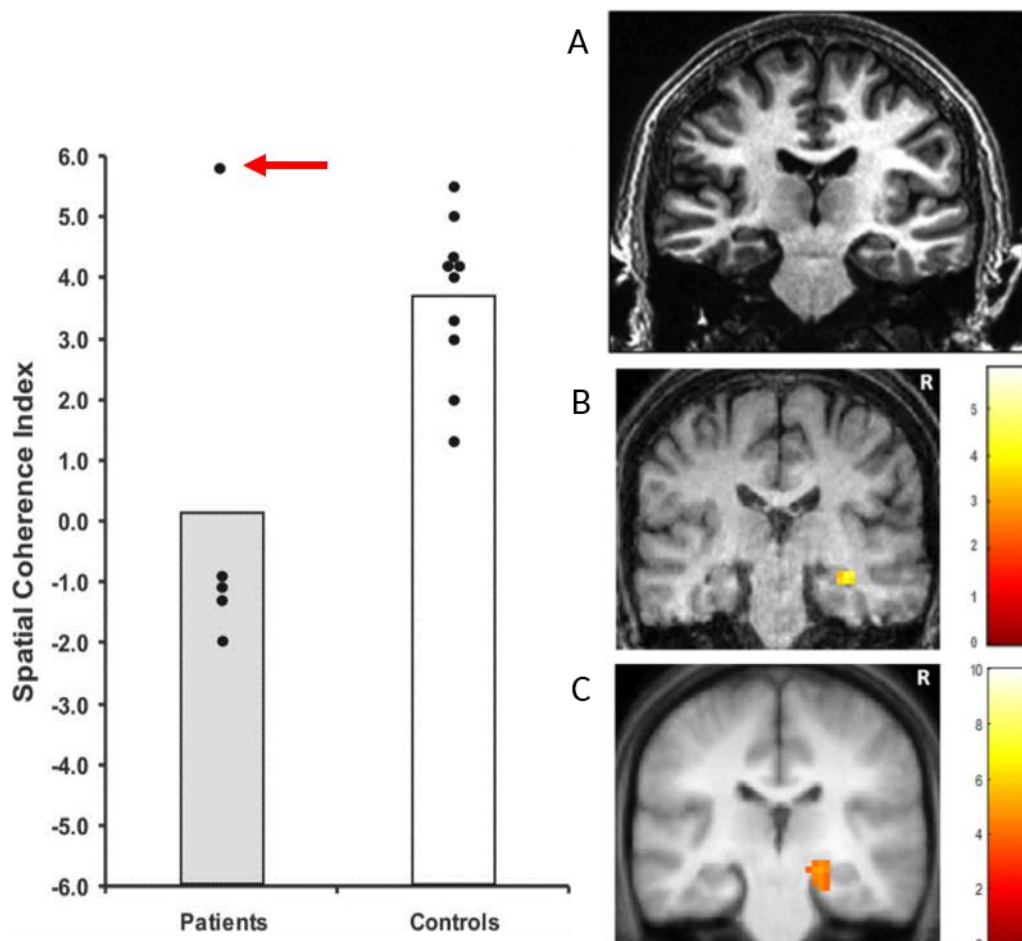


Figure 3.2. Adapted from Mullally et al. (2012) and Hassabis et al. (2007). Left: Spatial coherence index scores of patients with hippocampal lesions and healthy controls; the red arrow points the score of patient P01. Right - A: Anatomical MRI scan of patient P01 who presents hippocampal atrophy bilaterally; B: fMRI activation in the remnant hippocampus in patient P01 in the scene imagination task; and C: fMRI activation in the hippocampus in healthy controls in the same task.

between these three conditions, they identified a *scene representation* network that included the hippocampus, PHC, and retrosplenial cortex (Hassabis, Kumaran, & Maguire, 2007). Complementary to those results, they demonstrated that patients with lesions to the hippocampus were impaired in imagining new (fictitious) scenes (Hassabis, Kumaran, Vann, et al., 2007). Furthermore, they reported that it is the spatial coherence of the imagined scenes that lacks in those patients. Mullally et al. (2012) further investigated patient P01, described in the study by Hassabis and colleagues, who presents preserved scene construction, and especially preserved spatial coherence (figure 3.2, left). They showed that when performing the scene imagination task previously used in control subjects, patient P01 activated hippocampal remnants (figure 3.2, right). Based on those observations, they concluded that the construction of spatial scenes relies on the hippocampus, rather than the ability to project oneself in time, since newly-imagined fictitious scenes are not bound to a particular time (Hassabis & Maguire, 2007). They thus proposed the Scene Construction Theory (SCT; Hassabis & Maguire, 2009; Maguire & Mullally, 2013). Finally, Zeidman, Mullally and Maguire (2015) used fMRI to investigate the networks involved when participants viewed, imagined, and maintained (in WM) scenes. They reported that the hippocampus was particularly recruited by scene perception and imagination, but less recruited by maintaining these representations. Consistent with previous results (A. C. H. Lee & Rudebeck, 2010), the engagement of this region in WM for scenes would be due to the need to mentally construct a scene, rather than to the WM load.

Evidence in favour of the SCT

According to the SCT, the hippocampus would support the construction of spatially-coherent scenes. This capacity would be central to episodic memory, imagination, future thinking, and spatial navigation (figure 3.3). Scenes are here defined as “coherent object-containing spaces in which we can operate”; and a scene that extends over time constitutes an episode (Zeidman & Maguire, 2016). The SCT hence fits well with studies that have linked scene discrimination with the hippocampus in both lesion and fMRI studies (review in Graham et al., 2010; A. C. H. Lee et al., 2012). Scene discrimination was demonstrated to especially rely on the hippocampus when the images to discriminate are presented from different points of view, termed the *viewpoint effect* (Barens, Henson, et al., 2010; A. C. H. Lee, Bussey, et al., 2005). It was argued that this spatial manipulation would force the generation of an internal representation of the stimulus, which prevents the use of local low-level features (A. C. H. Lee et al., 2012), which is also coherent with the SCT view. Evidence for impaired priming for scene layouts (Ryan et al., 2000) and for spatial configurations (Chun & Phelps, 1999) in case of amnesia also point in that direction (see chapter I). McCormick et al. (2017) asked patients with lesions to the hippocampus and healthy controls to perform a possible/impossible judgement task with scene images. They divided the impossible scenes into two categories: semantic and constructive. Semantic impossible scenes depicted semantic violations (e.g., breathing underwater) whereas constructive impossible scenes depicted spatial violations (e.g., perspective errors). On average, patients with hippocampal lesions were impaired in the

constructive condition but performed as well as control subjects in the semantic condition. Taken together, those results confirm that the hippocampus support the spatial coherence of scenes.

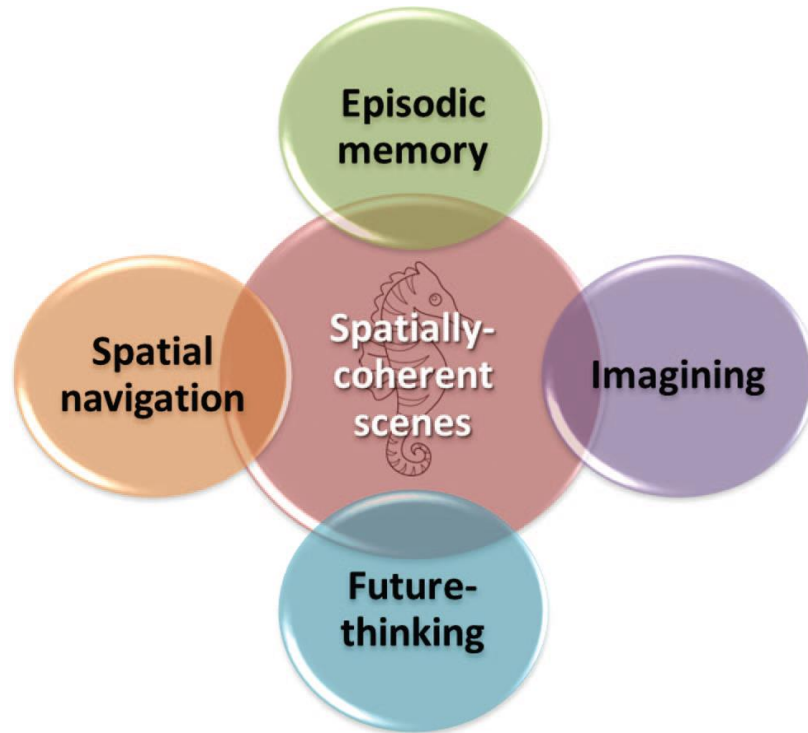


Figure 3.3. From Maguire & Mullally (2013): Scene Construction Theory. The construction of spatially-coherent scenes is the common brain mechanism between episodic memory, imagination, future thinking, and spatial navigation.

The Boundary Extension effect

Additional arguments in favour of the SCT came from studies on the Boundary Extension (BE) effect. The BE paradigm consists in a visual recognition task of natural/realistic scene images, in which normally-functioning subjects consistently tend to remember the images they previously saw as wider than they were, termed the BE effect (Intraub et al., 1998; Intraub & Richardson, 1989). This memory error would be due to an extrapolation of the perceived scene beyond its boundaries (figure 3.4). Chadwick et al. (2013) investigated the brain network underlying the BE using fMRI in healthy participants. They reported activation of the hippocampus and PHC as the result of the comparison between trials where the BE effect occurred to those where it did not occur. Additionally, using connectivity analyses they found that the hippocampus drove activity toward the PHC and back to the visual cortex. Consistently, it was demonstrated that the BE effect was markedly reduced in patients with damage to the hippocampus, resulting in a memory advantage for those patients as compared to control subjects (Mullally, Intraub, et al., 2012). These results suggest that the hippocampus is “responsible” for the BE effect, that is, the extrapolation of a scene beyond its perceived

boundaries. This also helps resolving the discrepancy between SCT and BVC models: whereas the BVC model considers boundaries as the physical limits of the space in which the individual is currently evolving, the SCT views boundaries as “the point from which the hippocampus must extrapolate the upcoming environment” (Maguire & Mullally, 2013). Thus according to the SCT, the hippocampus would continuously represent our perceived and unperceived spatial environment.

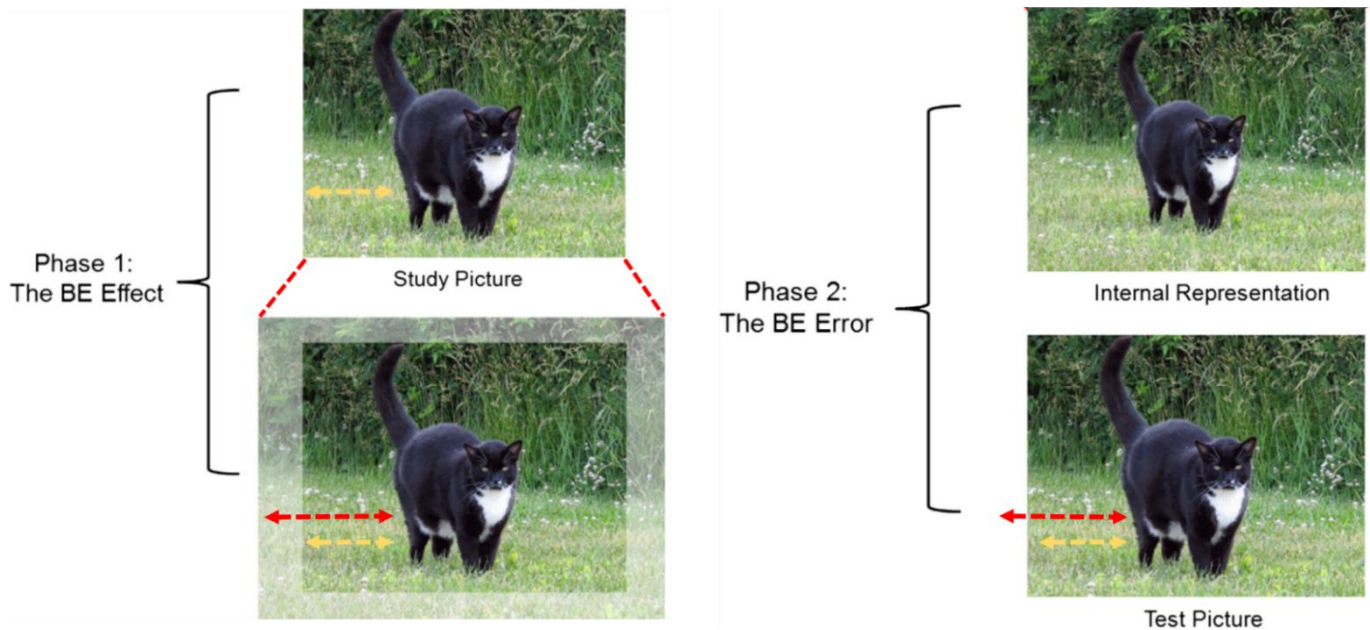


Figure 3.4. Adapted from Chadwick et al (2013): Boundary extension (BE) effect. During phase 1 when the study picture is presented, the subject extrapolates beyond its limits. The yellow arrow represents the distance between the object and the borders in the original image. The red arrow represents this distance distorted in the subject’s internal representation due to the extrapolation. During phase 2 the subject’s internal representation does not match the test picture (here the study and test pictures are the same), which leads to the BE error.

The HRB and SCT: opposed but complementary?

As we saw in this chapter, the HRB and SCT models both received considerable support from lesion and fMRI studies, and helped progressing in understanding how MTL regions contribute to a large variety of cognitive domains. However, these models seem in contradiction with each other in the specialisation they ascribe the hippocampus. The main principle of the HRB is the binding of high-resolution features, whereas for the SCT it is the representation of spatially-coherent scenes. When confronting these views emerges the question of how they explain the evidence that support the competing model. First, how does the HRB model explain the involvement of the hippocampus in spatial scene processing? As we presented earlier, with regard to the HRB, scenes rely on the hippocampus because they require the binding of multiple and precise elements, instead of being its core specialisation. More recently the authors also identified a specific *precise-location* impairment in navigation tasks in case of hippocampal damage (Kolarik et al., 2018). We may next ask: how does the SCT explain the role of the hippocampus in non-spatial associative processing? Consistent with

the main idea of the SCT, one proposed explanation is the mental imagery potential of the material, as supported by an fMRI study by Clark and colleagues (2018). The authors also identified scene construction as one, but not the only, key factor underlying various cognitive abilities that depend on the hippocampus (Clark et al., 2019). Hence the fundamental mechanisms ascribed to the hippocampus by the HRB and SCT may seem irreconcilable at first glance. Two approaches will be considered to resolve this discrepancy: an integrative theoretical account and the exploration of the hippocampus long-axis.

Synthesis

The MTL has been associated with functions other than long-term memory, such as WM, imagination, and visual perception. From the proposal that the hippocampus binds items and their context emerged the high-resolution binding model, to which the *precision* of the material processed is central. Concurrently, the hippocampus was also associated with scene construction, a view in which *spatial coherence* is crucial. These two models differ in the specialisation they ascribe to the hippocampus. In the next chapter, a model termed representational-hierarchical, which combines these two types of predictions, and gives an integrative account of the MTL, will be described.

Chapter IV – The representational-hierarchical view: An integrative model?

In the last chapter we showed that the hippocampus has been associated with high-resolution binding and scene construction functions, two fundamental principles that may seem incompatible. Moreover, despite proposals of whole-brain models (Baldassano et al., 2016; Barry et al., 2019; Summerfield et al., 2010), the HRB and SCT models lack a comprehensive theoretical account of MTL regions. In this chapter we will present the representational-hierarchical (HR) model, which integrates the predictions of the HRB and SCT models into a larger view of MTL and extra MTL regions.

1. *The representational-hierarchical approach*

The perceptual-mnemonic feature conjunction model

The RH view emerged from the observation of object perceptual discrimination impairments following PRC lesions in non-human primates (Buckley et al., 1997, 2001; Buckley & Gaffan, 1997, 1998; Goulet & Murray, 2001). Those results led Bussey, Saksida, and Murray (2005) to rethink the functional specialisation of this region: being at the junction between object recognition and object perception, they termed this function “object identification” (see also Murray & Bussey, 1999). To account for the different results reported in the literature, they proposed a neural-network based model: the perceptual-mnemonic feature conjunction (PMFC; further development of computational models related to this question can be found in Cowell et al., 2006). This model proposes to consider the PRC as part of the VVS (see chapter II for more details on the ventral and dorsal visual streams), and to focus on the hierarchical aspect of this pathway. The most caudal regions (i.e., posterior) would represent simple visual features, whereas more rostral regions (i.e., anterior) would process more complex features. Features are progressively assembled in a hierarchical way from posterior to anterior regions; hence the PRC conveys object representations resulting from the convergence of multiple visual features. In case of PRC lesion, the individual would need to rely on representations of lower complexity, held by more posterior regions (Bussey et al., 2005). Therefore, tasks that require to process the conjunction of visual features should be failed if the PRC is damaged only if they cannot be resolved using local visual features. Consistent with this proposal, visual-discrimination impairments in primates were sensitive to perceptual load, that is, the size of the stimuli set (Buckley & Gaffan, 1997). According to the PMFC, however, it is the degree of perceptual overlap between the stimuli to discriminate,

termed *feature ambiguity*, not the number of stimuli, that is crucial³. Bussey et al. (2002) manipulated feature ambiguity while maintaining the number of stimuli constant, and demonstrated feature-ambiguity dependant deficits in PRC-lesioned primates, thus supporting the PMFC view.

From non-human primates to humans

The paradigms used in subsequent studies to investigate visual discrimination in humans with MTL lesions were largely inspired from those used in the primate literature. Among those paradigms, the oddity judgement task has been widely used (A. C. H. Lee, Barense, et al., 2005). In this task, subjects are presented with several images (i.e., generally 3 to 6) and instructed to identify the *odd* stimulus, or the one stimulus that differs from the others. Concurrent discrimination tasks, in which participants must determine whether two stimuli are similar or different, and matching tasks, where they are asked to find which among two or more stimuli matches a reference stimulus, were also used (for review see Saksida & Bussey, 2010). Barense et al. (2005) tested patients with lesions either limited to the hippocampus or including both the hippocampus and PRC on a visual-discrimination task for single stimuli, and manipulated features ambiguity (figure 4.1). While patients with lesions to the hippocampus performed similarly to control participants, those with large MTL lesions that included the PRC

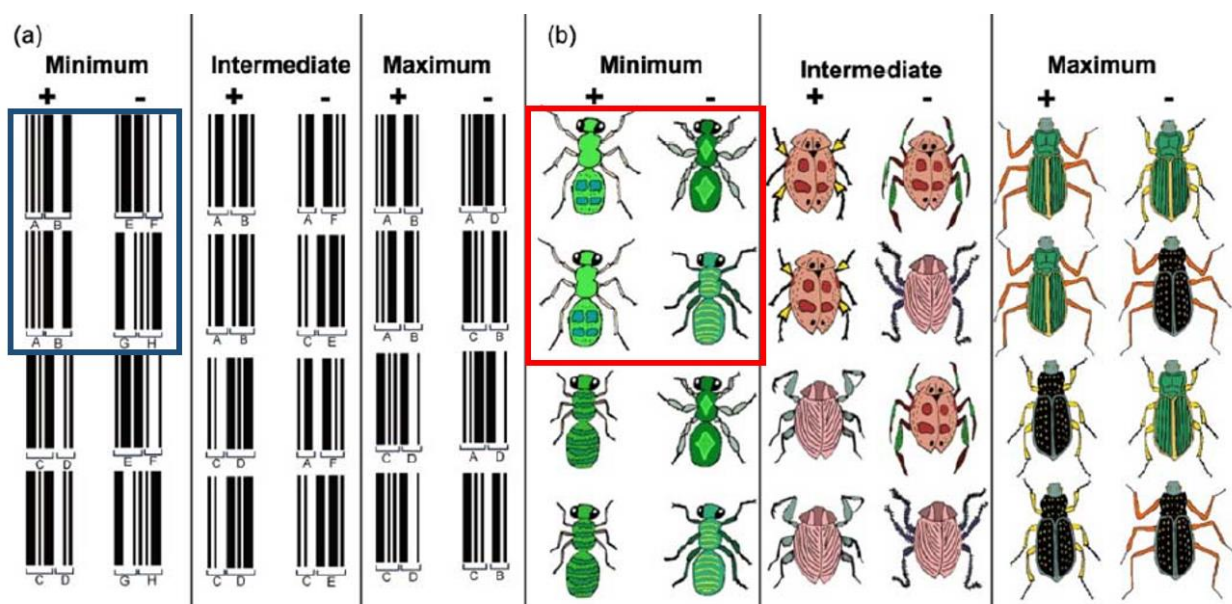


Figure 4.1. From Barense et al. (2005): Stimuli used to test the effect of feature ambiguity. One trial included 4 stimuli, presented in pairs. Blue and red squares represent the four stimuli constituting example trials in the barcode and bug conditions, respectively. Two stimuli were “targets”, here presented on the left of each trial, and two were “non-targets”. For each type of stimulus there were three ambiguity conditions: minimum, intermediate, and maximum, distinguished by the number of perceptual features that differentiated the targets from the non-targets. In the case of barcodes this manipulation was illustrated by letters for comprehension purposes.

³ In Buckley & Gaffan (1997), feature ambiguity and set size may have been confounded. More explanations can be found in Bussey, Saksida, and Murray (2005) and in Bussey & Saksida (2007).

were impaired for all types of items when feature ambiguity was high. Lee and colleagues (2005) used a similar design but tested discrimination for scenes, faces, objects, abstract art images, and colours. Expectedly, patients with MTL lesions were impaired in all conditions but the colour condition, whereas impairments in patients with selective hippocampal damage were limited to the scene condition. Similar to Barense et al., these impairments were revealed only in presence of a high overlap between the stimuli. In a concurrent study, the authors manipulated the presentation viewpoint in a face and scene oddity task (A. C. H. Lee, Buckley, et al., 2005). In “different view” trials, the stimuli to discriminate were presented from different angles, whereas in the “same view” condition, there were presented from the same angle. The scene-specific and scenes and faces deficits found in hippocampal and MTL patients, respectively, were observed only in the different view condition. Those results were replicated both in the same kind of patients (Barense et al., 2007) and in a double-dissociation between patients with primary lesions of the hippocampus due Alzheimer’s disease and patients with anterior temporal lesions (including the PRC) due to Semantic Dementia (A. C. H. Lee, Buckley, et al., 2006). It was proposed that in presence of a viewpoint manipulation, participants must rely on an internal, viewpoint-independent, representation of the stimuli to perform the task (Hartley et al., 2007; Barense, Henson, et al., 2010). In regard with the PMFC (and RH) view, presenting the stimuli from different viewpoints prevents the use of low-level visual features, and forces to rely on the conjunction of features that corresponds to the level of complexity of the stimuli presented (i.e., scenes/objects/faces; for reviews see Graham et al., 2010; A. C. H. Lee et al., 2012).

The representational-hierarchical model

Although contradictory results were reported (e.g., C. Stark & Squire, 2000), evidence from neuropsychological and neuroimaging studies strongly support the feature-conjunction mechanism assumed by the PMFC. Applying this proposal to humans, Bussey, Saksida, and Murray proposed the *representational-hierarchical* model (Murray et al., 2007; Saksida, 2009; Saksida & Bussey, 2010). This model extends the idea of feature conjunction along the VVS to the MTL, and hence unifies the principles of the PMFC and the hierarchical framework of content-based models presented in chapter II (figure 2.5; Shimamura, 2010). Accordingly, there is no MTL module dedicated to memory and segregated from a posterior module underlying perception (figure 4.2). In line with this proposal, the authors referred to the VVS as the ventral visual-perirhinal hippocampal stream (Saksida & Bussey, 2010). As proposed by the PMFC, *representations* are assembled in a *hierarchical* manner from posterior to anterior regions of the VVS, a mechanism termed *feature conjunction*. The representations processed by the PRC correspond to a-contextual whole objects; a class of stimuli later termed *entities* (Bastin et al., 2019). The hippocampus would sit at the highest level of this hierarchy and integrate object-level representation with contextual information stemming from the PHC. This is essential to form scenes representations (Graham et al., 2010), thus explaining the role of the hippocampus in scene processing. This mechanism also explains the involvement of the hippocampus in high-resolution binding, which can be seen as the conjunction of highly-

complex features. The RH model therefore encompasses the predictions of both the HRB and the SCT accounts detailed earlier. The main assumption of the RH view is that the brain regions involved in a given cognitive process would depend on the representational complexity of the stimuli, not on the psychological nature of the task. From *representational complexity* emerged the concept of *dimensionality*, which we will present in the next section.

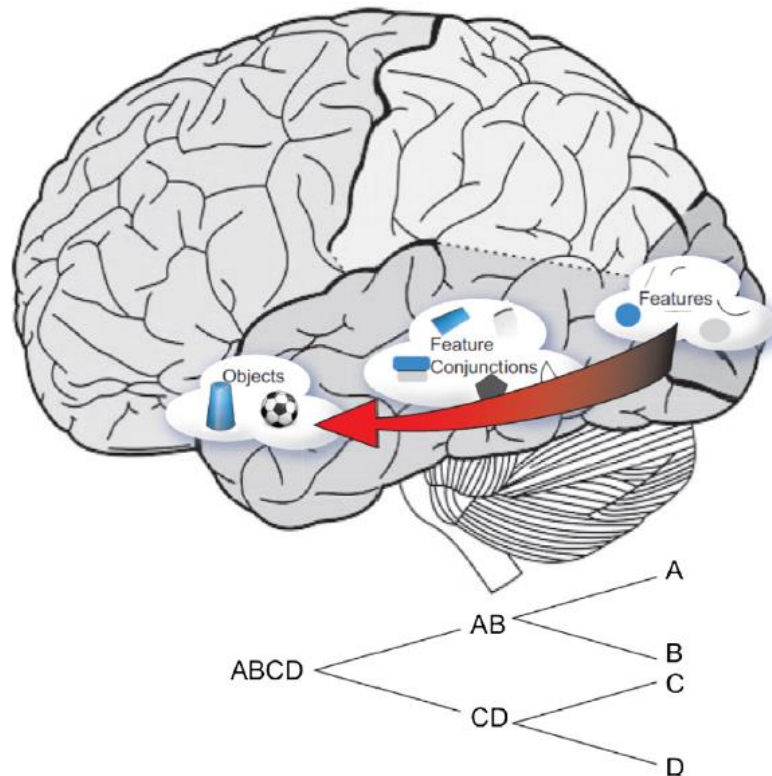


Figure 4.2. From Kent et al. (2016): Representational-hierarchical view of the ventral-visual stream and medial temporal lobe.

2. Representations, operations, and dimensionality

Breaking down cognitive processes

Recently, Cowell, Barense, and Sadil took the RH view a step further by proposing the representations versus operations breakdown (Cowell et al., 2019). Their starting point is that various theories have tried to explain the link between the hippocampus and PRC on the one hand and recollection and familiarity, respectively, on the other (see chapters II and III). They questioned the relevance of using those memory processes as labels in understanding the functions of MTL subregions. Recollection and familiarity, as we saw, are cognitive *processes*. Processes are, in Cowell and colleagues' view, mental phenomena that can be identifiable though introspection. Those phenomena would be too high-level to be mapped onto brain regions, rather, the authors argued that "these concepts are the phenomena to be explained, not the components of an explanatory mechanism". They thereby propose to decompose those processes into lower-level components, namely *representations* and *operations*. The

concept of representations, already used in several theories including the RH model (Saksida & Bussey, 2010), is here defined as a pattern of neural firing that represents (or “stands for”) a stimulus of the environment. Simple perceptual features, objects, faces, scenes, events, are all examples of representations. In contrast, operations are computations performed by the brain, that can be applied to various representations. Pattern-completion and pattern-separation are here considered neural operations. Cowell et al. took the example of recollection, the retrieval of a richly-detailed and contextualised memory. The operation underlying recollection is (akin to) pattern-completion⁴, or a memory reconstruction based on limited cues. In other words, it implies the retrieval of elements from memory that are not directly present among the test material. The representation involved in recollection is a contextualised and detailed memory of an event or episode. The crucial point is that the definition adopted by the authors of pattern-completion can be applied to any kind of representations. Reciprocally, operations other than pattern-completion can be applied to the representation involved in recollection. It is from the combination of these components that recollection emerges. Familiarity consists in generating a memory signal and assessing its strength, which we will term here *memory strength-signal*. The definition of familiarity frequently used in the literature assumes nothing on the kind of representation involved (a face, an object, a place, can feel familiar).

Representational dimensionality

Breaking down those processes into representations and operations allows one to investigate the influence of each component in isolation. Then the next question asked by Cowell, Barense, and Sadil is: does recollection rely on the hippocampus “because” of its pattern-completion-like retrieval, or because of the detailed and contextualised memory content it implies? More generally, does the operation or the representation constituting a given memory process explains the brain regions recruited by this process? Thereby two hypotheses emerge: one operation-based and one representation-based (figure 4.3). In an operation-based account, brain regions are dedicated to operations, therefore the same brain areas should be recruited by an operation, irrespective of the representations conveyed. In a representation-based account, in contrast, similar brain regions should be engaged by various operations as long as the representation is held constant (Cowell et al., 2019; see also Ross et al., 2018). The RH account assumes a representation-based functional organisation of the VVS and MTL, irrespective of the operations. Representations would be differentiated by their *dimensionality*. In keeping with the original PMFC/RH view, the concept of dimensionality is built around representational complexity, but encompasses the multi-modal aspect of hippocampal representations (figure 4.4): are considered high-dimensional the memories that

⁴ Cowell et al. (2019) acknowledge that other operations may be involved in recollection, such as expectancy violation (O’Connor et al., 2010) or prediction errors (Exton-McGuinness et al., 2015), but chose to focus on pattern-completion because it is the most central operation involved in recollection. We may add here that pattern-completion-like operations are often provoked in the paradigms used to assess recollection, as presented in chapter II (i.e., source memory, remember/know).

include “arbitrary associations between complex, crossmodal, or spatial elements” (Cowell et al., 2019). This kind of representation would rely on the hippocampus, regardless of the operation performed on it. Importantly, the RH view does not deny the existence of recollection or its relevance when studying human memory. Rather, it assumes that recollection *emerges* from the combination of a high-dimensional representation and the operation of pattern-completion-like retrieval, and relies on the hippocampus due to the representation involved. Accordingly, pattern-completion could happen anywhere along the VVS-MTL stream, depending on the dimensionality of the representation that is “completed”. Likewise, pattern-separation, or making similar memory representations more different to reduce later interference, has been associated with the hippocampus (Guzowski et al., 2004; see also Zotow et al., 2020), and can be considered as an operation. In the RH view, pattern-separation corresponds the use of feature conjunction of a given level of complexity to resolve lower level perceptual ambiguity, and thus can occur at any stage of the VVS-MTL hierarchy (Kent et al., 2016). While dimensionality is frequently manipulated experimentally by using different classes of stimuli (e.g., scenes and objects), it is also influenced by task instructions. For instance, the retrieval of simple representations in a cued-recall task may require the engagement of the hippocampus due to the association between the cue and target stimuli (Cowell et al., 2019).

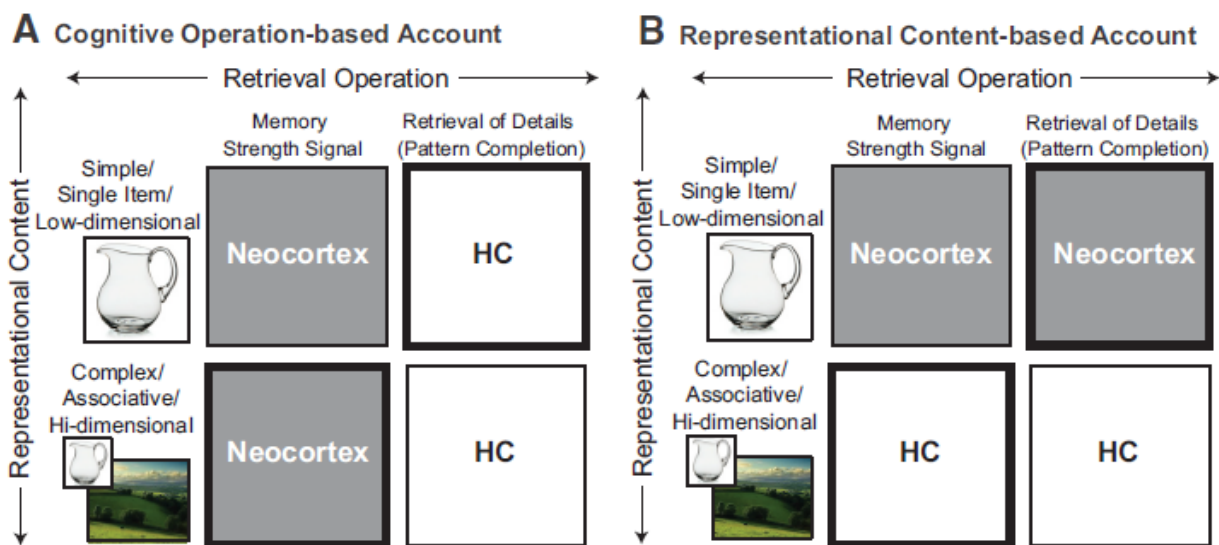


Figure 4.3. From Cowell et al. (2020). A: Operation-based account of the MTL; B: Representation-based account of the MTL. HC: hippocampus.

Predictions of the RH view

An assumption of this view that has been scarcely investigated is that regions outside the MTL, in particular regions of the VVS posterior to the MTL, should be engaged in memory for simple perceptual features. One study provided direct evidence in favour of this prediction by demonstrating associative learning between simple visual features in early visual areas using fMRI neurofeedback (Amano et al., 2016). In addition, Gorlin et al. (2012) used degraded images (i.e., the Mooney images) to study the effect of prior knowledge on visual identification

of simple objects with fMRI, and pinpointed regions posterior to the MTL as responsible for these reconstructions. In contrast, the assumption that MTL regions should be engaged by various, memory and non-memory, cognitive operations, has been widely studied. This claim is supported by numerous studies as exposed above and in the previous chapter (review in Graham et al., 2010). However, with the proposal to break down cognitive processes into operations and representation emerged new predictions. In particular, whether the involvement of the hippocampus in pattern-completion depends on representational dimensionality, remains debated.

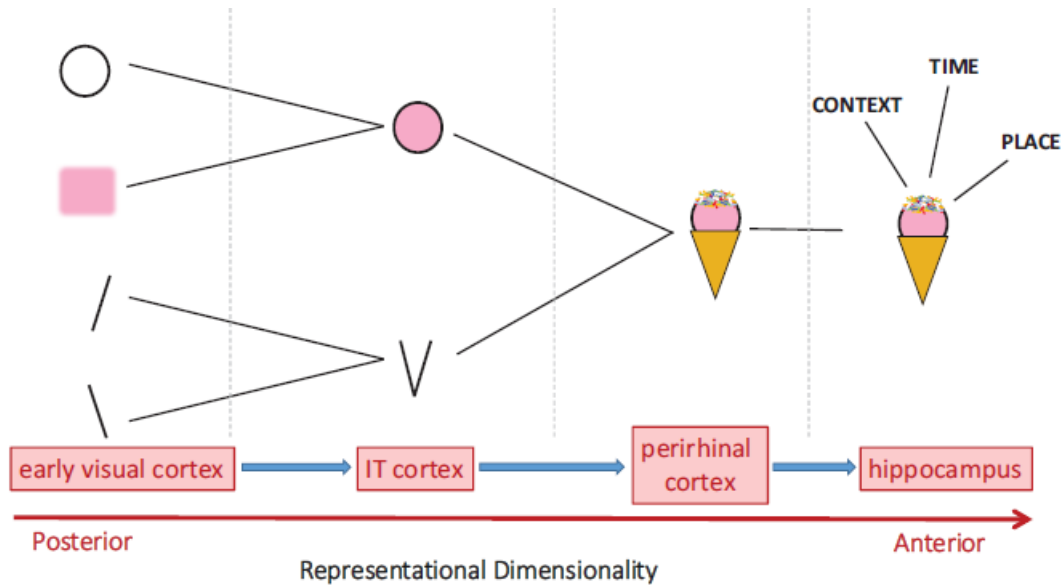


Figure 4.4. From Cowell et al. (2019): Theoretical illustration of the concept of dimensionality.

3. The patch protocol to investigate pattern-completion-like memory while manipulating representational dimensionality

Isolating pattern-completion from representational dimensionality?

As mentioned, whether the engagement of the hippocampus in pattern-completion is specific to high-dimensional representations remains to be demonstrated at this point. To answer this question, researchers needed to measure separately pattern-completion of low and high-dimensional representations. Methodological issues prevented the use of traditional recognition paradigms (presented in chapter II) to investigate this question. First, the retrieval of associated contextual information with the target stimuli is widely used to assess recollection, in paradigms such as the source memory and the PDP. In those paradigms, a stimulus and associated contextual information can be regarded as a high-dimensional representation in reason of its associative content. Therefore, pattern-completion like (or *recollective*) retrieval and high-dimensional representation are confounded. In contrast, the R/K procedure only consists in presenting the target stimulus and measuring subjective feelings, thereby avoiding this bias. However, presenting the same material during the

learning and test phases may trigger a strength-based memory operation, which would be confounded with pattern-completion. Thinking the problem in the other way, one could argue that when presented with the learned images in full at test, participants do not need to properly *complete* these images. Consistently, *remember* responses in R/K tasks usually reflect the retrieval of details associated with the cue during the learning phase (e.g., Migo et al., 2012). Therefore, the traditional R/K procedure also presents biases that needed to be overcome.

The patch-cue protocol as a solution

To solve this methodological challenge, Ross and colleagues proposed the patch-cue recognition paradigm (Ross et al., 2018). Patches are circular windows taken from the studied images, and used as partial visual cues for recognition (figure 4.5). Instead of being asked whether they specifically remembered seeing the items before, participants were instructed to attempt mentally reconstructing the original images from the patch cues. Therefore, R responses could be attributed to proper pattern-completion, given that participants did reconstruct the images from memory in those trials, and that those could not be contaminated by strength-based memory operations. For clarity and to avoid confusion with *Recollection* responses in traditional R/K paradigms, those R responses given by participants when presented with partial visual cues will be termed *Reconstruction* (or Rec) for the rest of this work. The authors manipulated representational dimensionality: half of the images were scenes whereas the other half were single objects; thus investigating pattern-completion of high- and low-dimensional representations, respectively. The crucial result of this study is that the hippocampus was engaged in the reconstruction of scene, but not object stimuli. Activity in the PRC, in contrast, did not differ between scene and object reconstruction. These results suggest that the high-dimensional representation, not the operation of pattern-completion, is responsible for the engagement of the hippocampus in recollection, which directly supports the representational hypothesis (Cowell et al., 2019). This crucial study raised a number of methodological and theoretical questions.

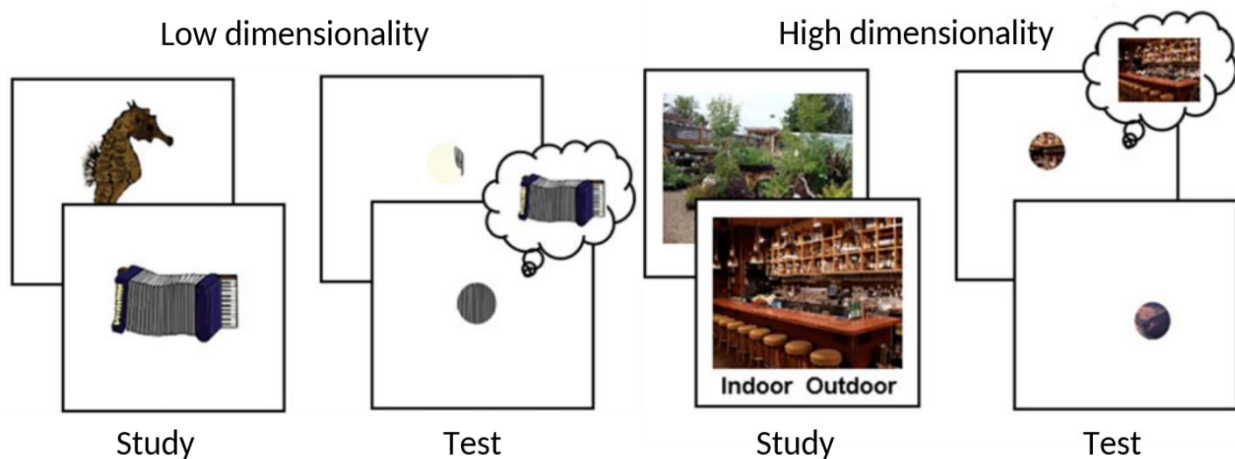


Figure 4.5. From Ross et al. (2018): Examples of low- and high-dimensional images presented during the study phase and patch cues presented during the test phase.

Methodological questions raised by the patch-cue protocol

First, the patch-cue recognition paradigm used by Ross and colleagues is inspired from the R/K paradigm. As such, one may wonder how these two versions of the paradigm differ from one another. Remember responses in the original R/K task are believed to reflect recollection. In contrast, reconstruction responses in the case of patch cues reflect the mental reconstruction of the original stimuli from the cues; an operation assumed to be equal when performed on high- and low-dimensional representations. In keeping with the RH view, the reconstruction of high-, but not low-dimensional stimuli, is akin to recollection. Recollection, however, is not limited to the dimensionality of the content that is retrieved, but is usually accompanied with a particular sensation of reliving one's personal past, or mental-time travel (Tulving, 1985b, 1989). Because mental-time travel certainly relies on the hippocampus, emerges the question of how this phenomenon contributed to reconstruction responses given by the participants for scene and object stimuli. The second methodological question raised by this protocol is whether reconstruction *is* comparable for scenes and objects. Said differently, is the operation of pattern-completion unmodulated by representational dimensionality? One could argue that these dimensions are not orthogonal, and that the operation performed on high-dimensional representations differs from that performed on low-dimensional representations, which could explain the differences in brain activity found between these conditions.

Theoretical questions raised by the patch-cue protocol

The second kind of questions raised by those results is theoretical. If the representation, not the operation, determines the engagement of the hippocampus and PRC in a given process, then the pattern of activity found for scenes and objects during pattern-completion should be observed for any other operation. One of the most extensively studied memory processes is familiarity. In the RH view, familiarity is underpinned by the operation of strength-signal memory, which can be applied to different representations such as scenes and objects (Cowell et al., 2019). In the patch-cue paradigm, when participants recognised a patch but could not reconstruct the original image, they responded "familiar" as in the R/K paradigm. Yet, since patch cues were used, it is those partial cues, not the entire images, that were judged as familiar. This does not allow to explore strength-signal memory for scenes and objects, as those patches do not present the full complexity of those representations. The demonstration by Ross and colleagues is therefore limited to pattern-completion, while according to the RH view this pattern of results should apply to any operation.

Synthesis

The RH model gives an integrative account of the functional specialisation of the VVS and MTL, that is, representation-based and hierarchically organised. Further, it was proposed to break down cognitive processes into operations and representations, and that

representations are the key factor determining the functional organisation of the MTL. The patch-cue protocol was designed to investigate pattern-completion of low- and high-dimensional representations. This procedure raises methodological and theoretical questions, which will be addressed in this work (see Thesis objectives section).

Chapter V: The anterior-posterior axis of the hippocampus and hemispheric specialisation

The RH model gives an integrative theoretical account that encompasses the vast majority of the results presented so far. If this model presents the advantage of incorporating MTL functions into a larger account of the VVS functional organisation, it lacks predictions regarding two other axes of brain organisation. The first is the anteroposterior (or long) axis of the hippocampus; the second is the hemispheric specialisation. In this chapter we will introduce these two axes, and ask how they interact with the RH principles of organisation.

1. The RH model and the anterior-posterior axis of the hippocampus

Dividing the hippocampus into long-axis segments

Until this point we have considered the hippocampus as a unitary structure, in compliance with the models presented so far. However, it was argued that this structure is heterogeneous, and that its different subregions may not be functionally equivalent (e.g., Fanselow & Dong, 2010). Functional differences were searched across hippocampal subfields in the first place (i.e., CA1-CA4, subiculum, dentate gyrus), but the long-axis specialisation gained growing interest in the last decade (Poppenk et al., 2013). To investigate functional differences across the long-axis of the hippocampus, two sections are usually distinguished. The anterior hippocampus (aHC) is delimited posteriorly by the apex of the uncus and broadly

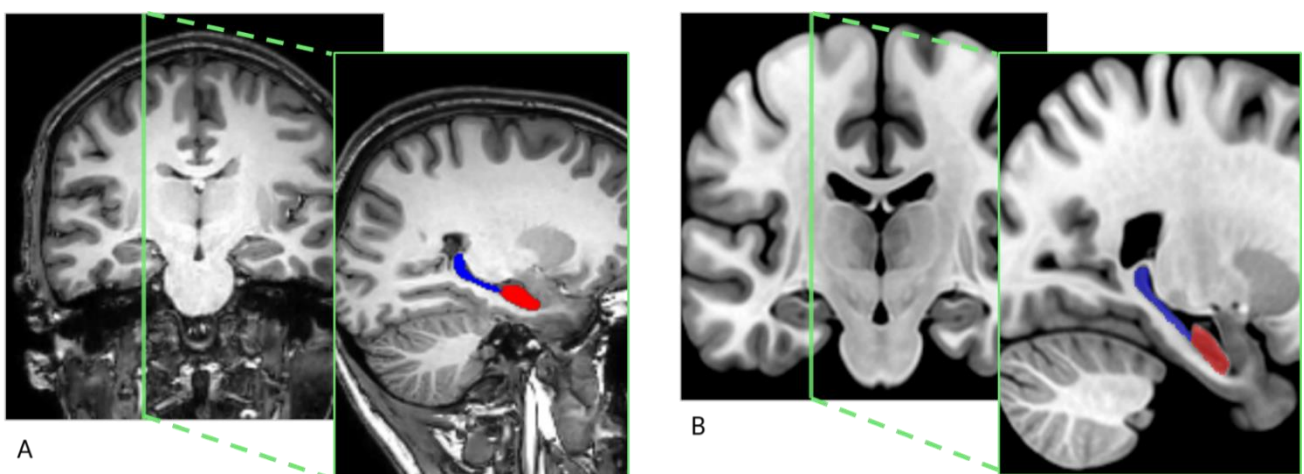


Figure 5.1. Segmentation of the posterior and anterior hippocampus. A: example of native anatomical T1 scan from one participant of Study 3. Posterior (blue) and anterior (red) hippocampus segmented using the Automated Segmentation of Hippocampal Subfields procedure (ASHS; see Chapter VII - methods section) are projected on the sagittal view. The position of the sagittal slice is indicated on the coronal slice by the green line. B: Approximately equivalent positions on the MNI152 template (see Poppenk et al., 2013).

corresponds to the anterior third of the hippocampus; the two thirds posterior to this landmark constitute the posterior hippocampus (pHC) (figure 5.1; Poppenk et al., 2013). Although other segmentations were proposed (see e.g., Strange et al., 2014; Brunec et al., 2018) and will be discussed later in this work, we will focus on this 2-sections framework for the moment. The first instance of long-axis model is the Hippocampal Encoding/Retrieval (HIPER) model, proposed by Lepage, Habib, and Tulving in 1998 after reviewing 52 position emission tomography studies. In this view, the aHC would perform memory encoding whereas the pHC would be responsible for memory retrieval. Evidence was reported against (Schacter & Wagner, 1999) and in favour of the HIPER model (Spaniol et al., 2009; for further development with the HERNET model, see Kim, 2015). One of the main criticisms of this account is that the encoding/retrieval effects are often confounded with novelty processing (Poppenk et al., 2010, 2013). Moreover, this dichotomy only applies to the memory domain, leaving aside other domains such as WM, imagination, and visual perception, in which the hippocampus is involved (see chapters III and IV).

The hippocampus long-axis specialisation: reunifying the SCT and HRB models?

In the case of the SCT, Zeidman and Maguire (2016) identified the anterior hippocampus specifically as being responsible for constructing spatial scenes. Precisely, a region situated in the medial portion of the anterior hippocampus resulted from the overlap between the fMRI activity found for the perception and the imagination of scenes (figure 5.2). Taking this question a step further, Dalton et al. (2018) investigated the contribution of the hippocampus to scene construction, array construction, and object imagination, using high-resolution fMRI. Crucially, in the array construction condition, participants were asked to imagine a 2-dimensional grid and to position objects at given locations on this grid. Therefore, while the scene construction condition taps into the core mechanism of the SCT model, the array construction condition reproduces the object-location tasks failed by patients with lesions to the hippocampus (Olson, Page, et al., 2006). In addition to confirming the previously reported specialisation of the anterior hippocampus for scene construction, they revealed a partially different network underlying object-array association, which included a posterior region of the hippocampus, as well as anterior ERC. Finally, in the object imagination condition a region in the anterior-lateral hippocampus was recruited. Care must be taken, however, when interpreting this latter result, since fMRI is only correlational and unlike scene construction and object-array association, object imagination is not impaired following damage to the hippocampus. The same authors (McCormick et al., 2021) furthered this investigation by disentangling the respective contributions of the hippocampus to scene layout and scene complexity processing. Participants were presented with pairs of scene images, and instructed to look for differences between the two images either in the spatial layout or in the colour of the scenes. Using this design (i.e., using the same stimuli but varying the instructions) they could counterbalance the images across the conditions. Also manipulating the complexity of the images (i.e., the amount of perceptual features), the colour-complex condition was thus akin to the task used by Aly and colleagues presented earlier (2013). Whereas the layout

condition recruited the anterior hippocampus, the colour condition was associated with the posterior hippocampus; and those effects were not modulated by the complexity of the images. Taken together, those results show that the HRB and SCT models may be compatible when considering the hippocampus not as a whole but as a heterogeneous structure: scene construction would rely on the anterior part of the hippocampus and high-resolution processing on its posterior part.

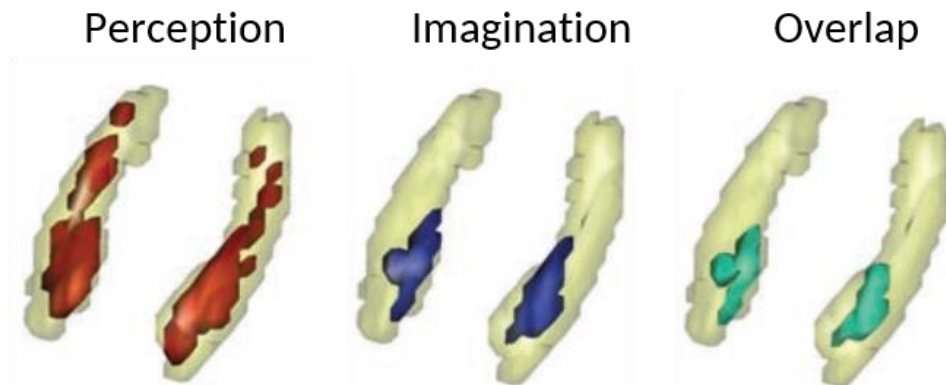


Figure 5.2. Adapted from Zeidman & Maguire (2016): fMRI activity projected on a template of the hippocampus for the perception and imagination of scenes, and the overlap between them.

The broad-to-sharp model of the hippocampus as an extension of the RH view

A substantial amount of studies investigated the long-axis specialisation of the hippocampus, and were reviewed by Poppenk, Evensmoen, Moscovitch, and Nadel (Poppenk et al., 2013). To explain the variety of evidence reported in these studies, positive versus negative motivational processing, memory encoding versus retrieval, cognitive versus spatial, vestibular versus visual, global versus local, gist versus details, and pattern-completion versus pattern-separation, dichotomies of the aHC versus pHC (respectively) were proposed. Poppenk and colleagues claimed that although there is evidence in favour of each of these models, none of them can account for the diversity of results reported in the literature alone. Based on these observations, and on the different connexions of the aHC and pHC with brain regions inside and outside the MTL, they proposed an integrative model of the hippocampus long-axis organisation. With prevailing inputs from the PRC and temporal pole (through the anterior ERC), the aHC would represent broad, global information, including global spatial representations. This would contribute to creating “sketches”, or gist representations of events. The pHC, in contrast, with prevailing PHC connexions (through posterior ERC), would represent sharp/detailed information, including local and precise spatial positions. This is consistent with the distribution of place cells, the density of which is weaker in the aHC, with larger receptive fields, compared to the pHC. This view encompasses the results presented above: scene construction can be regarded as the construction of a global spatial representation, and thus taps into the specialisation of the aHC; whereas high-resolution binding recruits the pHC through the association of sharp/detailed information. However,

Poppenk et al.'s model also overpasses these functions, as global representations are not limited to scenes, and local sharp representations are not limited the association of details. Rather, this view applies to any kind of representation, the determinant characteristic of which would be its "grain" of resolution (Poppenk et al., 2013; also Brunec et al., 2018; Robin & Moscovitch, 2017). This grain-based principle of organisation seems compatible with the RH view, since it is independent of the operations performed on the representations. Indeed, while the authors acknowledge that the internal connectivity of the hippocampus biases its anterior portion toward pattern-completion and its posterior part toward pattern-separation, they propose that these operations are not segregated to these two regions of the hippocampus.

Locating recollection in the long-axis of the hippocampus

When examining the compatibility between the RH model and the broad/gist to sharp/detail account of the hippocampus proposed by Poppenk and colleagues, the case of recollection is particularly interesting. Recollection was found to be associated with the pHC volume specifically (Poppenk & Moscovitch, 2011). Because recollection ability was measured using source memory, this relation reflects the role of the pHC in retrieving contextual details associated with the cue stimulus (Snytte et al., 2022). This differs from the patch-recognition apparatus presented above (Ross et al., 2018), in which no associative details must be retrieved; rather, recollection is approximated through scene reconstruction. Considering the hypothesised role of the aHC in representing global spatial information, and particularly in scene construction (McCormick et al., 2021; Zeidman & Maguire, 2016), one could expect scene reconstruction from patches to rely particularly on the aHC. In other words, this view predicts that the aHC should have been engaged by scene reconstruction more than by object reconstruction. In contrast, since participants were not asked to retrieve associated details (or any other kind of sharp information), the pHC should have been engaged similarly by the scene and object conditions. Ross and colleagues, however, divided the hippocampus into three equal-length segments (i.e., anterior, middle, and posterior), and reported the exact same scene > object pattern of activity in the three segments. This result hence hardly fits into the broad-to-sharp model of the hippocampus, and calls for further investigation.

2. The RH model and hemispheric specialisation

Most neuroimaging studies that investigated MTL functions in a representational perspective have drawn conclusions bilaterally (e.g., Chadwick et al., 2013; Clark et al., 2018; Hodgetts et al., 2017; Ross et al., 2018; Zeidman et al., 2015; but see Dalton et al., 2018). Reciprocally, most patients in studies reporting representation-specific impairments in non-memory tasks presented bilateral lesions (e.g., Aly et al., 2013; Barense et al., 2007; Hartley et al., 2007; Hassabis, Kumaran, Vann, et al., 2007; A. C. H. Lee, Buckley, et al., 2005; A. C. H. Lee, Bussey, et al., 2005). Little is known, therefore, on the hemispheric specialisation of these functions (Zeidman & Maguire, 2016). Considering the massive memory impairment found in

patients with bilateral MTL damage, they represent the optimal experimental situation to evidence the consequences of these lesions on other functions than memory. However, patients with unilateral lesions and domain-specific memory deficits might present with more slightly impaired functions such as visual perception or working memory when assessed in a representational perspective, that is, with high-dimensional stimuli.

Material-dependant memory impairments in case of unilateral MTL damage

Whereas bilateral MTL lesions lead to severe amnesia (Allen, 2018), unilateral lesions produce material-specific impairments. Lesions to the left MTL are usually associated with deficits of verbal memory (Baxendale, 1997; Frisk & Milner, 1990; Golby et al., 2001; Kumaran & Maguire, 2007; T. M. C. Lee et al., 2002; Rocchetta & Milner, 1993), but also of sequence learning (Igloi et al., 2010; Lehn et al., 2009; Schendan et al., 2003), and autobiographical recall (Burgess et al., 2001; Maguire & Mummery, 1999; Stern et al., 1996). Right MTL regions, in contrast, are essential in the visual (Jones-Gotman, 1986; C.-H. Lee et al., 2016; Spiers, Burgess, et al., 2001) and spatial aspects of memory (Maguire et al., 1996, 1997, 1998; Worsley et al., 2001). Consistent results were reported in fMRI studies concerning the MTL in general (e.g., Klamer et al., 2013; Sidhu et al., 2013; Wagner et al., 2005), and the hippocampus specifically (for a meta-analytic review, see Persson & Söderlund, 2015). This material-based hemispheric specialisation of memory can be seen as an extension of the overall preferential involvement of left and right brain regions in verbal (Vigneau et al., 2011; for a historical perspective, see Manning & Thomas-Antérion, 2011) and visuo-spatial processing (Thiebaut de Schotten et al., 2011), respectively. The experimental studies that supported the development of the RH model consistently used visual-discrimination tasks, either in patients with MTL lesions or using functional neuroimaging (Graham et al., 2010). The rare studies that investigated the lateralisation of the brain network involved in this class of paradigm showed that processing the spatial position of stimuli preferentially engaged the right hemisphere whereas left regions were involved in the categorical identity of the stimuli (Laeng, 1994; Saneyoshi et al., 2006). This principle of hemispheric specialisation is compatible with the RH model, and may constitute a modulation of the representational specialisation of VVS-MTL regions.

Extending the lateralisation to the RH specialisation of the MTL

Because the tasks used in studies that evidenced impairments outside the memory domain in case of MTL lesion usually rely on visuo-spatial differences between the stimuli (e.g., Barense et al., 2007; A. C. H. Lee, Bussey, et al., 2005), we can hypothesise that they rely on right MTL regions specifically. Some studies argue in favour of this hypothesis. Concerning entity representation, Besson et al. (2020) tested patients with progressive atrophy due to early Alzheimer's disease, and demonstrated that the PRC and antero-lateral ERC⁵ volumes in

⁵ BA 35 of the PRC together with the antero-lateral part of the ERC form the *trans-entorhinal cortex*, a region that is affected very early in the development of Alzheimer's disease.

the right hemisphere, specifically, were predictive of entity familiarity capacities (for evidence of feature conjunction in the right temporo-parietal junction, see Pollmann et al., 2014). Consistently, Spiers et al. (2001) found that right (RTLE) but not left (LTLE) MTL surgery for drug-resistant epilepsy impaired visual recognition when targets and lures were highly similar. Regarding memory for scenes, RTLE but not LTLE has been associated with scene-layout recognition impairments (Baxendale et al., 1998; Pigott & Milner, 1993; Spiers, Burgess, et al., 2001). Whereas memory for the objects identity was impaired in all patients with RTLE, the position of the objects in the scene was dependant on the degree of hippocampal removal (Baxendale et al., 1998; Pigott & Milner, 1993). Consistently, the imagination of new spatial scenes was found to engage the right hippocampus preferentially (Hassabis, Kumaran, & Maguire, 2007) and viewpoint manipulation in scene discrimination modulated activity in the right posterior hippocampus (Barense, Henson, et al., 2010). Furthermore, Mullally et al. (2012) documented the case of P01, a patient with bilateral hippocampal atrophy whose scene imagination capacity is preserved (first reported in Hassabis, Kumaran, Vann, et al., 2007; see chapter III) using fMRI. They found this preservation to be supported by activation of his remnant right hippocampus while no compensatory activation appeared when compared with control subjects. Coherent results were reported by Irish and colleagues (2017), who showed that scene construction was impaired in case of right, but not left, selective hippocampal lesion. To explore the inter-hemispheric and hippocampus long-axis patterns of activation found for encoding and retrieval of visual and verbal stimuli, Persson and Soderlund (2015) conducted a meta-analysis on 94 fMRI studies. Encoding of verbal material was associated with left aHC activity whereas encoding of visual material was related to bilateral but right-dominant activity in the pHC. In contrast, memory retrieval was mainly associated with bilateral pHC activity, irrespective of material type. Taken together, those results suggest that the principles of functional organisation ascribed to the MTL by the RH model, and to the hippocampus by the broad-to-sharp model of Poppenk and colleagues, may apply differently to the right and left hemispheres. In particular, high-dimensionality as a continuum of perceptual complexity may be specific to the right hemisphere, while in the left hemisphere, verbal and semantic complexity could play a more important role.

Synthesis

Investigating the hippocampus long-axis reveals distinct functional specialisations of its anterior and posterior segments. It was proposed that these segments are differentiated according to the sharpness of the representations they process, an assumption that may constitute an extension of the RH principles within the hippocampus. In addition, these principles may interact with hemispheric lateralisation, as left and right MTL regions process different types of material. Thereby, analysing how the RH view applies to these two axes of brain organisation raises new predictions, which will be the focus of this work.

Thesis objectives

Neuropsychological studies showed that long-term declarative memory relies on MTL regions, whereas WM, procedural memory, and priming, do not. More precisely, episodic memory has been associated with the hippocampus, whereas anterior temporal cortical regions would be responsible for semantic memory. The diversity of results reported in recognition memory studies further led researchers to conceptualise and study two memory *processes*: recollection, which depends on the hippocampus, and familiarity, which rather depends on the PRC. The observation that material type is critical to understanding the involvement of MTL subregions in recognition memory gave rise to models that explain this functional organisation in terms of memory *content* and associative *binding*. Furthermore, it was demonstrated that those regions are critical to functions outside the memory domain (such as WM, imagination, or visual perception), depending on the material used. Two key mechanisms were proposed to explain the diversity of cognitive phenomena that depend on the hippocampus: *high-resolution binding*, and *scene construction*. The representational-hierarchical (RH) model encompasses the predictions of these two models, and gives a full account of the MTL and VVS functional organisation based on representational dimensionality (thus not limited to the hippocampus).

Recently, it was proposed to decompose cognitive processes into operations and representations. The RH view predicts that representational dimensionality exclusively determines the engagement of MTL sub-regions in a given process. The case of recollection is critical in this regard, and Ross and colleagues used a patch-cued paradigm to show that the hippocampus is engaged in memory reconstruction of scenes but not objects. The design used by the authors is highly relevant in that it allows to decompose the process of recollection, but it raises methodological questions. In this apparatus, recollection is approximated by the combination of a pattern-completion like retrieval and a high-dimensional stimulus. Yet, the contribution of proper recollection (i.e., mental-time travel based) to those retrievals remains unknown, and may constitute a bias if it varies depending on dimensionality. In addition, the operation of pattern-completion, or visual reconstruction, is assumed to be equivalent between scenes and objects. Importantly, if this assumption was wrong and the operation was to differ depending on representational content, it would question the results obtained by Ross and colleagues. Two behavioural studies, gathered in a first experimental chapter (i.e., chapter VI), aim at characterising the patch-cue paradigm. This cognitive characterisation is crucial to refine the experimental procedure and instructions used in subsequent study 3. Therefore, studies 1 and 2 aim at:

- Evaluating the degree to which proper recollection contributes to the visual reconstruction of scene and object stimuli: Study 1.

- Assessing the precision of visual reconstruction with and without prior exposure to the original image for scene and object stimuli: Study 2.

Following these two behavioural studies, study 3 (chapter VII) aims at investigating the theoretical questions raised by Ross and colleagues' results. As we saw, the patch-cue protocol does not allow to measure any operation other than pattern-completion. According to the RH model, the pattern of results found in the hippocampus and PRC for scene and object reconstruction should be reproducible across other operations. This is crucial, since if this pattern was to be specific to pattern-completion, then both the representation *and* the operation would determine the involvement of these regions in memory processes. In study 3, the original paradigm is reproduced while (1) rigorously controlling the instructions given to the participants, and (2) designing two parallel versions, one assessing patch-cued reconstruction and the other measuring proper recollection versus familiarity with whole images. Study 3 has 2 first objectives:

- Assessing the replicability of the results reported by Ross and colleagues.
- Extending these results to operations other than pattern-completion: memory-strength recognition (i.e., the operation underlying familiarity), memory-strength rejection (i.e., familiarity-based rejection), and visual discrimination.

Next, we saw that taking into account the long-axis specialisation of the hippocampus helped understanding the diversity of mechanisms that rely on this region. In particular, the broad-to-sharp model can be regarded as an extension of the RH principles within the hippocampus. Study 3 thus includes a second level of objectives, consisting in:

- Investigating how the patterns of results found in the hippocampus vary depending on long-axis segments.
- Testing the predictions of the broad-to-sharp model of the hippocampus.

Finally, the results reviewed in chapter V suggest that the representational organisation of MTL regions is modulated by hemispheric specialisation. In particular, high dimensionality as assessed with complex visual stimuli (i.e., spatial scenes and entities) may correspond to the functional specialisation of right MTL regions specifically. This assumption is addressed in chapter VIII both by assessing the lateralisation of the fMRI results from Study 3 and with a behavioural investigation of patients with unilateral MTL damage (i.e., Study 4), with the following objectives:

- Exploring how the activity patterns found in the MTL vary depending on brain hemisphere: Study 3 reanalysis.
- Testing the hypothesis that representational specialisation assessed using complex visual-perception paradigms (e.g., Barense et al., 2005; A. C. H. Lee, Buckley, et al., 2005) relies on right MTL regions specifically, by applying a paradigm of this class to patients with damage limited either to left or to the right MTL: Study 4.

Experimental chapters overview. The objectives, population studied, methods used, and corresponding studies, are summarised.

Chapter VI

Objective: Characterisation of the patch-cue protocol.

- Study 1 (behavioural, healthy controls)
- Study 2 (behavioural, healthy controls)

Chapter VII

Objectives: Test of the RH predictions, hippocampus long-axis.

- Study 3 (fMRI, healthy controls)

Chapter VIII

Objective: Hemispheric lateralisation.

- Study 3 (fMRI, healthy controls)
- Study 4 (behavioural, TLE patients)

RH: Representational-hierarchical, fMRI: Functional magnetic resonance imaging, TLE: Temporal lobe epilepsy.

Materials: General

Because most of the effects studied in this work strongly rely on the stimuli used, a set of stimuli was specially designed during this thesis, and was used in the four studies. Three kinds of paradigms needed to be allowed by the so built images: a visual-matching task (i.e., studies 3 and 4), a traditional recognition task (i.e., studies 1 and 3), and a patch-cued reconstruction task (i.e., studies 2 and 3). Because the same stimuli are used in the four experiments, their main characteristics are described in this section.

1. Classes of stimuli

Stimuli needed to be manipulated in 3 dimensions, thus realistic 3-dimensional models were used instead of real pictures. Three classes of stimuli were built in order to manipulate representational content. The first two are scenes and objects, as widely used in previous studies (e.g., Hodgetts et al., 2017; Ross et al., 2018; Staresina et al., 2011; Zeidman et al., 2015). Scenes were built using a freely available software (<https://unity.com>) and depict outdoor and indoor spatial scenes (e.g., a bedroom, a street). These scenes include central elements (e.g., buildings such as a house, furniture such as a bed in case of an indoor scene) as well as spatial landmark (i.e., the ground, sky or ceiling). Objects were built using a commercially available software (<https://www.sketchup.com>), and depict familiar 3-dimensional objects (e.g., a suitcase, a wrench) with no spatial landmark. A third class of stimuli, termed “building” was built in the aim of presenting a higher degree of visual complexity than objects but without the spatial landmarks included in scene stimuli (see Study 4). Buildings were built in the same way as scenes but all spatial landmarks were removed, keeping the central structure only (e.g., a barn, a bridge, a church). All stimuli were emotionally neutral. Figure M.1 presents an example of each stimulus type. All stimuli are available in the OSF project page associated with study 3 (https://osf.io/cbds5/?view_only=8dff7226148143c2b8a9a4a4efcfab01).

Because low-level characteristics influence the cortical processing of visual stimuli, we sought to minimise differences between stimulus classes that could be confounded with the stimulus type manipulation. One important factor is spatial frequency (e.g., Vuilleumier et al., 2003), which usually differs between scenes and other types of stimuli. Therefore, objects and buildings were positioned on noise grayscale backgrounds that were randomly generated in order to reproduce the spatial-frequency power spectrum of scenes (figure M.1). Luminance was also controlled by the backgrounds, and equalised between all images, resulting in grayscale images. Finally, because the main aim was to use those images in the MRI scanner, we had to adapt their format to the screen resolution available in the IRMaGe MRI facility

(Grenoble, France). The screen resolution is 1366 x 766 pixels; thus all images resolution is 640 x 360 pixels.

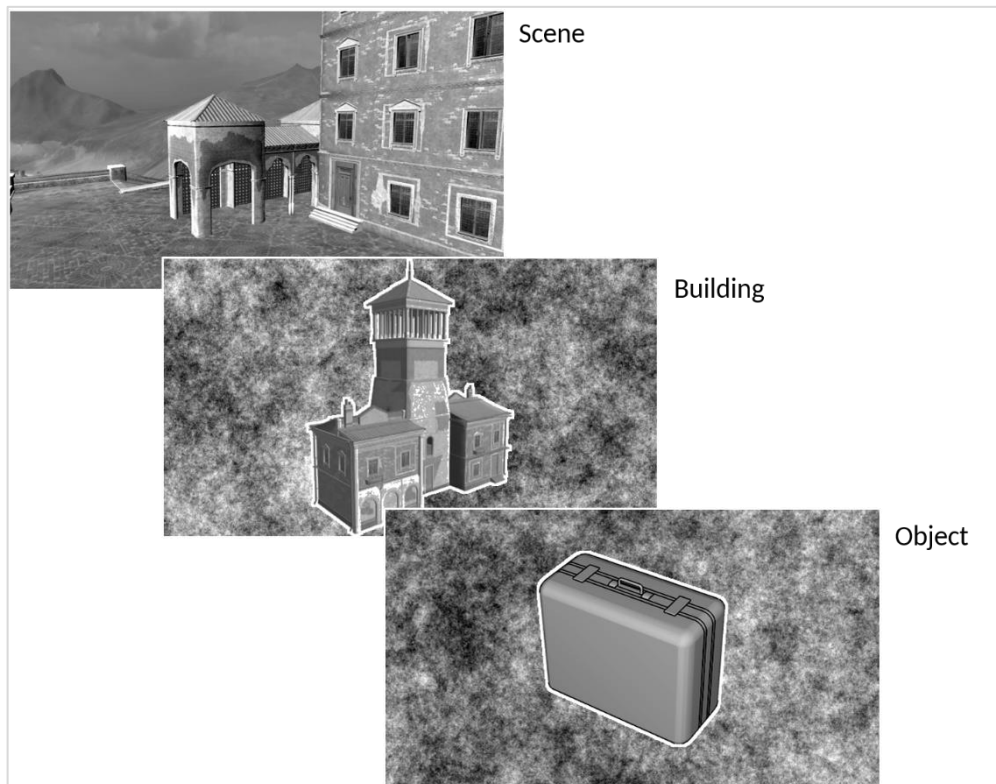


Figure M.1. Examples of the three classes of stimuli.

2. Manipulations in the Matching task

To measure high-order visual perception, we built a visual-matching paradigm: three stimuli are presented at the same time, and participants are instructed to determine which of two choices of response (i.e., the target and lure) matches the third stimulus (i.e., the reference). The matching depends on stimulus identity, such that the target always displays the same stimulus (i.e., the same scene, building, or object) as the reference. The lure displays a modified version of the stimulus (figure M.2.A). The modifications performed concern the size, proportions, position, or orientation, of structural parts of the images (for similar designs, see e.g., Barense, Henson, et al., 2010; A. C. H. Lee, Buckley, et al., 2005; A. C. H. Lee, Bussey, et al., 2005; A. C. H. Lee & Rudebeck, 2010). Presentation viewpoint was manipulated in half of the trials, consisting in a 40- to 60-degree shift in point of view either to right or to the left. Importantly, the point of view between the target and lure is always the same, but differs from that of the reference in “different viewpoint” trials as opposed to “same viewpoint” trials (figure M.2.B). Sixty-four trials per stimulus class were built, resulting in 576 images (192 trials composed of 3 images).

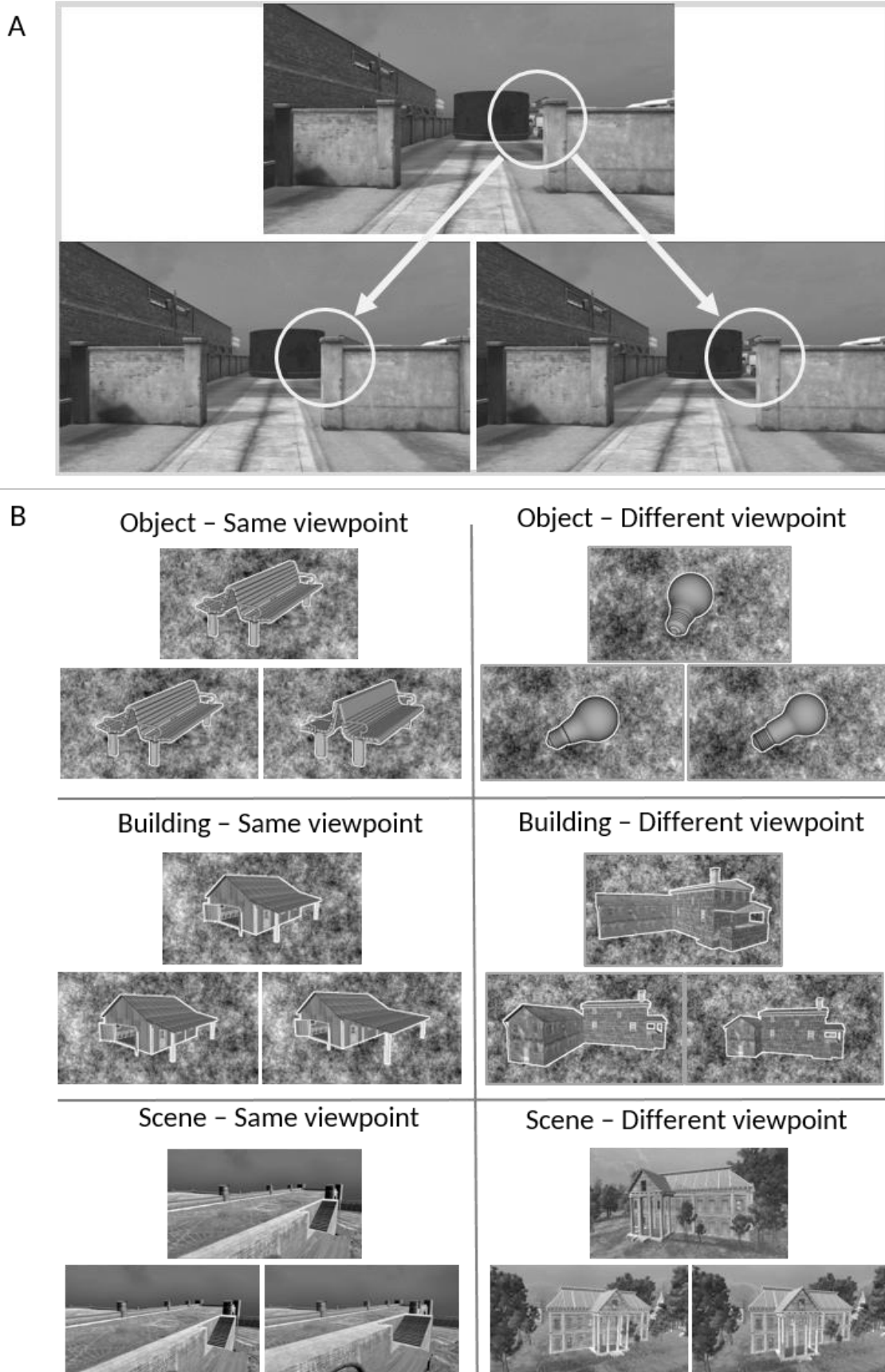


Figure M.2. A: Example of manipulation in the scene – same viewpoint condition. B: Examples of trials from the Matching task in all experimental conditions.

Higher-order visual perception paradigms rely on feature overlap, or the degree of shared visual features between the images constituting a trial (see chapter IV). Additionally, the manipulation of presentation viewpoint prevents the use of low-level perceptual features to perform the task. The difficulty of such paradigms must thus be controlled, in order to prevent from floor and ceiling effects. In functional neuroimaging and neuropsychological studies, an average of 70-90% of correct responses is generally required in healthy controls, to allow correct interpretation of the results and meaningful comparisons with patients, respectively. Therefore, 12 pilot subjects were recruited to explore trial-by-trial proportions of correct responses. Trials that were judged too difficult (i.e., < 60 %) or too easy (i.e., > 90%) were removed or modified to adjust task difficulty.

3. Recognition task and visual patches

Among the objectives of this work is the replication of the results reported by Ross and colleagues using the patch-cue recognition task. Because the encoding task in Study 3 is the matching task, we built new patches for the recognition task (instead of re-using the original material). Patches are 150-pixels diameter circular windows taken at various places from the original images (figure M.3). We refer to the original images from which are taken the patches as the “whole-item” version. A patch version of each stimulus that was the reference image in the matching paradigm was built, so that all reference images, as well as new stimuli, exist both in patch and whole-item versions (i.e., 84 whole-item and 84 patches per stimulus class). Patches were positioned on noise backgrounds generated in the same manner as for constructing object and building stimuli, and of the same size as the whole-images (i.e., 640 x 360 pixels). We chose to locate the patches on these backgrounds at the same position as they were in the original images (instead of the centre of the background systematically). Similar to the original study, patches positions were carefully chosen to avoid displaying critical elements of the images that would make reconstruction (or guessing) too easy, but to contain enough information to make recognition/reconstruction possible. This was confirmed by checking for trial-by-trial aberrant recognition performance distribution in the pilot subjects.

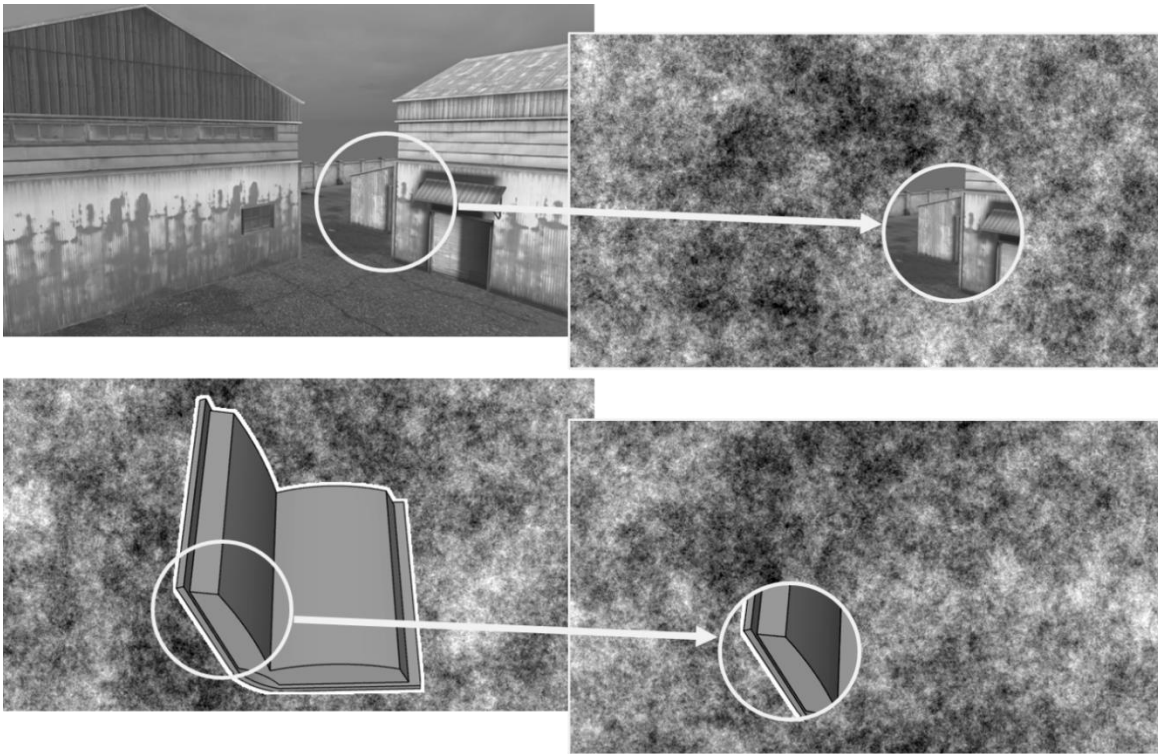


Figure M.3. Examples of patches and their position in the original images in the scene and object conditions.

Chapter VI – Characterising the patch-cue protocol: what is reconstruction?

This first experimental chapter aims at addressing the methodological questions that emerged from the patch-cue paradigm. Study 1 was built in the aim of characterising the cognitive outcomes associated with reconstructing images from patches, and particularly measuring the contribution of proper recollection. Study 2 was designed to determine whether reconstructing a scene and reconstructing an object both rely on the prior encounter of the stimulus (i.e., on memory representation rather than on generic representation). Both studies 1 and 2 were conducted in healthy young participants, with no neurophysiological data being recorded. The results from these studies are critical regarding the behavioural paradigm and instructions used in the subsequent fMRI study (Study 3).

The results from Study 1 were presented at the Interdisciplinary congress of the CNRS memory research group (GDR mémoire) in October 2021 in Vers (France) in a poster communication under the title: Pattern completion and recollection : The subtleties of measuring recognition memory with partial visual cues (Gardette et al.).

Contents of chapter VI

| | |
|--|-----------|
| Chapter VI – Characterising the patch-cue protocol: what is reconstruction? | 71 |
| Study 1 – Reconstruction versus recollection: Remember/know investigation of the patch-cue paradigm..... | 73 |
| Introduction..... | 73 |
| Methods | 74 |
| Results | 77 |
| Discussion | 79 |
| Study 2: Comparable contribution of memory representations to scenes and objects reconstruction? | 80 |
| Introduction..... | 80 |
| Methods | 81 |
| Results | 84 |
| Discussion | 86 |
| Synthesis..... | 87 |

1. Study 1: Reconstruction versus recollection: Remember/know investigation of the patch-cue paradigm

Introduction

This first study aimed at characterising the memory mechanisms used by participants in the patch-cue paradigm, as compared a traditional, *whole-item*, R/K paradigm. The main process of interest here is recollection, defined as a detailed and contextualised memory retrieval (Tulving, 1989). Several methods were designed to measure recollection, most of which are based either on retrieving details from the encoding period or on the subjective feeling of episodic recollection (see chapter II). The patch-cue paradigm aims at decomposing the representation (i.e., high- vs low-dimensional) and operation (i.e., pattern-completion-like retrieval) involved in recollection, in order to determine which of these components is “responsible” for the engagement of the hippocampus. Thus recollection is approximated by the reconstruction of scene images. One of the interrogations raised by this apparatus is whether proper recollection, that is, mental-time travel based retrieval, contributes to image reconstruction. Here we define image reconstruction as the mental completion of the visual stimulus from which the partial cue originates. This definition relies on the assumption that recollection can be separated from visual reconstruction; that is, reconstruction can occur with or without recollection. If so, we should be able to measure the rate of recollection during reconstruction, and reconstruction without recollection should appear.

Importantly, those two memory mechanisms may have been confounded in the original study, as participants were asked whether they “**remembered** the scene/object from the first part of the study” (Ross et al., 2018). *Remembering* the image can mean to visually reconstruct the image; but also to remember the moment they saw the image the first time, which would imply proper recollection even when facing an object patch. Recollection-based responses in this case surely encompasses image reconstruction, as the participant would then recall the full image, but it also overpasses it, since details from the encoding would be recalled, as it is usually the case in R/K paradigms (Migo et al., 2012; Montaldi & Mayes, 2010). This is of particular importance given the role of the posterior hippocampus in detail retrieval (Poppenk & Moscovitch, 2011) and the inconsistency between the results of this study and the broad-to-sharp account of the hippocampus long-axis.

In the present study, we aimed at estimating the contribution of recollection to patch-cued reconstruction. We therefore used a patch-cue protocol similar to that of Ross and colleagues, with a parallel (control) whole-item R/K task. Similar to the original study, we used object and scene images; although those were new images designed for this series of experiments (see Materials: General section). Crucially, reconstruction and recollection were measured sequentially in the patch-cue condition. Reported recollection were verified using oral reports, which were rated independently by two judges. The first aim was to quantify the contribution of recollection to image reconstruction; we thus explored the rate of justified

recollections among reconstructions. We expected reconstruction to be at least partly independent from recollection. Second, because a difference in recollection between scene and object reconstruction would be critical in regard to the interpretation of neuroimaging results obtained with this procedure, we compared the recollection rates between these conditions.

Methods

Participants

Since no previous study have documented similar analyses, we could not estimate an adequate sample size a priori on the basis of the reported effect size. We therefore chose a minimal sample size of $N=60$, in order to ensure a minimum of 25 participants per condition (i.e., patch-cue/whole-item) after excluding outliers. This way, group sizes were comparable to those in the subsequent fMRI study (see chapter VII). Sixty-six young participants hence took part in this study (18 to 25 years old, 54 females). All were students in the Savoie-Mont Blanc University and were recruited in exchange for course credits. All had normal or corrected to normal vision, and none had any neurological or psychiatric disorder (self-declared). Before taking part, each participant gave their informed written consent. Participants were randomly assigned either to the patch-cue or to the whole-item condition. The average experiment duration was 30 minutes.

Material

The experiment was conducted using OpenSesame, version 3.3.8 (Mathôt et al., 2012; <https://osdoc.cogsci.nl/3.3/>) on a laptop computer with a 1366 x 768 pixels resolution. 120 stimuli were used, 60 scenes and 60 objects, all taken from the image based constructed for this project. Of these stimuli, 30 scenes and 30 objects were randomly selected for each participant and presented during the study phase, being the *old* items, whereas the 60 remaining images were the *new* items. During the test phase, 80 images were presented, of which 20 scenes and 20 objects were randomly selected among the old images, and 20 scenes and 20 objects were taken from the new images. In the whole-item condition, all images were presented in full in both phases. In the patch-cue condition, images were presented in full during the encoding phase and in the form of patches during the test phase (see Materials: General for details on the construction of patches).

General procedure

In the first phase, participants were presented with the 60 old images, one at a time and in a random order. They were asked to rate how pleasant they found each image on a scale ranging from 1 – very unpleasant, to 5 – very pleasant (3 was “neither pleasant nor unpleasant”). Similar to the fMRI study and original study from Ross and colleagues, participants were not asked to remember the images: encoding was thus incidental. Once a pleasantness response was given, the response options disappeared from the screen, but the image systematically

remained for six seconds to ensure equal encoding time for all stimuli (this duration is similar to that of the encoding phase in the fMRI study). Twice during the encoding phase (i.e., when 20 and 40 stimuli out of 60 had been presented), a break was proposed to the participant: the experiment paused and they were told to press the space key when they were ready to start again. Between the encoding and the test phases, the experimenter explained the test phase and ensured that the subject understood properly the instructions by providing examples (appendix A1). During the test phase, images were also presented one at a time in a random order. The participants provided their responses by pressing keyboard buttons.

Instructions and R/K procedures

The procedure is summarised in figure 6.1. **In the whole-item condition**, participants were instructed to judge for each item if⁶:

1. They **specifically remembered seeing the image** during the encoding period (response “R”)
2. They only found the image familiar (response “F”)
3. They thought the image was new (response “N”).

For each “R” response given, the experiment paused and they were asked to justify their response by describing “what made them give this answer”. The experimenter recorded their oral descriptions using an audio recorder. They then pressed the space key to continue the experiment.

In the patch-cue condition, participants were instructed to judge for each item if:

1. They **could reconstruct the original image** from memory, that is, they could see it with their “minds eyes” (response “Rec”)
2. They only found the patch familiar (response “F”)
3. They thought the patch was new (response “N”)

For each “Rec” response given, they were asked whether it was accompanied with a recollection. When they reported a recollection, they were asked to justify this answer and their description was recorded as in the whole-item condition.

⁶ All three response options were proposed concurrently. Alternatively, we could have asked participants (1) to judge whether the image was old or new, and (2) if they responded *old*, asked the familiarity/recollection question. However, in the fMRI protocol, all response options are proposed immediately, to avoid delaying the response from the spontaneous brain response measured with BOLD fMRI since additional memory mechanisms may occur in the meantime; we thus chose to stick to this procedure in the present study.

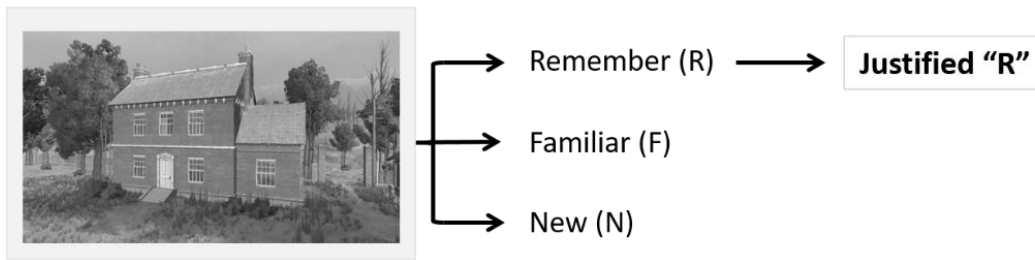
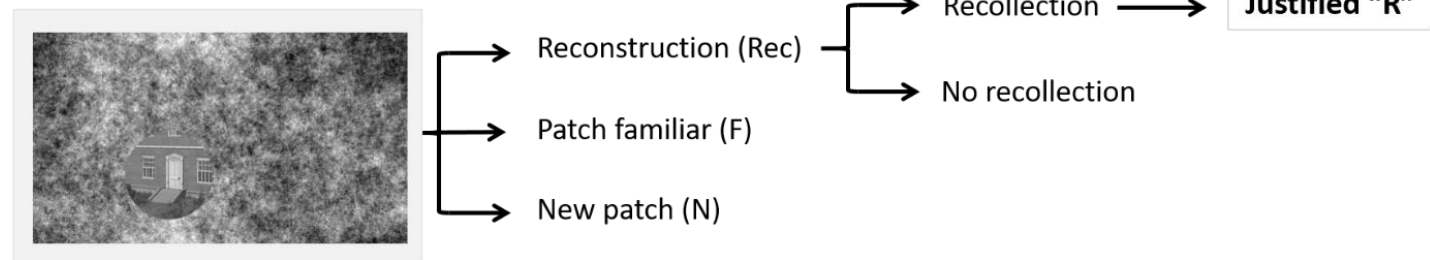
Whole-item condition**Patch-cue condition**

Figure 6.1. Procedure in the whole-item and patch-cue conditions of study 1.

Measures and recollection ratings

Hit and FA rates were derived from participant's responses (see chapter II for the definitions of these indices) and used as a control measures to ensure that participants performed the task properly. Pleasantness judgements recorded during the study task were not of interest, but were explored to check that participants did maintain their attention on the images. The proportions of R/K/N responses were recorded in the whole-item condition, while in the patch-cue condition, the proportions of Rec/F/N responses and the proportion of "R" reported following a Rec response were recorded. In both conditions, the justifications of reported "R" were recorded. All descriptions were rated as justified/unjustified "R" separately by 2 judges (ML and JG), then inter-judge agreement was calculated. In case of disagreement, the description was discussed until a consensus was reached. The rating method was adapted from the criteria by Curran and colleagues (Curran et al., 1997), which mainly use the retrieval of details from the study phase. The criteria were as follows:

1. For a "R" to be considered justified, the description had to include content that fell into (at least) one of the following categories (1a, 1b, and 1c). This criterion, based on the third criterion by Curran and colleagues, was used to ensure that in any justified answer, participants provided additional information, that is, other than "I remember that image from earlier".

1a. *Reference to the study phase.* For example: "I remember this image was the first image after the first break", or "I particularly liked this image". In contrast, justifications that referred to past event but were unrelated to the study phase were not accepted (e.g., "Yesterday I thought of my dog", Curran et al., 1997).

1b. *Autobiographical reference.* For instance: "That reminded me of my grandparent's house" or "I thought this image looks like a place I usually go on holiday".

- 1c. *Self-reference*. For instance: “I remember thinking that I am particularly bad at DIY” in case of a tool image, or “I remember this image because I play the guitar myself and so it made me think of that” for the guitar image.
2. For a “R” to be considered justified, the description had to be in the past tense or be of the form “I remember [X]” (where the justification was rated on the content of the X information). Any justification in the present (e.g., “I love going to the beach”) was not accepted.
3. For a “R” to be considered justified, the content of the justification had to include information that were not directly present at test, so that information related to the image itself or experiment background were not sufficient. Importantly, in the patch-cue condition, the information provided had to overpass the content of the full image, which indeed differentiates proper recollection from visual reconstruction.

Statistical analyses

After checking for the statistical assumptions, general linear model analyses were performed using R (R. Team, 2014). Condition (patch-cue vs whole-item) was analysed as a between-subject variable, whereas stimulus type (scenes vs objects) was analysed as a within-subject variable. The overall number of justified “R” responses, and proportions of justified “R” among reconstruction responses in the patch-cue condition, were analysed.

Results

Overall performance and exclusions

First, four participants in the whole-item condition had to be excluded because they never responded “remember”, and four because they did not understand or follow the instructions properly (as agreed by both judges when analysing the oral descriptions). Considering overall correct response rates, one subject was excluded because they responded below chance level (i.e., < 50 %; Haaf et al., 2021). Finally, using the FA and Hit rates, two subjects were identified as outliers because they had a FA rate of 0.6. These subjects were found to be outliers using the FA > 0.4 rule (Alghamdi & Rugg, 2020), the z score method (van den Bos et al., 2020; Williams & Lindsay, 2019), and the median absolute deviation method (Leys et al., 2013). Pleasantness judgements did not reveal any extreme value. Of the 55 remaining participants, 29 were in the whole-item condition and 26 in the patch-cue condition. Hits and FA rates indicated that there was no ceiling or floor effect, neither in the whole-item nor in the patch-cue condition (figure 6.2.A and B).

Inter-judge agreement

Given that only two rating options were available (i.e., justified/unjustified), inter-rater reliability was binary. Because measures such as Cohen’s kappa are influenced by the number of possible values, we calculated the percentage of cases in which the two raters chose the same option. Agreement was high both in the whole-item (86.14 %) and in the patch-cue condition (86.14 %), and was comparable to that of similar studies (e.g., Mihaylova et al., 2019;

Selmecky & Dobbins, 2014). In addition, Fleiss’s kappa showed these distributions were statistically different from chance (both $p < .01$).

Justified Recollection analyses

Overall, the vast majority of reported “R” were appropriately justified ($M = 92.64\%$; $SD = 11.22\%$), suggesting that participants (apart from those excluded from the analyses) understood the instructions properly. The total number of justified “R” was descriptively higher in the whole-item condition ($M = 11.31$; $SD = 9.95$) than in the patch-cue condition ($M = 7.92$; $SD = 6.4$), but no significant difference was found, $t(53) = -1.48$, $p = .143$.

In the patch-cue condition, the proportion of justified “R” that followed a reconstruction varied steeply between subjects, ranging from 0 to 100% ($M = 41.9\%$; $SD = 30\%$; figure 6.2.C). The overall number of justified “R” was slightly higher in the object ($M = 4.73$; $SD = 4.33$) than in the scene condition ($M = 3.19$; $SD = 2.6$), $t(25) = 2.7$; $p < .05$. Proportions of justified “R”

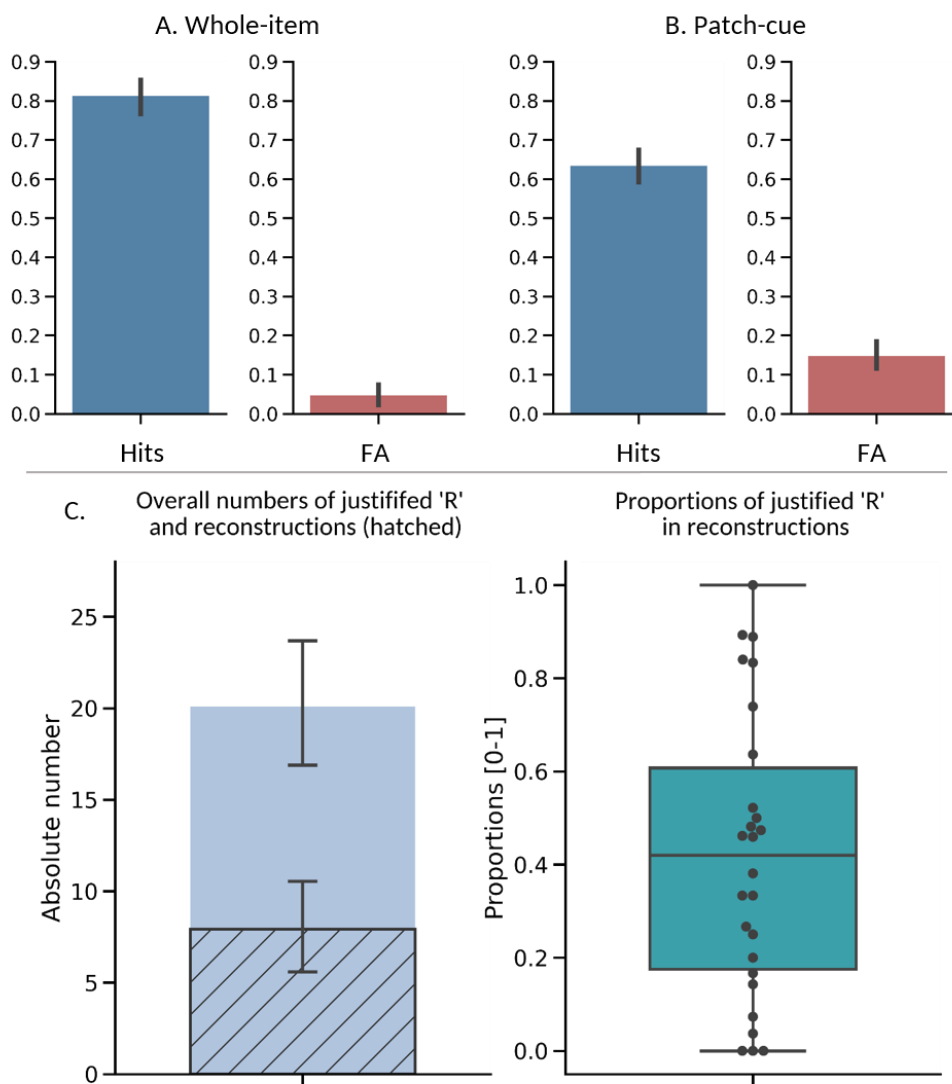


Figure 6.2. Hits and false alarms (FA) rates in the whole-item (A.) and patch-cue (B.) conditions. C. Justified “R” among reconstructions in the patch-cue condition. Left: overall number of reconstructions (blue) and of justified “R” (hatched) in the sample. Right: by-subject proportions of justified “R” among reconstructions.

among reconstructions, were highly variable both for object ($M = 39.63\%$; $SD = 30.85\%$) and scene ($M = 48.55\%$; $SD = 37.08\%$) images, and did not differ significantly between these conditions, $t(25) = -1.89$, $p = .069$.

Discussion

The aim of this study was to estimate the contribution of proper recollection to the reconstruction of images from visual patches. We thus combined a justified R/K procedure to the patch-cue recognition paradigm, with a parallel traditional R/K condition. We assumed that recollection and visual reconstruction would be separable, that is, we would identify reconstructions with and without recollection. The proportions of justified “R” responses among reconstructions revealed that (1) the majority of reconstructions occur without associated recollection (figure 6.2 left); while (2) reconstruction and recollection do co-occur; and (3) the proportion of recollections among reconstructions presents a high inter-subject variability (figure 6.2 right). Those proportions did not differ significantly between scene and object reconstruction, and were highly variable in both conditions.

These results show that it is possible to visually reconstruct an image without resorting to proper recollection. Additionally, the contribution of recollection does not seem to vary depending on the type of the stimuli reconstructed. This strengthens the relevance of the patch-cue paradigm in measuring the pattern-completion-like retrieval of different classes of representations.

However, those results also reveal that recollection does occur in certain trials when participants are asked to visually reconstruct images. It is to be noted that to measure its contribution to the task, we had to explain the concept of recollection to the participants, and to ask them for each reconstruction whether they experienced it or not. We cannot rule out the possibility that this experimental set up maximised the occurrence of recollection in the patch-cue condition. Accordingly, only asking participants to visually reconstruct images without mentioning recollection should lower the likelihood of this process to occur spontaneously. The term “remember”, used by Ross and colleagues in the original study, might have been confusing in this regard. Yet, if recollection contributed to reconstruction in this study, then it should have led to similar increases in pHC activity for objects and scenes due to comparable recollection of contextual details in both conditions. Therefore, how can the scene > object pattern found by the authors in the pHC be explained? This reinforces the need for replication of those results, which is one of the aims of Study 3. Importantly, based on the observations of the present study, the recognition instructions in Study 3 will be adapted: participants will be asked if they “remember” the image in the whole-item condition, to measure recollection; but only to “reconstruct” the original images in the patch-cue condition, to measure visual reconstruction, or pattern-completion-like retrieval.

2. Study 2: Comparable contribution of memory representations to scenes and objects reconstruction?

Introduction

The results from study 1 provided us with insights on the contribution of recollection to reconstruction, and showed that the latter can occur without the former. Yet, the question remains as to the nature of reconstruction without recollection; in particular, the contribution of episodic memory. The aim of the patch-cue protocol is to measure pattern-completion-like retrieval of different kinds of representations. Scene and object images are therefore used to manipulate representational dimensionality. This apparatus relies on the assumption that the pattern-completion of high- and low-dimensional representations is equivalent, and that the difference in the brain regions engaged between these conditions is due to the representation processed exclusively (Cowell et al., 2019). In regard to the patch-cue paradigm, visually reconstructing a scene and an object image from memory would be equivalent, although the complexity of the memory representation that is retrieved is not.

An alternative hypothesis would be that the complexity of the image and the nature of the reconstructive processes are not orthogonal, that is, the former influences (or modulates) the latter. Taking this argument a step further, one could assume that due to lower perceptual complexity, the reconstruction of objects implies an operation of a different nature than that of scenes. In particular, object images could be (re)-constructed without memory representations, using generic (or semantic) object representations. In contrast, because of their high visual complexity, scene images would require the use of memory representations to be reconstructed. Crucially, such difference could explain any effect found in hippocampal recruitment in terms of memory-based versus non-memory-based reconstruction rather than in terms of representational dimensionality.

To rule out this possibility, Ross and colleagues used a post-scan naming test, in which subjects were asked to identify the items for which they had responded “remember”. They showed that naming accuracy was reliable and comparable between objects and scenes. However, this control task only provides information on the conceptual identification of the item (e.g., “a library” [scene]; “a bike” [object]), but does not provide information regarding the contribution of episodic memory representation to reconstruction. The present study, in contrast, was designed to investigate how (re)-construction evolves throughout successive presentations of the original image. We therefore presented patches and asked participants to mentally (re)-construct each image, with and without prior presentation of the original image, using both scenes and objects. The similarity between the imagined image and the original image was measured both subjectively and objectively. Importantly, participants in this study were not explicitly instructed to “remember” seeing the images before, only to try imagining the image from which the patch originated, as precisely as they could. This way, a shift from imagination to memory, or from construction to reconstruction was expected.

If the reconstruction of object images does not, whereas that of scenes does, depend on memory representations, then different effects of presentation on similarity should be found between those conditions. In the scene condition, the shift from imagination (i.e., without prior exposure) towards memory reconstruction (i.e., following exposure) should result in an increase of the similarity between the imagined and the original scenes. In contrast, if no such shift occurs for object images, then the similarity ratings with and without prior exposure to the original image should be comparable in this condition. In line with the RH account, we hypothesised that the operation of pattern-completion is independent of the representation reconstructed. Thus the reconstruction of both types of images should imply memory representations⁷, and we expected similarity ratings to increase with exposures both for scenes and for objects.

Methods

Participants

Again, given that no effect size was available to estimate the required sample size via a power analysis, we chose a minimal sample size of N=60. Seventy-six young healthy participants took part in this study (68 females, 1 non-binary gender, age 16 to 44 years old, M = 19.86; SD = 3.55). They were recruited in the Savoie Mont-Blanc University and participated in exchange for course credits. All participants had normal or corrected-to-normal vision. They gave their informed written consent before taking part.

Material

Similar to Study 1, the experiment was conducted using OpenSesame, version 3.3.8 (Mathôt et al., 2012; <https://osdoc.cogsci.nl/3.3/>) on windows computers (1920 x 1080 pixels resolution). Because they would be presented several times, only nine scenes and nine objects were selected from the image base constructed for this project (see Materials: General section). Images were selected to be of medium difficulty (i.e., patches judged as too prototypical, too “guessable”, or containing too few information were not selected) to avoid masking the effects of interest of this study. Both the whole and the patch versions of each image were used, resulting in 36 stimuli overall.

Procedure and instructions

All the instructions were explained to the participants before beginning the experiment. Illustrations (appendix A2) as well as examples of the task were provided to ensure a good understanding of the procedure. In all trials, participants were presented with the patch version of an image, and were asked to imagine the remaining of the original image.

⁷ This hypothesis is specific to this apparatus, which is designed in the aim of measuring reconstruction from memory. However, we acknowledge that in different contexts, image reconstruction may not rely on prior exposure but only require generic representations (e.g., conceptual identification from perceptually degraded images).

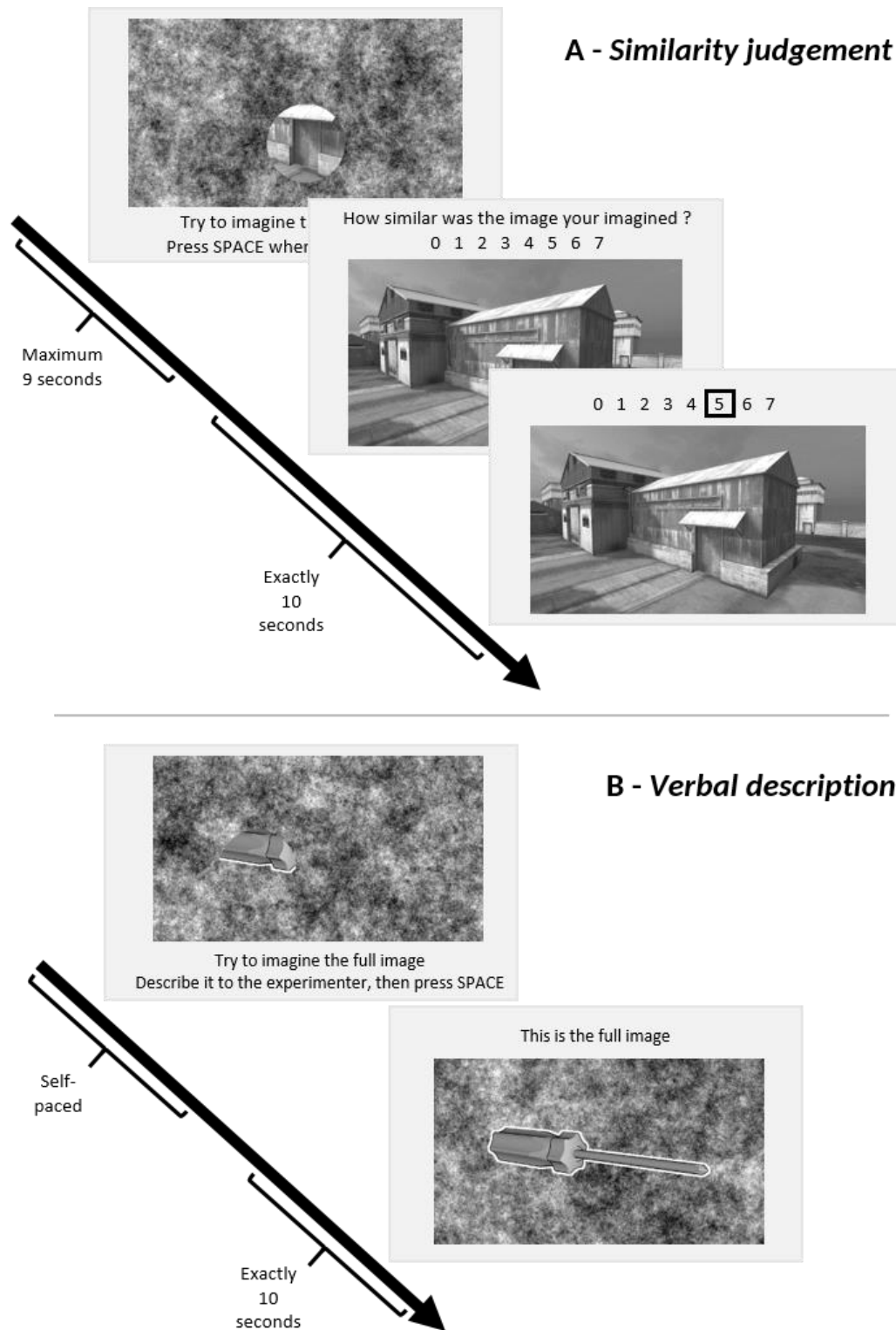


Figure 6.3. Experimental procedure in Study 2. A: example of similarity judgment trial. B: example of verbal description trial. Note that instructions were in French; here short translations were chosen to fit in the figure size. See main text for the detailed instructions.

Importantly, the same instruction was given before and after the first presentation of the whole image. Once they were ready (i.e., they had a clear image in mind), they pressed the space key. The maximum duration of this step was 9 seconds, a duration chosen based on

pilot participants. There were two kinds of trials: similarity judgements (i.e., subjective rating) and verbal descriptions (i.e., for later objective rating), illustrated in figure 6.3. In similarity judgements trials, the original image appeared in full immediately when the subject had pressed the space key. While the full image remained on screen, they were asked to rate the similarity between the image they had imagined and the original one from 0- “not similar at all” to 7- “completely similar”. Once they had given an answer, the question disappeared from the screen (to inform the subject that their answer had been recorded) but the image was systematically displayed during 10 seconds, to equalised the encoding time across images.

In verbal description trials, participants were instructed to verbally describe the image they had imagined to the experimenter, who recorded it using an audio recorder. Specifically, they were asked to describe it “like if someone else was going to listen to this description and try imagining the image they had imagined as closely as possible”. This instruction was given (during the briefing session) to ensure that participants would provide details beyond the simple conceptual identification of the image (e.g., “it’s a screwdriver”, “it’s a bedroom”). The experimenter prompted for details exactly once for each verbal description of each participant to reduce discrepancies in the amount of detail due to variables not of interest such as personality traits. This step was self-paced, that is, participants pressed the space key once they had finished describing the image, with no time limit. Subsequently, the original image appeared on screen for 10 seconds as in similarity judgement trials.

The experiment was divided into three successive phases. All 18 stimuli were presented once during each phase, so that subjects had never seen the full images during phase 1, they had seen them all once when starting phase 2, and twice during phase 3. Whereas phase 2 only consisted in similarity judgements, verbal description trials were intermixed with similarity judgement trials in phases 1 and 3. Four to six images during phase 1, and 3 to 6 during phase 2, were randomly assigned to the verbal description condition, whereas the remaining images were assigned to the similarity judgement condition⁸. All items were presented in a random order.

Rating of verbal descriptions

The verbal descriptions were rated on their degree of similarity to the original images on a scale ranging from 0 to 3. Correct and incorrect details for central and peripheral elements were considered, as shown in table 4.1. All descriptions were analysed independently by two raters (CB1 and CB2⁹), then inter-rater reliability was calculated. Once an agreement was reached, ratings were averaged by condition, resulting in four scores per participant (i.e., scene phase 1, scene phase 3, object phase 1, and object phase 3).

⁸ This variable distribution of verbal description / similarity judgment trials was unintentional and was caused by a technical mistake in the experiment script. Seven subjects were excluded from the analyses of the verbal descriptions for this reason (see results section). Note that equal overall numbers of scene and object stimuli were ascribed to both types of trials.

⁹ The two raters have the same initials.

Table 4.1. Criteria used to rate the similarity between verbal descriptions and the original images.

| | Correct description | Errors |
|---|--|--|
| 0 | No central element Extrapolation based on the patch | Several errors on central or peripheral elements |
| 1 | Central element(s) mentioned No peripheral details | One error on central element(s). Amount of details \approx amount of errors |
| 2 | Central element(s) mentioned, peripheral details | No error on central elements, one/two errors on peripheral elements |
| 3 | Detailed description of all/almost all elements | No error |

Statistical analyses

Statistical analyses were performed using R (R. Team, 2014). Data from both the similarity judgements and verbal descriptions violated the homoscedasticity assumption of the general linear model as revealed by Levene's test, therefore non-parametric tests were used (i.e., Freidman's and Wilcoxon's tests). Presentation (i.e., 1st, 2nd, 3rd) and material type (i.e., scene, object) were analysed as within-subject factors. Similarity judgements and ratings of verbal descriptions were analysed. In the case of verbal descriptions, the variable Presentation consisted in two modalities only (i.e., 1st, 3rd).

Results

Similarity judgements

One subject was excluded from the analyses because of difficulties in understanding the instructions, and another subject was identified as statistical outlier in regard to the distribution of similarity judgements data, thus 74 participants were included in final analyses. Freidman's Anova revealed a main effect of presentation, $Q(2) = 117$, $p < .001$ (figure 6.4). Specifically, mean similarity increased both between the first ($M = 3.24$; $SD = 0.88$) and second ($M = 5.88$; $SD = 0.65$) phases, $W = 0$; $p < .001$; and between the second and the third ($M = 6.07$; $SD = 0.62$) phases, $W = 694$; $p < .001$. Planed comparisons revealed a significant increase in similarity between the first and second phases both for scenes [$Q(1) = 74$; $p < .001$] and for objects [$Q(1) = 58.9$; $p < .001$]. A main effect of material type was also found, with a higher overall similarity for objects ($M = 5.31$; $SD = 1.89$) than for scenes ($M = 4.82$; $SD = 1.27$), $W = 2328$; $p < .001$. There was a significant presentation \times material type interaction, $Q = 82$, $p < .001$. In the first phase (i.e., without prior exposure), similarity judgements were higher for scenes than for objects, $W = 636$, $p < .001$. In contrast, in the second ($W = 2480$; $p < .001$) and third ($W = 2659$; $p < .001$) phases, similarity judgements were higher for objects than for scenes.

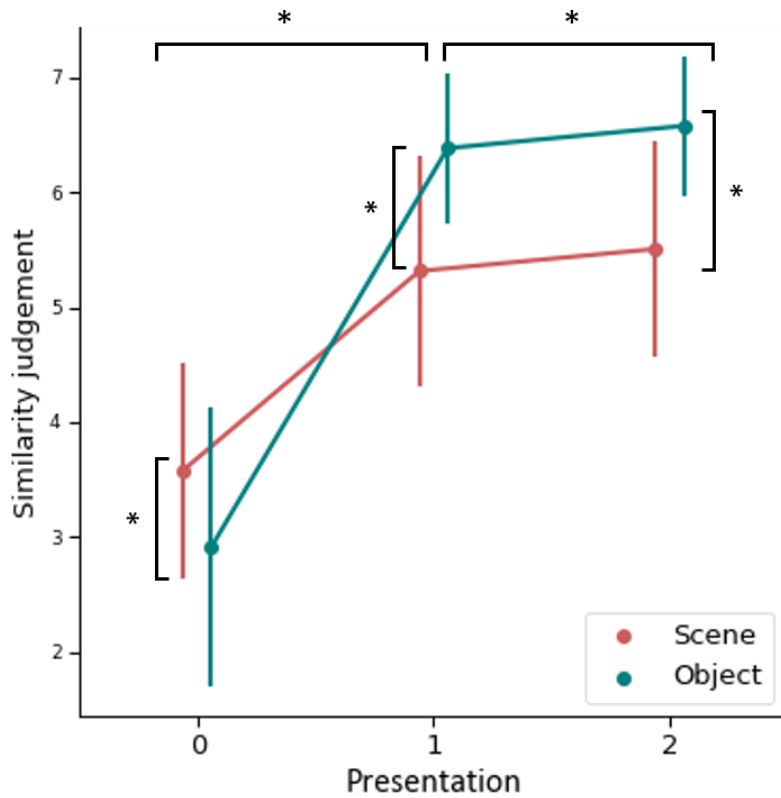


Figure 6.4. Results from Study 2: similarity judgements as function of presentation phase (1st, 2nd, and 3rd) and material type (scenes and objects). Presentation 0 means no prior exposure. Means and 95% confidence intervals are depicted. *: $p < .001$.

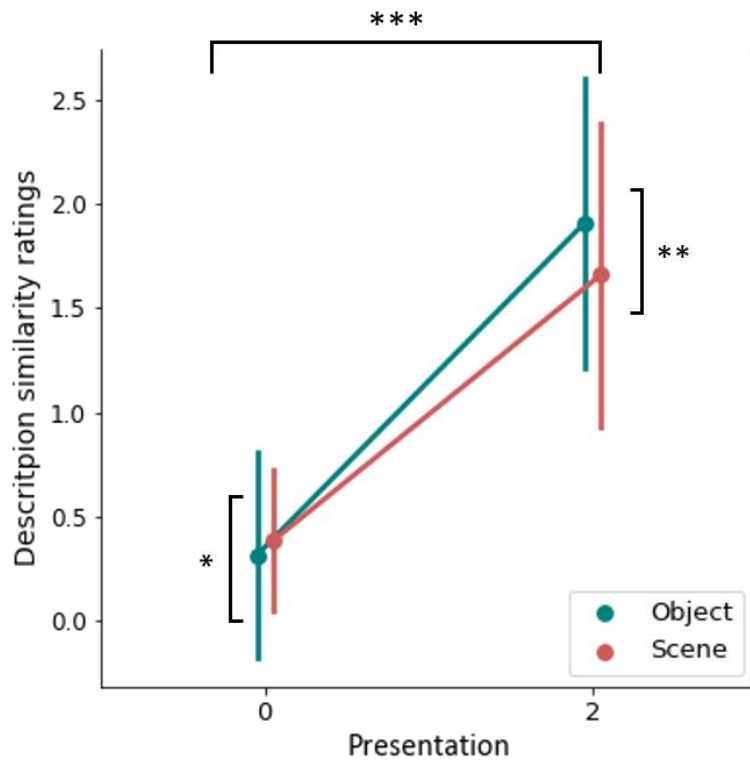


Figure 6.5. Results from Study 2: ratings of verbal descriptions as function of presentation phase (1st, and 3rd) and material type (scenes and objects). Means and 95% confidence intervals are depicted. *: $p < .05$; **: $p < .01$; ***: $p < .001$.

Ratings of verbal descriptions

Weighted Cohen's kappa showed high inter-rater reliability ($k = .90$). The data from seven subjects were excluded from the analyses because of insufficient verbal description trials, none were identified as outliers, thus 69 participants were included in final analyses. An increase in description similarity between phase 1 ($M = 0.34$; $SD = 0.42$) and phase 2 ($M = 1.78$, $SD = 0.72$), was observed, $W = 2$, $p < .001$ (figure 6.5). There was no main effect of material type ($W = 1253$; $p = .155$), but a significant interaction between presentation and material type: the increase between phase 1 and phase 3 was steeper for objects than scene stimuli ($W = 1570$, $p < .01$). Consistent with the results observed with subjective similarity judgements, description similarity in phase 1 was rated higher for scenes ($M = 0.38$; $SD = 0.33$) than for objects ($M = 0.31$; $SD = 0.49$), $W = 499$; $p < .05$. The reverse effect was found in phase 3, with higher description similarity for objects ($M = 1.9$; $SD = 0.69$) than scenes ($M = 1.65$; $SD = 0.72$), $W = 1256$; $p < .01$.

Discussion

In this study we aimed at determining whether mentally reconstructing a scene and an object image similarly relies on prior exposure. Participants were thus presented with patches taken from these two types of stimuli, and were instructed to imagine the full image as precisely as possible. The accuracy of the reconstruction as function of prior exposure (i.e., none, once, and twice) was measured both subjectively (i.e., self-judgements) and objectively (i.e., ratings of verbal descriptions).

As expected, similarity judgements increased with exposure to the original image, which was objectified by verbal description ratings. This reflects the shift from imagination to memory reconstruction. This increase was steeper for objects than for scenes, with (slightly) higher similarity for scenes prior to exposure, but higher similarity for objects after the first exposure. Importantly, if memory representations contributed less to the (re)-construction of objects than to that of scenes, the reverse pattern should have occurred. Besides, since an increase in similarity was found in both conditions when analysed separately (i.e., simple effects), those results rather suggest that both types of stimuli benefited from exposure, that is, from memory encoding. One could argue that the lower similarity ratings for objects prior to exposure may only result from the lower number of details available to describe in those images. However, participants were asked to rate the similarity between the imagined and original images, not the absolute number of details they recalled. The fact that the pattern was reverse after the first exposure also argues against this hypothesis. Finally, similarity also increased with the second exposure, which can be attributed to the strengthening of the memory representation (or memory *trace*).

Overall these results show that exposure to the whole stimulus causes a shift from construction to reconstruction. These findings must be interpreted cautiously regarding two aspects. First, we studied *reconstruction*, a cognitive mechanism, with no associated measure

of brain activity. Therefore, the conclusions drawn at the cognitive level do not indicate the exact nature of the underlying brain computation, here assumed to be pattern-completion. In other words, these results provide information on the patch-cue reconstruction protocol, but do not constitute a demonstration that pattern-completion of scene and object representations is equivalent at the neural level. Second, this study differs from the patch-cue recognition protocol, since there were no old and new stimuli, rather, participants tried imagining all images with and without prior exposure. However, the facts that (1) in the patch-cue paradigm participants are explicitly instructed to reconstruct the images *from memory*, and (2) having shown that reconstruction of both scenes and objects benefits from prior exposure, support that memory reconstruction can be measured for both types of stimuli through the patch-cue paradigm.

Synthesis

Study 1 demonstrated that reconstruction is separable from proper recollection, and stressed the importance of controlling the instructions given to participants when measuring this operation. Study 2 showed that the reconstruction of both scenes and objects relies on episodic memory representations. Taken together, these results indicate that the operation of reconstruction from visual patches can occur without recollection, but is a memory operation. This paradigm is therefore suited for measuring pattern-completion like retrieval of low- and high-dimensional representations. Accordingly, this procedure will be used in study 3. Instructions will be adapted in order to avoid confusions between reconstruction and recollection, which will be measured separately in a patch-cue and whole-item versions of the task, respectively.

Chapter VII: Hippocampal and perirhinal engagement in memory and visual perception: the role of representational content (Study 3)

The demonstration that the hippocampus is involved in pattern-completion of scenes but not objects provides a strong argument in favour of the representational-hierarchical (RH) account of MTL regions. However, this model predicts that the same effect should apply to any other operation, which remains to be tested. Studies 1 and 2 confirmed that the patch-cue protocol is suited for measuring such memory operation, and supported the relevance of dissociating it from recollection versus familiarity, which are better evaluated through a whole-item traditional remember/know paradigm. Study 3 aims at (1) replicating the results reported by Ross and colleagues (2018); (2) assessing whether those results can be extended to other memory and non-memory operations; and (3) investigating how these results apply to the long-axis of the hippocampus.

This chapter is adapted from the article Gardette, J., Cousin, E., Bourgin, J., Torlay, L., Pichat, C., Moreaud, O., & Hot, P. (2022). Hippocampal activity during memory and visual perception: The role of representational content. *Cortex*. <https://doi.org/10.1016/j.cortex.2022.09.004>

This article was published in the registered-report format, therefore the stage 1 approved protocol, data, as well as analysis codes, are fully available on the OSF project page: https://osf.io/cbds5/?view_only=8dff7226148143c2b8a9a4a4efcfab01

A subset of the results from this study were presented at the Organisation of Human Brain Mapping (OHBM) conference in Glasgow in June 2022 under the title: fMRI evidence for representational-based MTL specialisation across memory operations (Gardette et al.).

Contents of chapter VII

| | |
|--|-----------|
| Chapter VII: Hippocampal and perirhinal engagement in memory and visual perception: the role of representational content (Study 3)..... | 88 |
| Introduction..... | 90 |
| Methods | 92 |
| Results | 100 |
| Summary of the main results | 108 |
| Discussion | 108 |
| Synthesis..... | 113 |

Introduction

According to the RH model, recollection is the combination of the operation of *pattern completion* and a complex, associative representation that includes a temporal and/or spatial context. In contrast, the process of familiarity involves the operation of generating a memory-strength signal and assessing its strength. Crucially, the definitions of pattern-completion and strength-signal memory are independent of the memory content, or representation (Cowell et al., 2019). The interest in breaking cognitive processes into operations and representations is to consider the influence of one in isolation from the other, which leads to two competing hypotheses: one operation-based, the other representation-based. In line with the RH hypothesis, the representation processed would determine the MTL regions involved in a given cognitive process, independently of the operation performed on it. Ross and colleagues (2018) showed that the recruitment of the hippocampus in pattern-completion like memory reconstruction is specific to scenes, as compared to objects. The first aim of Study 3 is to replicate these results, which strongly support the RH view.

This demonstration, however, only concerns pattern-completion. If MTL structures are specialised according to representations and not operations, then the pattern of results observed in this study should be found for other operations such as the generation of a memory-strength signal, or even visual perception. K responses reflect familiarity, or memory-strength signal recognition. Ross and colleagues reported no activation of the hippocampus associated with K responses for scenes. One interpretation of this result could be that the function of the hippocampus is, after all, recollection, which involves *both* the operation of pattern completion *and* a complex, associative memory content. However, given that recognition was performed on patch stimuli, participants judged only these visual patches as familiar, not the whole stimuli. Consequently, the representations processed in these trials were not scenes but parts of scenes, which cannot be regarded as high-dimensional representations. In other words, if these stimuli were complete, the hippocampus would have been recruited during K responses for scenes, according to the RH model. The second aim of the present study is to test whether the representational specialisation found for pattern-completion can be extended to strength-signal recognition, by measuring familiarity for whole-item scenes and objects.

We therefore expect K responses for whole-item scenes to elicit hippocampal activations in comparison to whole-item objects. This prediction results from the hypothesis that the representation (i.e., scenes or objects), and not the operation (i.e., memory-strength-signal) determines the MTL structures involved in familiarity-based memory. Yet, whether the signal that is generated is strong enough to trigger a familiarity judgement does not affect the dimensionality of the representational content, which depends on the cue stimulus only. Therefore, whether a memory-strength-signal does trigger a familiarity judgement or not should not affect the MTL structures involved in this process, which should instead be recruited according to the dimensionality of the stimulus. Correctly rejecting high-dimensional stimuli should thus activate the hippocampus similarly to recognising the same kind of stimuli

via familiarity. We hence expect new whole-item scene processing to recruit the hippocampus in comparison to new whole-item object processing (i.e., correct rejections; figure 7.1).

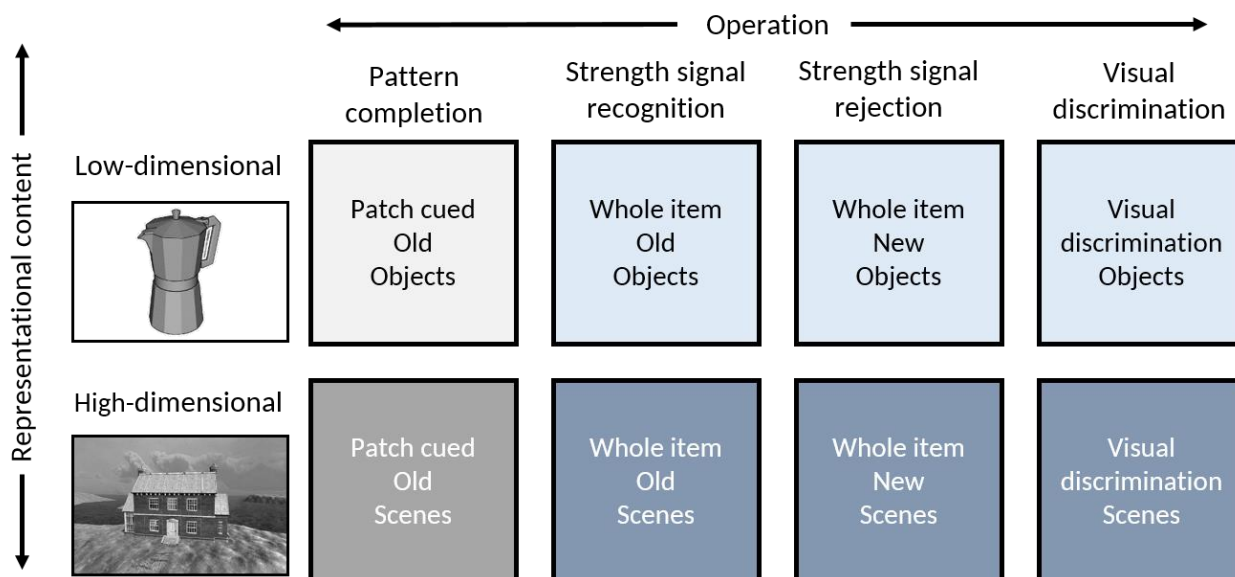


Figure 7.1. Schematic illustration of the matrix taken from Ross et al (2018) extended to additional operations. Grey boxes represent conditions investigated by Ross and colleagues; blue boxes represent conditions added in the present study.

As detailed in chapters III and IV, there is ample evidence showing the involvement of MTL regions in non-memory processes such as visual perception, both in neuropsychological (Aly et al., 2013; Barense et al., 2007; A. C. H. Lee, Buckley, et al., 2005; A. C. H. Lee, Bussey, et al., 2005; for review, see A. C. H. Lee et al., 2012) and fMRI studies (e.g., Barense et al., 2010; Hodgetts et al., 2017; Lee et al., 2008; McCormick et al., 2021; McCormick & Maguire, 2021; Zeidman et al., 2015). Notably, some results suggest that presenting the stimuli from different viewpoints is crucial to demonstrate such results in visual-discrimination tasks (A. C. H. Lee, Buckley, et al., 2005, 2006; see also Barense, Henson, et al., 2010; review in Graham et al., 2010). When contextualising these results in the representational view, visual discrimination can be considered an operation in the same way as pattern-completion and memory strength signal. Therefore, we used a visual-discrimination task as the encoding phase for subsequent recognition task, thus using the same stimuli across all investigated operations.

Finally, research highlighted the interest of exploring the hippocampus long-axis, as differences in functional specialisation are found across its segments (e.g., Kim, 2015; Poppenk et al., 2013; Zeidman & Maguire, 2016; see chapter V). In particular, a broad-to-sharp account provides an extension of the RH model within the hippocampus. Whereas the anterior hippocampus (aHC) would process broad/gist representations, the posterior hippocampus (pHC) would process sharp/detailed representations. Crucially, this view claims that operations such as pattern-completion can occur in both segments, depending on the “grain” of the representation processed. The results from Ross and colleagues, however, do not fit in this account, as the pHC was more activated by scene than by object reconstruction. It is

possible that proper recollection was confounded with reconstruction in this paradigm (see chapter VI). Having clarified the instructions for measuring visual reconstruction and recollection, the present study aims at investigating the predictions of the broad-to-sharp model of the hippocampus long-axis. In particular, this model predicts that whereas the aHC should be engaged in the reconstruction of scenes specifically, recollection of both types of stimuli should rely on the pHC.

In summary, the aims of the present study were:

- To replicate the results from Ross and colleagues (2018) concerning hippocampal versus PRC engagement during pattern-completion
- To extend these results to other memory operations (i.e., memory-strength recognition and rejection), and to a non-memory operation (i.e., visual discrimination)
- To assess the broad-to-sharp model of the hippocampus internal specialisation

To that end, we used an fMRI protocol based on the original paradigm with additional experimental conditions. Participants first performed a visual discrimination task with scenes and objects where presentation viewpoint was manipulated; they then performed an incidental recognition task in which scenes and objects were presented in full to one group of participants and in the form of visual patches to the other group.

Methods

Power analysis

To calculate the size required for an adequately powered sample, we used the software G*power. For each of the main hypotheses, we estimated an effect size based on previous studies that reported similar effects. From these effect sizes, we estimate the minimal sample size required to achieve a statistical power of 0.9 with a threshold of $\alpha = .02$ ¹⁰. Concerning pattern-completion, the estimated sample size was $n = 22$ (Ross et al., 2018; effect size .589). For the whole-item recognition task, required sample sizes were $n = 22$ for familiarity effects (Hassabis, Kumaran, & Maguire, 2007; effect size = .655), and $n = 20$ for correct rejections (Rombouts et al., 2001; effect size 0.606). The estimate sample size in the matching task was $n = 18$ (Hodgetts et al., 2017; Lawrence et al., 2020; A. C. H. Lee et al., 2008; Zeidman et al., 2015; effect sizes > .694).

Therefore, the minimal sample size required for the visual-discrimination task was $n = 18$, whereas the minimal sample size required for the recognition task was $n = 22$. Given that the recognition task was designed between-subjects (i.e., half of the participants were assigned to the whole-item condition whereas the other half were assigned to the patch-cue condition), and that the preregistered hypotheses for this task concern only one of these conditions, a

¹⁰ This unusual threshold was advised during the stage 1 review of the registered-report in a replication perspective (Ross and colleagues reported the effect of interest with at $p = .019$).

minimum of 22 subjects was required per group. Our study therefore needed 50 participants overall, with 25 participants per group in the recognition task.

Participants

A total of fifty-nine healthy young adult participants were recruited through posters at the Grenoble-Alpes University campus (Grenoble, France). Two participants were excluded because of technical difficulties, and one due to excessive head motion during scanning. After applying exclusion rules for behavioural responses (see *Planned analyses - behavioural data*), 51 participants were included in the analyses of the visual-discrimination task, and 25 in each condition of the recognition task analyses. All participants were native French speakers, right-handed, and had normal or corrected vision. Mean age was 21.3 (SD = 2.1; range 18-30; 13 males). Before taking part in the study, participants were screened for MRI safety and gave their informed consent. This study was governed by French law (Jardé, Décret n° 2016–1537; 16 November 2016) and the protocol has been approved by the National French Ethics Committee for the Protection of Human Subjects (CHUGA promotion; CPP 2020-A01592-37; ClinicalTrials ID NCT04562974).

Inclusion criteria

- Having normal or corrected-to-normal visual acuity, allowing normal perception of the experimental material.
- Giving written informed consent before taking part in the study.
- Age between 18 and 35 years.
- Having no contraindication to MRI scanning.
- Being affiliated with the French social security system (healthcare system).

Exclusion criteria

- Existence of a severe general health condition (e.g., heart or respiratory, haematologic, renal, hepatic, cancerous)
- Pharmacological treatment likely to modulate brain activity (e.g., benzodiazepines, antidepressants, neuroleptic, lithium)
- Diagnosed psychiatric or neurological condition (e.g., cerebrovascular accident, epilepsy)
- Alcohol ingestion before examination
- Claustrophobia
- People concerned by L1121-5 to L1121-8 of the French public health code (i.e., pregnant or breastfeeding women, subjects under 18 or over 18 years protected by the law, and subjects under administrative or legal surveillance).
- Uncorrected visual disorder
- Cognitive deficit (criterion: Mini-Mental State Examination score of <27)

Procedure

The experimental procedure began with a short neuropsychological examination, including the Mini-Mental State Examination (Kalafat et al., 2003) and the Trail-Making Test, Part A and B (Lezak et al., 2004; Mitrushina et al., 2005)¹¹. Participants then underwent a training session for the matching task. During the training phase only, feedbacks were given on the accuracy of each response; in the case of an error, the stimuli remained on-screen until the participant pressed a key, to provide enough time to resolve the trial. After ensuring that participants understood the instructions and were familiarised with the task, they underwent the scanning session. The protocol was composed of two experimental tasks, both performed during MRI scanning. Stimuli were displayed with OpenSesame software (Mathôt et al., 2012) and projected onto a translucent screen (1366 x 768 pixels) at the rear of the MRI scanner, visible via a mirror placed on the head coil. Participants provided their responses manually.

Matching task

Task procedure

During the matching task, each trial was composed of three visual stimuli: one (i.e., the reference) positioned above the other two (i.e., the target and the lure; figure 7.2). Participants were given the instruction to determine which of the two images presented below matched (i.e., described the same stimulus as) the reference image. Each trial lasted 6 sec. After an answer was given by the participant, the lure and target images disappeared, but the reference image remained on-screen. Each reference stimulus was thus displayed for the same duration (i.e., 6 sec), hence controlling for encoding time. Two variables were manipulated: stimulus type (scenes vs. objects), and viewpoint (same vs. different), resulting in four experimental conditions. There were 32 stimuli per condition (i.e., 128 trials overall). Trials were paired into 12-sec pseudo-blocks (figure 7.2). The task was divided into two functional runs of 10 min, each including 32 task blocks and 6 rest blocks consisting in a fixation cross displayed for 12 sec. Blocks were separated by 4-sec inter-stimulus intervals, consisting of a grey fixation dot displayed on a black screen. Response accuracy and response time were recorded.

¹¹ The versions of these tests used can be found in appendices C1 and C2.

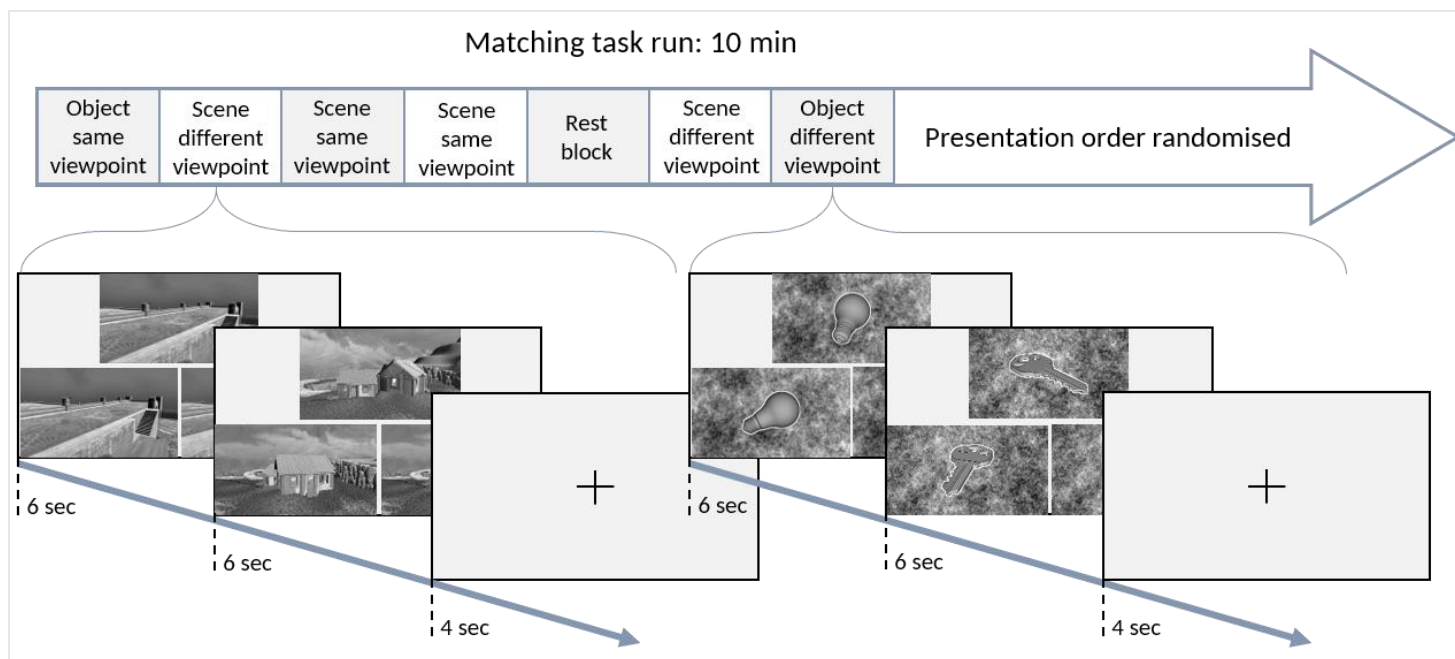


Figure 7.2. Design of the matching task. Pseudo-blocks were composed of 2 trials of the same condition. Pseudo-blocks composition and presentation order were randomly determined for each participant. Six rest blocks were intermixed with task blocks.

Recognition task

Task procedure

During the recognition task, scenes and objects from the matching task were presented again to the participants, mixed with new stimuli of the same type. A trial was composed of one stimulus displayed in the centre of the screen for 6 secs (figure 7.3). The task was divided into two runs of 64 trials (i.e., 128 trials overall). Each run lasted 11 minutes and included 24 old and 8 new scenes and 24 old and 8 new objects, as well as 32 baseline trials (i.e., null events), consisting in a fixation dot displayed for 4 sec. Events (i.e., scenes, objects, and null events) were presented in a pseudo-randomised order. Half of the participants ($N = 25$) underwent the whole-item condition, whereas the other half underwent the patch-cue condition. Participants were randomly assigned to one of the conditions. Participants were not given the instruction to try to remember stimuli during the first task, thus ensuring incidental encoding. Both groups of subjects were instructed to determine whether or not each stimulus had been presented during the previous task, but with different specific instructions. When an answer was given, the displayed image disappeared and was replaced by the inter-stimulus fixation cross, thus informing the participant that their response had been recorded.

Instructions in the patch-cue condition

In the patch-cue condition, stimuli were presented in the form of visual patches. Participants had three response options: '1' if they were able to *visually reconstruct the original image from the patch* (Rec responses); '2' if the patch seemed familiar to them but they could not

reconstruct the original image (K responses); and '3' if they thought the patch had not been presented before (new responses).

Instructions in the whole-item condition

In the whole-item condition, stimuli were presented in the same form as during the matching task (i.e., entirely). Participants had three response options: '1' if they *specifically remembered seeing the stimulus during the first task* (R responses); '2' if the stimulus seemed familiar to them but they did not specifically remember seeing it before (K responses); and '3' if they thought the stimulus had not been presented before (new responses).

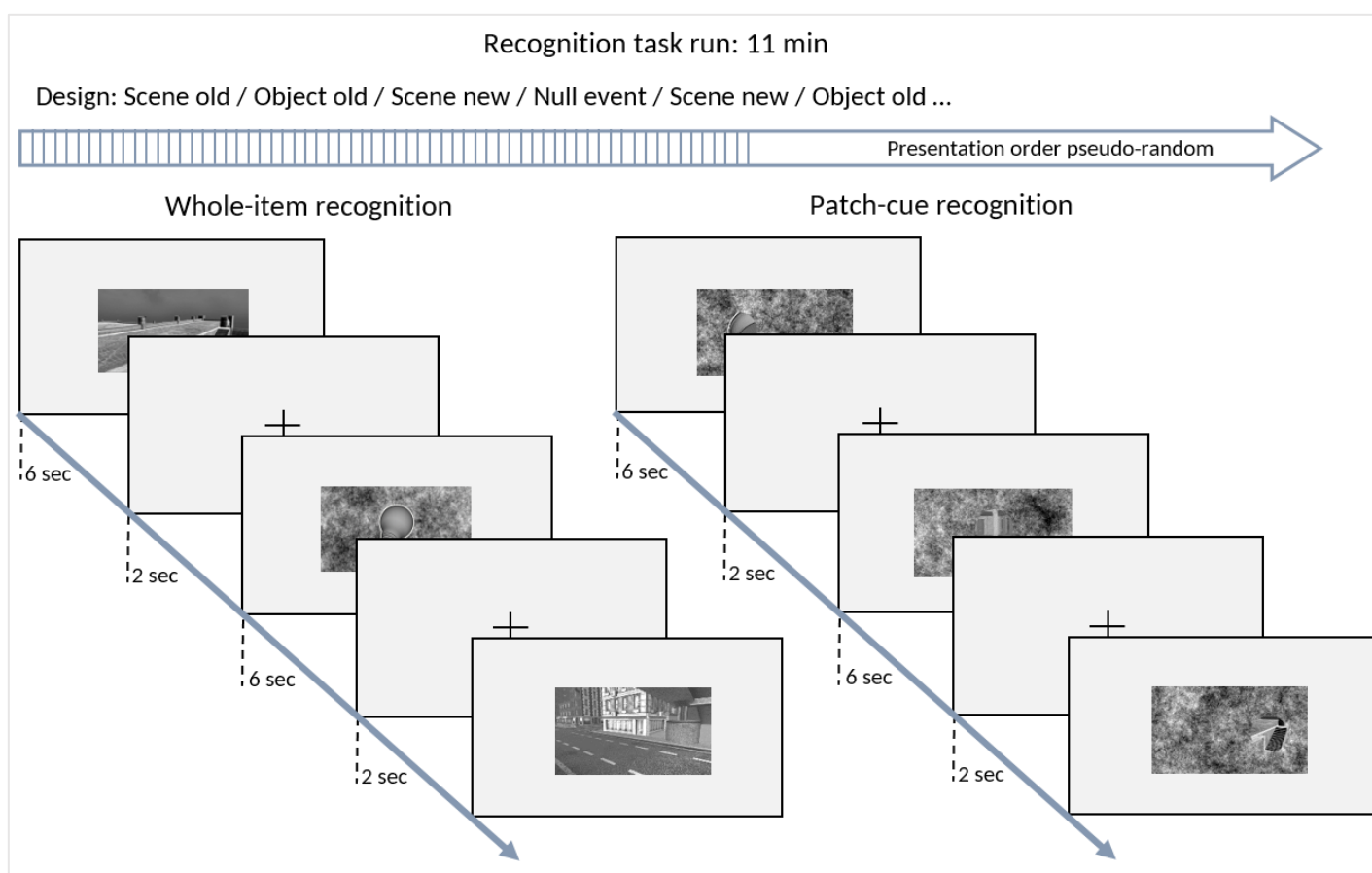


Figure 7.3. Event-related design of the recognition task. Old and new scenes and objects were presented in a pseudo-randomised order, intermixed with baseline trials (i.e., null events).

Briefing and debriefing sessions

Remember/know paradigms are very powerful to investigate the nature of memory retrieval, by relying on participants' subjective feeling; it hence comes with a briefing and a debriefing session (Diana et al., 2006; Migo et al., 2012; Rajaram, 1993). First, we ensured that each participant had fully understood the R/K instructions before the task began. To do so, we provided participants with examples of the subjective feeling associated with each type of response, and encouraged them to ask questions until they had a good comprehension of what each response option meant (i.e., Rec vs. K in the patch-cue condition and R vs. K in the

whole-item condition). They were explicitly told to respond according to their subjective feeling. At the end of the experiment, participants also underwent a debriefing session, in which we ensured that they responded according to R/K instructions. As was done in Ross et al. (2018), participants were aware that a debriefing session would take place at the end of the recognition task, thus encouraging them to respond as accurately as possible.

Stimuli and manipulation

The stimuli used in this study were taken from the stimuli base constructed for this series of experiments (see Materials: General section). Scenes and objects were used, in the whole-item and patch-cue versions. In the matching task, there were 64 scene and 64 object trials, thus including 384 images (3 images per trial). In the recognition task, there were 64 scene and 64 object trials, comprising 48 old and 16 new items, thus 128 images overall, either in the whole-item or in the patch-cue version.

MRI data acquisition and preprocessing

Scanning parameters

MRI and fMRI data were collected using a 3T scanner (Achieva dStream 3.0T TX, Philips Medical Systems, Best, NL) with a 32-channel head coil at the IRMaGe MRI facility (Grenoble, France). First, T1-weighted, high-resolution, 3D anatomical scans were acquired (field of view (FOV) = 256 x 192 x 220; resolution = 1 x 1 x 1 mm; acquisition matrix = 256 x 256 pixels, reconstruction matrix = 256 x 256 pixels). Functional data were then acquired using a BOLD-sensitive T2*-weighted echo-planar imaging (EPI) method. According to the hypotheses and in order to increase spatial resolution, a reduced FOV (100 x 240 x 60) was used, focused on ROIs (i.e., MTL areas; for methodological considerations on this point, see Nau, 2019). Each volume was composed of 40 slices, acquired sequentially in an ascendant mode. Slice thickness was 1.5 mm. The in-plane voxel size was 1.27 x 1.27 x 1.5 mm (166 x 160 pixels data matrix; 192 x 192 pixels reconstruction matrix). The main sequence parameters were: TR = 2s; TE = 30 msec; flip angle = 80°. One whole-brain EPI image was acquired for the coregistration preprocessing step.

Preprocessing

fMRI data were preprocessed with SPM 12 (SPM, Wellcome Department of Imaging Neuroscience, London, U.K; www.fil.ion.ucl.ac.uk/spm) implemented in MATLAB (Mathworks Inc., Sherborn, MA, USA). First, a realignment step was performed to correct for subtle head movements. Realigned functional images were then coregistered to the whole-brain image. A second coregistration step served to replace the anatomical image onto the whole-brain functional image. Finally, functional images were smoothed with a 3-mm FWHM (Full Width at Half Maximum) Gaussian kernel. Noise and signal drift were removed by using a high-pass filter (1/128 Hz cut-off). Preprocessed data were then statistically analysed.

Exclusion rules for MRI data

Motion parameters from the realignment step were then analysed using ART (Artifact Detection Tool, Gabrieli Lab, Massachusetts Institute of Technology, available at: https://www.nitrc.org/projects/artifact_detect). Were considered as outliers those volumes that showed more than 1.5 mm interscan movement in translation, 0.02 rad in rotation, or 3 SD global interscan signal intensity relative to the session mean. Participants who had more than 15% of scans marked as outliers were excluded from the study (N=1).

*Planned analyses**Behavioural data*

Behavioural data from the matching task included rates of correct responses (CRs) and errors (response times were not of interest to our purposes) for each participant for each run. The study being conducted among healthy young participants, we expected them to succeed in all conditions of the task. To be included in the analyses, the rate of CRs for a participant had to be at least 70%, thus ensuring that participants performed the task properly (for similar designs, see Barense, Henson, et al., 2010; Hodgetts et al., 2017; A. C. H. Lee et al., 2008). Behavioural data from the recognition task included CR and error rates as well as rates of remember and know responses, for each participant for each run. Correct responses consisted in correct recognitions (R/rec or K for old items) and correct rejections (New for new items); errors consisted in false alarms (R/rec or K for new items) and omissions (New for old items). To be included in the analyses, the rate of CRs of a participant had to be at least 70%, and rates of correct R/rec and K responses had to be of at least 20%, thus insuring that participants performed the task properly, and that all response types were represented.

*Statistical fMRI analyses**Statistical design*

Following preprocessing, statistical analyses were performed using the general linear model (GLM) as implemented in SPM12. Runs from the matching paradigm were analysed as a block design, including 2 factors: stimulus type (i.e., scenes vs. objects) and viewpoint (i.e., same vs. different). These 4 experimental conditions were modelled as a boxcar function of 12-sec duration (i.e., the duration of a pseudo-block) and convolved with the canonical hemodynamic response function to create regressors of interest. Recognition task runs were analysed as an event-related design including 2 factors: stimulus type (i.e., scenes vs. objects) and subject-driven correct response (i.e., R/Rec, K, and new). These 6 experimental conditions were convolved with the canonical hemodynamic response function to create regressors of interest. Movement parameters obtained by realignment corrections were included as noise (regressors of no interest).

Regions of interest (ROIs)

ROIs were defined on each individual's non-normalised structural brain image. The Automated Segmentation of Hippocampal Subfields approach (ASHS; Yushkevich et al., 2015) was first performed, then ROIs were manually edited by using MRICron (<https://www.nitrc.org/projects/mricron>). The sub-regions of the parahippocampal gyrus (including Brodmann areas 35 and 36) were combined into the parahippocampal region, and controlled following the principles described by Allen et al. (2005). This parahippocampal region was then subdivided into three sections of equal length: an anterior segment corresponding to the PRC, a posterior segment corresponding to the PHC, and a middle segment corresponding to the transition zone between these regions (Ross et al., 2018; for a similar approach, see also Hannula et al., 2013). Using the same approach, we divided the hippocampus longitudinally into three segments corresponding to the anterior, middle (midHC), and posterior hippocampus (figure 7.4). ROI drawings were checked by a researcher (MD) with extensive neuroanatomy experience, including that related to the hippocampus and MTL structures, and were adjusted where necessary in discussion with the research team. Parameter estimates were then extracted from these ROIs across the experimental conditions by using the Nilearn python module (<https://nilearn.github.io/index.html>). After verifying the homogeneity of variances using Levene's test, and removing extreme values, these parameter estimates were entered into specific within-subjects mixed regressions. Stimulus type (Scene/Object), viewpoint (Different/Same), and hippocampus segment (aHC/midHC/pHC) were analysed as within-subject variables.

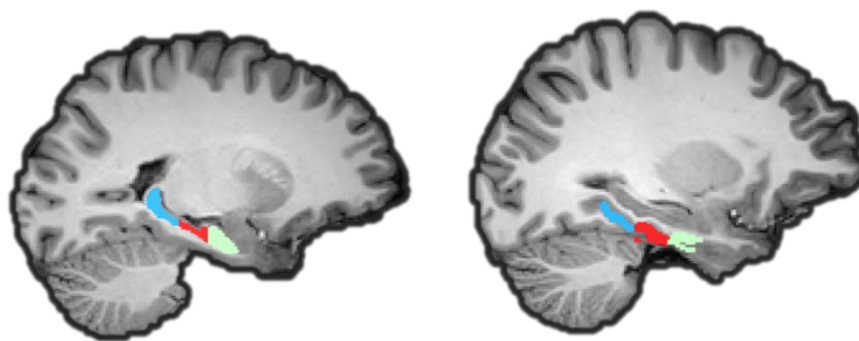


Figure 7.4. Regions of interest drawn on one sample subject's anatomy. Left: posterior, middle, and anterior hippocampus. Right: posterior, middle, and anterior (perirhinal cortex) parahippocampal gyrus.

ROIs validation analysis

The approach we used to define the ROIs differs from that used in the original study. Specifically, the anterior border of the PRC extends more anteriorly in the anatomical criteria followed by Ross and colleagues (Pruessner et al., 2000, 2002) than with the ASHS-driven segmentation. We chose this procedure in order to be more conservative on what is included in the PRC regions. However, to rule out the possibility that any discrepancy between our results and those reported in the original study would be due to the difference in the

segmentation procedures, we conducted a validation analysis: all anatomical scans were re-segmented manually using the original criteria. Signal from all conditions of the matching paradigm (as this task includes all subjects, unlike the recognition tasks) was then extracted from the two versions of the PRC ROI. Correlation analyses revealed that the two methods led to extremely similar results (all $r > .975$; all p -values $< .001$). Finally, all analyses presented in the results section were performed again using the extended PRC masks instead of the initial masks, which did not yield any appreciable difference.

Additional whole-brain analyses

The main analysis procedure reported in this work (and in the associated publication) is ROIs-based, similar to that of the original study, since this procedure is most suitable to test region-specific hypotheses. We completed this procedure by a whole-brain approach to provide more comprehensive and contextualised information. This approach was used to locate the clusters of voxels that showed significant signal change between scene and object processing both (1) within the ROIs (e.g., in the medial-lateral axis of the hippocampus) and (2) outside the ROIs (e.g., the parahippocampal cortex). To this end, anatomical data from each participant were normalised to the Montreal Neurological Institute (MNI) space. The anatomical normalisation parameters were subsequently used to normalise functional volumes. Statistical parametric maps generated at the individual level with the Scene > Object contrast were finally entered into a one-sample t -test at the second level, constituting the group analysis for each hypothesis (i.e., Matching, Pattern-completion, Strength-signal recognition, Strength-signal rejection, and Recollection). Activity clusters found in the hippocampus are categorised as aHC or pHC depending on the y coordinate, with $y = -21$ (in MNI space) being considered the posterior border of the aHC (Poppenk et al., 2013). Finally, an exploratory conjunction analysis was performed in order to test the hypothesis that a scene specialisation could be identified in the hippocampus across all operations studied (Friston et al., 2005). For clarity, the results from whole-brain analyses are displayed as a complement to each ROI analysis, projected on a MNI template. The full results of the whole-brain analyses, and the procedure and results of the conjunction analysis, are available in appendix B.

Results

Behavioural data

Neuropsychological screening confirmed that all participants presented normal global cognitive functioning ($M_{MMSE} = 29.86$; $SD = 0.34$) and visuo-spatial abilities ($M_{TMT A} = 17.97$; $SD = 4.32$; $M_{TMT B} = 36.49$; $SD = 8.84$). Only participants who met the inclusion criteria were included for further analyses (cf. *Planned analyses - behavioural data*). Behavioural data confirmed that participants properly performed both the matching task ($M_{correct} = 82.64\%$, $SD = 4.62$) and the recognition task ($M_{correct} = 83.03\%$, $SD = 8.22$). Rates of R/K/N responses were comparable in the whole-item and patch-cue conditions (Whole-item: $M_R = 43.27\%$, $M_K =$

32.15, $M_{\text{new}} = 24.57$; Patch-cue: $M_R = 46.25\%$, $M_K = 33.15$, $M_{\text{new}} = 20.59$ of all correct responses).

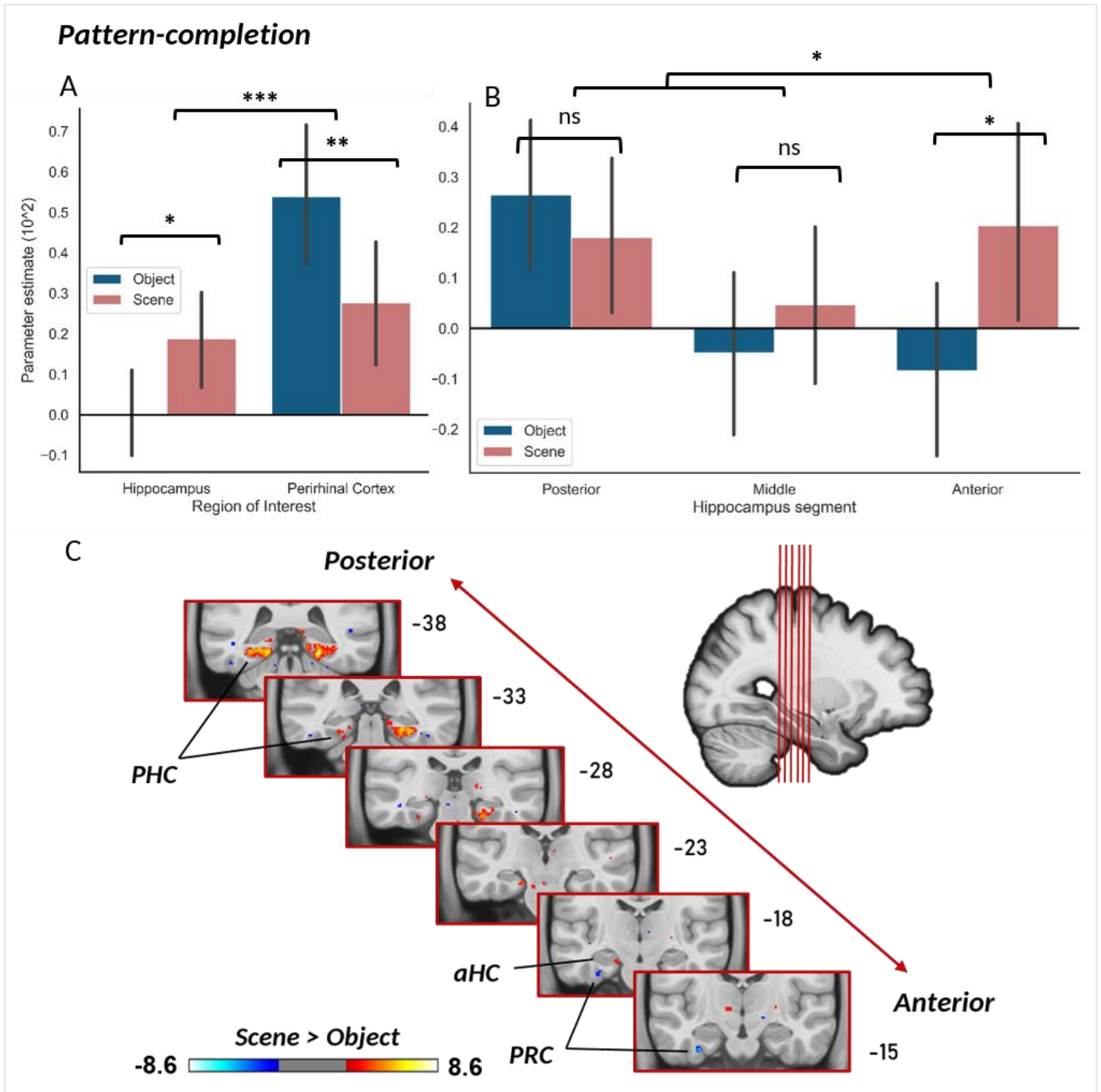


Figure 7.5. Results from pattern-completion trials (i.e., Reconstruction responses in the patch-cue condition). A: Parameter estimates extracted from the hippocampus and perirhinal cortex regions for scenes and objects (means and 95% confidence intervals). B: Parameter estimates extracted from each long-axis segment of the hippocampus. C: Significant clusters of activity resulting from the scene > object contrast in whole-brain normalised data with a threshold of $T = 3$, projected on a MNI template. Ns: non-significant; PHC: parahippocampal cortex; aHC: anterior hippocampus; PRC: perirhinal cortex. *: $p < .05$, **: $p < .01$, ***: $p < .001$

Pattern-completion

As predicted, we observed a significant stimulus type \times ROI interaction during pattern completion, $F(1,22) = 26.64$; $p < .001$ (figure 7.5). Consistent with the original study, the hippocampus was significantly more engaged during pattern completion of scenes than of objects $F(1,22) = 5.26$; $p < .05$. In contrast, the PRC was more engaged during pattern completion of objects than of scenes $F(1,22) = 8.65$; $p < .01$. When decomposing the hippocampus long axis, we found no main effect of stimulus type ($p = .29$), but a Long-axis segment \times stimulus type interaction, $F(1,47) = 4.89$; $p < .05$. Whereas no effect of stimulus type was found in the posterior ($p = .173$) and middle ($p = .371$) segments, the anterior hippocampus showed greater engagement for pattern completion of scenes than of objects, $F(1,22) = 4.77$; $p < .05$.

Strength-signal recognition

Similar to pattern-completion, we observed an ROI \times stimulus type interaction during correct familiarity-based responses, $F(1,22) = 9.28$; $p < .01$ (figure 7.6). Whereas hippocampal activity was higher for scene than for object processing, $F(1,22) = 4.53$; $p < .05$, the reverse pattern was found in the PRC, $F(1,22) = 4.46$; $p < .05$. When investigating the hippocampus long axis, we found a trend for main effect of stimulus type, $F(1,23) = 4.19$, $p = .051$; a main effect of segment, $F(2,22) = 24.66$, $p < .001$; and a stimulus type \times segment interaction, $F(2,46) = 3.95$, $p < .05$. Activity was higher in the pHC than midHC, $F(1,23) = 12.17$, $p < .01$, and higher in the midHC than in the aHC, $F(1,23) = 6.29$, $p < .05$. Signal was enhanced for scene as compared to object processing in the aHC, $F(1,23) = 7.56$, $p < .05$, but not in the midHC ($p = .09$) and pHC ($p = .69$).

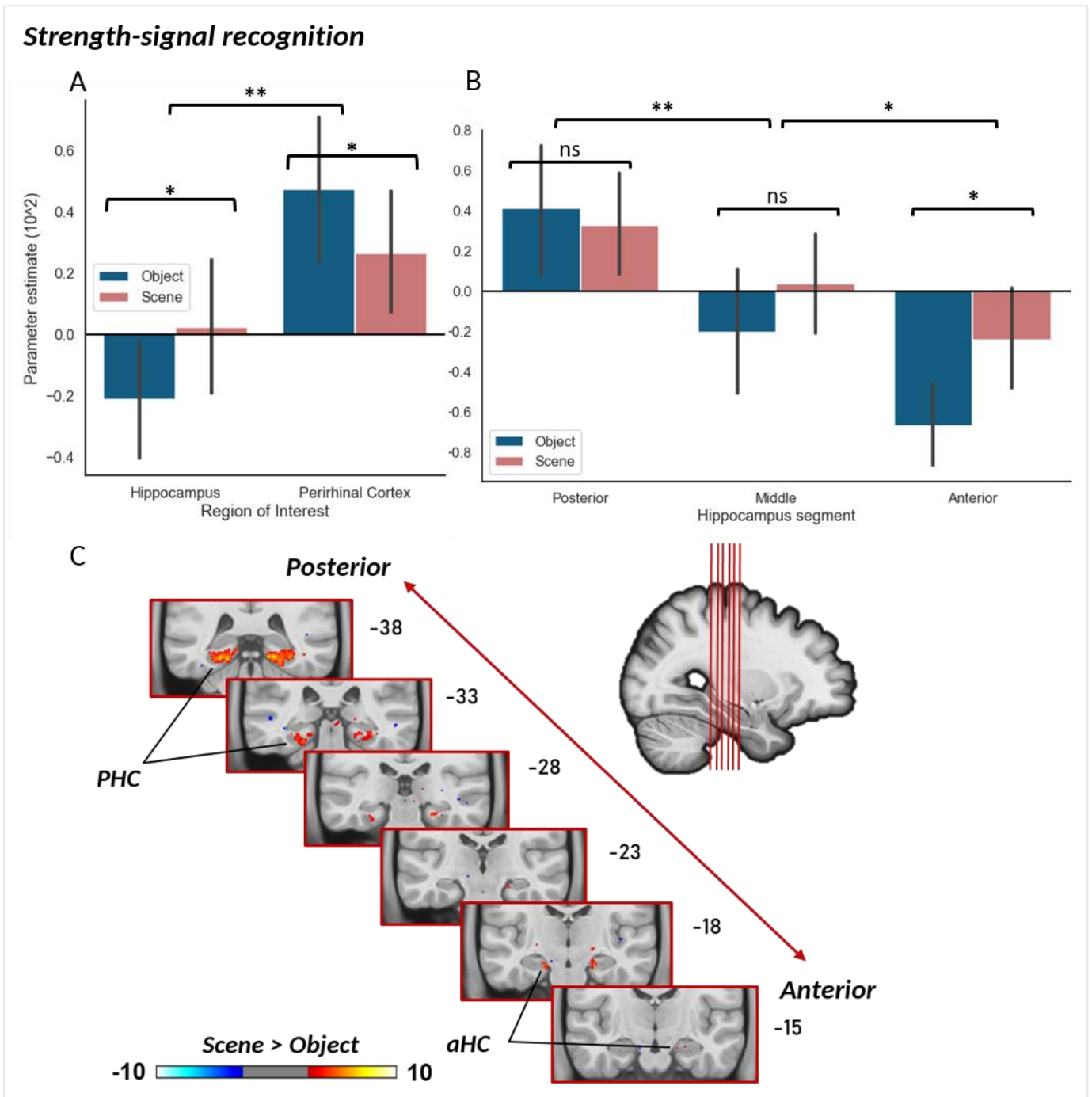


Figure 7.6. Results from strength-signal recognition trials (i.e., Familiarity responses in the whole-item condition). A: Parameter estimates extracted from the hippocampus and perirhinal cortex regions for scenes and objects (means and 95% confidence intervals). B: Parameter estimates extracted from each long-axis segment of the hippocampus. C: Significant clusters of activity resulting from the scene > object contrast in whole-brain normalised data with a threshold of $T = 3$, projected on a MNI template. Ns: non-significant; PHC: parahippocampal cortex; aHC: anterior hippocampus; *: $p < .05$, **: $p < .01$

Strength-signal rejection

Consistent with our hypothesis, we found a stimulus type \times ROI interaction for correct new responses, $F(1,21) = 15.45$, $p < .001$ (figure 7.7). The hippocampus was more activated by

correct rejection of scenes than of objects, $F(1,22) = 4.57$, $p < .05$, whereas no effect of stimulus type was found in the PRC ($p = .30$). Concerning the hippocampus long-axis, an effect of segment was found, $F(1,23) = 6.8$, $p < .05$, whereas there was no significant effect either of stimulus type or stimulus type \times segment interaction (both $p > .1$). Specifically, trends for higher activity in the pHC compared to the aHC, $F(1,23) = 4.06$, $p = .055$, and to the midHC, $F(1,32) = 3.38$, $p = .078$, were observed. There was no difference between midHC and aHC engagement ($p = .84$). Finally, scene processing recruited significantly more the aHC than object processing did, $F(1,23) = 6.96$, $p < .05$, whereas no effect of stimulus type was found in the midHC ($p = .55$) and pHC ($p = .68$).

Visual discrimination

We observed an ROI \times stimulus type interaction during visual discrimination, $F(1,195) = 131.74$, $p < .001$; (figure 7.8.A)¹². Hippocampal activation was higher for scene than for object processing, $F(1,49) = 42.89$, $p < .001$, whereas the PRC was more recruited by object than by scene processing $F(1,49) = 34.70$, $p < .001$. There was no stimulus type \times viewpoint interaction for the hippocampus ($p = .65$). In contrast, such an interaction was found in the PRC $F(1,48) = 9.43$, $p < .01$ (figure 7.8.C). Simple effects revealed that PRC activity was enhanced in the different as compared to same viewpoint for object processing, $F(1,45) = 16.43$, $p < .001$, but not for scene processing ($p = .91$). When we analysed the hippocampus long-axis segments, we found a main effect of hippocampus segment, $F(2,48) = 22.23$, $p < .001$, as well as a stimulus type \times segment interaction, $F(2,343) = 15.48$, $p < .001$ (figure 7.8.B). Signal was higher for scene than for object discrimination in the aHC, $F(1,147) = 31.93$, $p < .001$, and midHC, $F(1,152) = 65.94$, $p < .001$, but not in the pHC ($p = .085$).

¹² Negative vs positive parameter estimates values are due to an implicit global normalisation step during the statistical processing procedure in SPM. Interpretations are based on relative differences found between experimental conditions and regions.

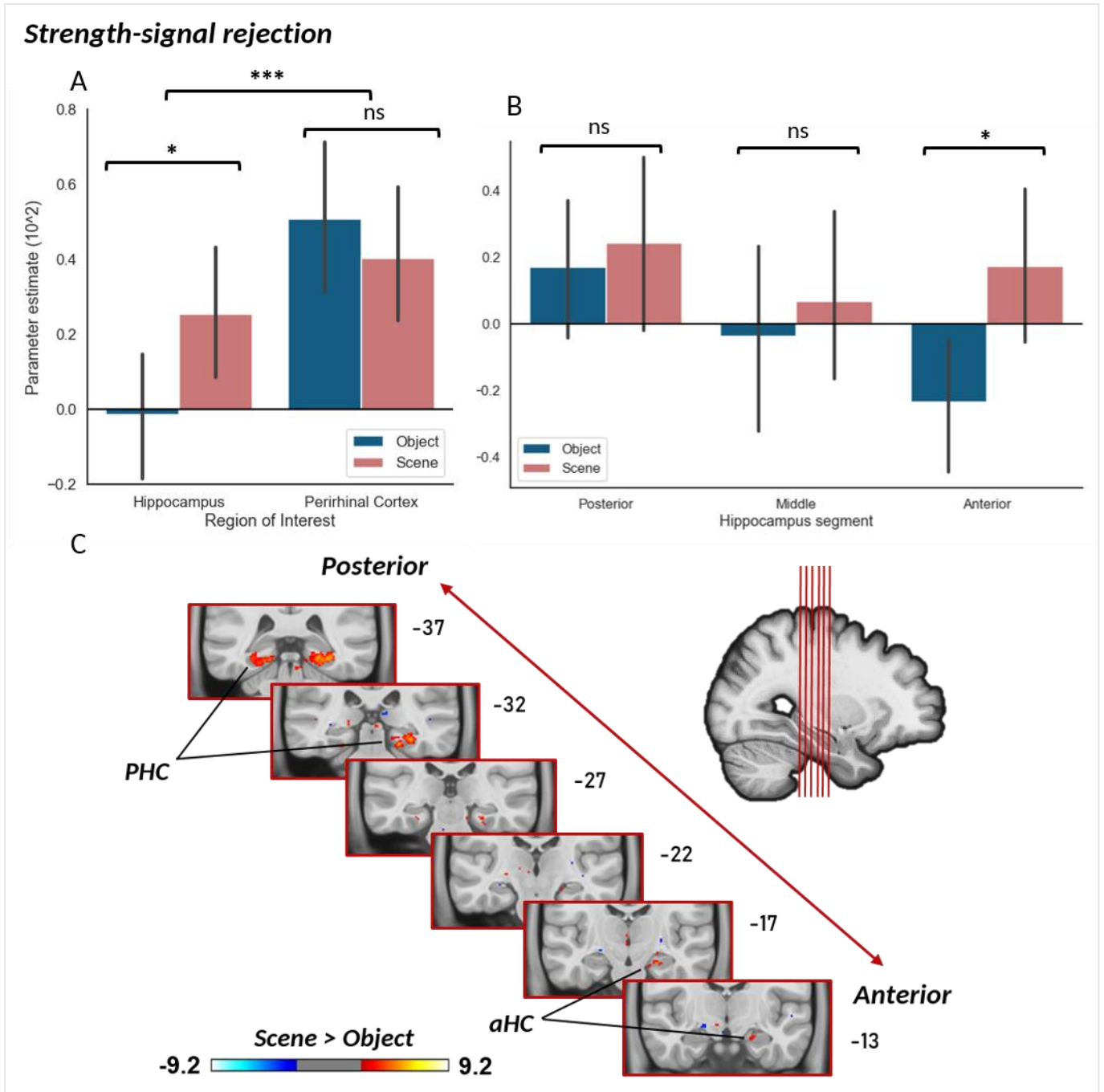


Figure 7.7. Results from strength-signal rejection trials (i.e., New responses in the whole-item condition). A: Parameter estimates extracted from the hippocampus and perirhinal cortex regions for scenes and objects (means and 95% confidence intervals). B: Parameter estimates extracted from each long-axis segment of the hippocampus. C: Significant clusters of activity resulting from the scene > object contrast in whole-brain normalised data with a threshold of $T = 3$, projected on a MNI template. Ns: non-significant; PHC: parahippocampal cortex; aHC: anterior hippocampus; *: $p < .05$, ***: $p < .001$

Recollection

We then analysed the activity patterns during proper recollection (i.e., R responses in the whole-item condition) across the hippocampus long-axis and PRC. Main effects of segment, $F(1,22) = 11.57$, $p < .001$, and of stimulus type, $F(1,23) = 5.49$, $p < .05$, as well as segment \times

stimulus type interaction, $F(2.46) = 5.32, p < .05$, were observed (figure 7.9.A). The pHC was more recruited than the midHC, $F(1,23) = 12.76, p < .01$, and the aHC, $F(1,23) = 21.75, p < .001$, whereas engagement of the aHC and midHC was comparable ($p = .15$). The effect of stimulus type was significant in the aHC, $F(1,23) = 9.14, p < .01$, but no in the midHC ($p = .073$) and pHC ($p = .84$). Finally, the PRC was more recruited by object than scene processing, $F(1,24) = 5.32, p < .05$ (figure 7.9.B).

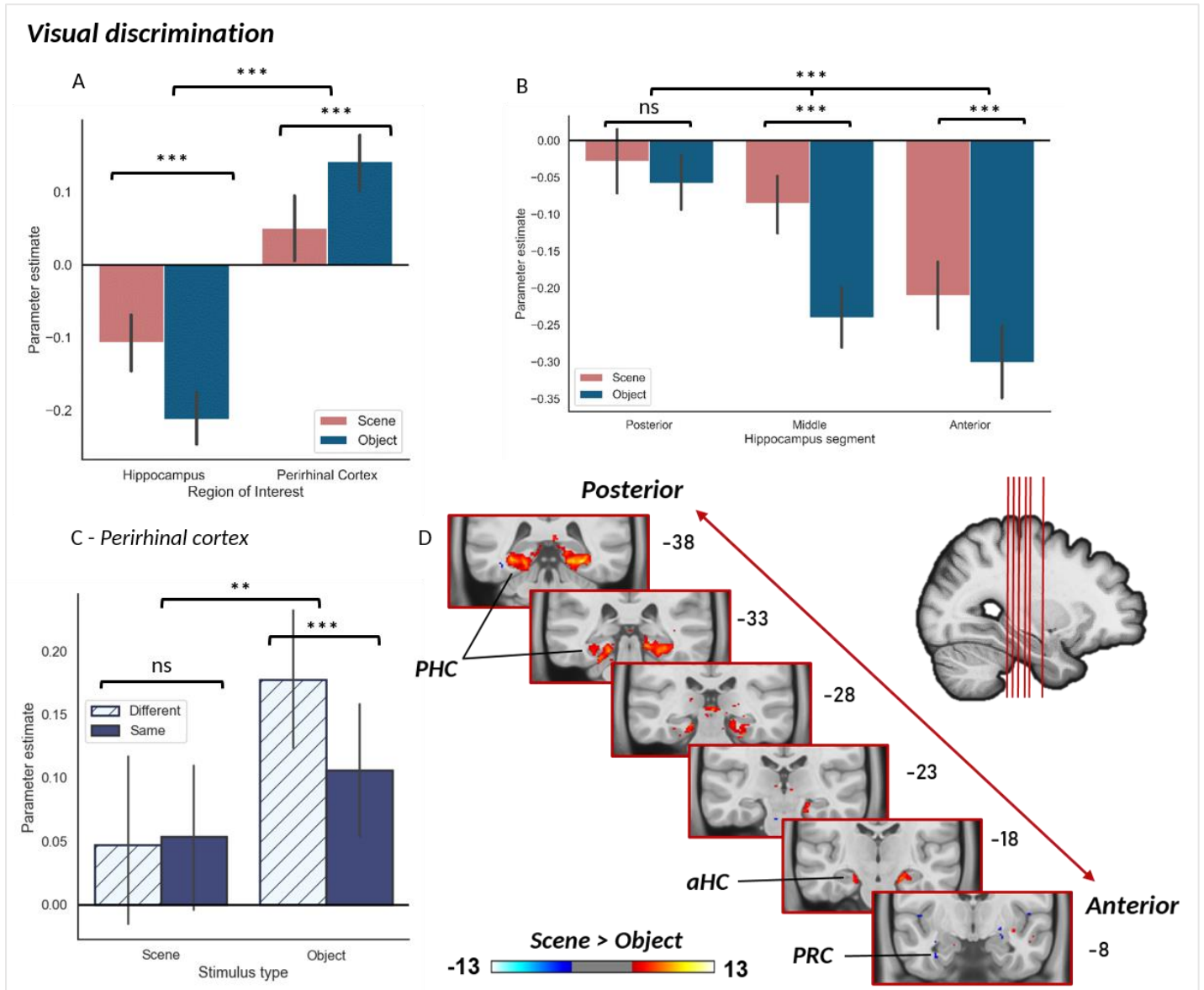


Figure 7.8. Results from matching task. A: Parameter estimates extracted from the hippocampus and perirhinal cortex regions for scenes and objects (means and 95% confidence intervals). B: Parameter estimates extracted from each long-axis segment of the hippocampus. C: Parameter estimates extracted from the perirhinal cortex as function of stimulus type and viewpoint. D: Significant clusters of activity resulting from the scene > object contrast in whole-brain normalised data with a threshold of $T = 3.5$, projected on a MNI template. ns: non-significant; PHC: parahippocampal cortex; aHC: anterior hippocampus; PRC: perirhinal cortex. *: $p < .05$, **: $p < .01$, ***: $p < .001$

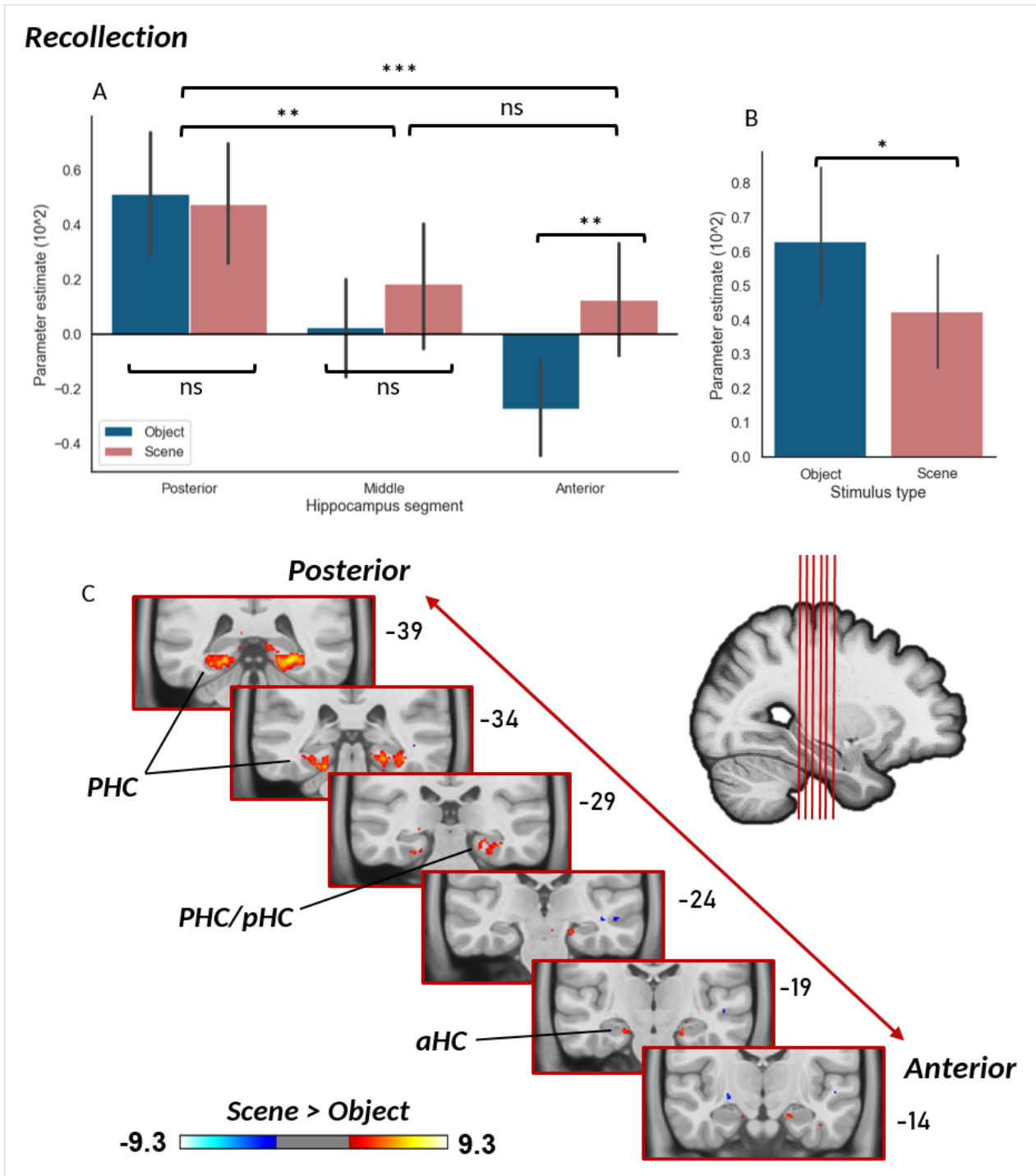


Figure 7.9. Results from Recollection trials (i.e., R responses in the whole-item recognition task). A: Parameter estimates extracted from the hippocampus long-axis segments for scenes and objects (means and 95% confidence intervals). B: Parameter estimates extracted the PRC. C: Significant clusters of activity resulting from the scene > object contrast in whole-brain normalised data with a threshold of $T = 3$, projected on a MNI template. Ns: non-significant; PHC: parahippocampal cortex; pHC: posterior hippocampus, aHC: anterior hippocampus. *: $p < .05$, **: $p < .01$, ***: $p < .001$

Summary of the main results

ROI analyses

Table 7.1. Summary of the main fMRI results: representational specialisation (i.e., scene vs. object preferential engagement of the hippocampus/PRC) and hippocampus long-axis patterns for each operation investigated.

| Operation | Effect of stimulus type | | Hippocampus long-axis pattern |
|-----------------------------|-------------------------|---------------------------|-------------------------------|
| | Scene > Object | Object > Scene in the PRC | |
| Pattern-completion | aHC only | Yes | pHC = midHC = aHC |
| Strength-signal recognition | aHC only | Yes | pHC > midHC > aHC |
| Strength-signal rejection | aHC only | No | pHC = midHC = aHC |
| Visual discrimination | aHC and midHC | Yes | pHC > midHC > aHC |
| Proper recollection | aHC only | Yes | pHC > midHC = aHC |

aHC/mid/pHC: anterior, middle, and posterior hippocampus, PRC: perirhinal cortex.

Whole-brain analyses

Whole-brain analyses aimed at locating activations resulting from the comparison between scene and object processing. Significant activations resulting from the Scene > Object contrast were found in the aHC for all operation investigated. More precisely, these clusters were consistently located in the medial part of the aHC. This was confirmed by the conjunction analysis, which revealed that this region was the same as that identified by Zeidman and Maguire (2016; see appendix B5). This contrast also revealed strong activations in the parahippocampal cortex across all operations. Negative values, that is, clusters of voxels that showed more signal change for object than for scene processing, were found in the PRC region.

Discussion

In this study, we assessed the hypothesis that the engagement of MTL regions in various cognitive operations is determined by representational content. In particular, we aimed at replicating the results reported by Ross and colleagues (2018): a specific recruitment of the hippocampus for the pattern-completion of scenes as compared to objects, and extending it to the operations of strength-signal recognition and rejection, and visual-discrimination. We also investigated how those patterns apply to the long-axis of the hippocampus, and explored the activity found for the process of proper recollection.

1. *Representational specialisation across operations*

a. *Replication of the original results*

As expected, the hippocampus and PRC responded differently to scenes versus objects in reconstruction trials of the patch-cue paradigm. Specifically, the hippocampus was more recruited by pattern-completion like retrieval of scenes than that of objects, while the pattern was reverse for the PRC. This preregistered replication strengthens the original demonstration that the contribution of the hippocampus to memory recall is determined by representational content rather than by the retrieval process. Contrary to the original findings, the PRC was more activated by pattern completion of objects than that of scenes (potential reasons for this discrepancy are discussed in section 3 of this discussion). This effect is consistent with the representational hypothesis, in which it is expected that pattern completion is not limited to the hippocampus. Rather, this operation could happen at any stage of the VVS, depending on the dimensionality of the memory content, and the observed involvement of the hippocampus in processes such as recollection would reflect its specialisation in scene processing (e.g., Barense et al., 2005; Maguire & Mullally, 2013; Mullally & Maguire, 2014; Zeidman et al., 2015). Overall, this pattern of results supports the representational hypothesis: the contribution of MTL regions to memory recall is determined by the dimensionality of the representation retrieved, while pattern-completion would not be specific to the hippocampus.

b. *Generalisation to other memory operations*

We next investigated whether this pattern of results could be extended to operations other than pattern completion (figure 7.1). The representational account makes a clear prediction: this result should be generalisable to any operation, as long as the representations are held constant (Cowell et al., 2019). We first examined familiarity-based memory, or strength-signal recognition and rejection. Because “familiar” and “new” judgements made on visual patches cannot properly elicit such operations, we used a whole-item R/K paradigm to test this hypothesis. As predicted, MTL activity for whole-item familiar responses was modulated by representational content. Yet, whereas the object specialisation observed in the PRC was similar between strength-signal recognition and pattern completion, the scene specialisation of the hippocampus in strength-signal recognition seemed weaker than that found in pattern completion (figure 7.6.A). One possible explanation for this discrepancy is that the hippocampus would be required when a scene representation needs to be constructed (Hassabis, Kumaran, & Maguire, 2007; Maguire & Mullally, 2013; Mullally & Maguire, 2014) or re-constructed as in pattern completion, but not in strength-signal memory. Yet, patients with hippocampal lesions elicit stimulus-dependent deficits in both familiarity and recollection memory (Bird et al., 2007; Cipolotti et al., 2006). Wais et al. (2010) also reported hippocampal involvement in familiarity-based recognition memory in fMRI. Notably, the authors controlled for memory strength confound by using confidence ratings, and argued that previous studies may have failed in demonstrating hippocampal activations in familiarity-

based recognition because the memories associated with familiarity responses were too weak to generate a signal measurable with fMRI. It is possible that memory strength was confounded with remember-vs.-familiar responses in the present study, thus weakening the hippocampal response to strength-signal recognition. Controlling for confidence rating in familiarity-based recognition memory while manipulating representational dimensionality may constitute an interesting lead for future research. Another explanation is that this effect is specific to the aHC, as revealed both by the ROIs-based analysis of the hippocampus long-axis, and whole-brain analyses (see next discussion section), and thus appears weakened when considering the hippocampus in a unitary manner. Similar to pattern-completion and strength-signal recognition, the hippocampus was more recruited by strength-signal rejection of scenes than objects. In contrast, no effect of stimulus type was found in PRC activity in this condition. This result further shows that the representational specialisation of the hippocampus is not specific to pattern-completion, which directly supports the RH model.

c. Generalisation to a perceptual operation

The results observed in the visual discrimination task further argue in favour of the RH view: the hippocampus was more activated for scenes than for objects, whereas the pattern was reversed for the PRC. Crucially, this shows that the representational specialisation found in memory also applies to non-memory operations. A viewpoint effect was reported in previous fMRI studies (Barens, Henson, et al., 2010; also A. C. H. Lee & Rudebeck, 2010). In the present study, however, this effect was restricted to the PRC¹³. The theoretical explanation behind viewpoint manipulations is that presenting the stimuli from different viewpoints prevents the use of low-level perceptual features to resolve the task. In other words, it forces the use of an internal representations of the intended dimensionality (Graham et al., 2010). One interpretation of our results could be that the scene stimuli used in the visual matching task presented a sufficient degree of feature ambiguity to prevent the use of low-level perceptual features. Further investigation of this question will be provided in the next chapter, as hemispheric specialisation will be explored. In regard to the RH view, task variables such as viewpoint manipulations can modulate the dimensionality of the representation (Cowell et al., 2019). Although fMRI does not allow to determine whether or not same-viewpoint scene discrimination critically depends on the hippocampus when feature ambiguity is high, some patients studies suggested so (Aly et al., 2013; A. C. H. Lee, Bussey, et al., 2005). Our results show, however, that scene/object specialisation of the hippocampus/PRC can be evidenced without manipulating presentation viewpoint, and the involvement of MTL regions in visual discrimination is determined by representational dimensionality similarly as in the other operations studied. Taken together, these results support the RH account by showing that the results reported by Ross and colleagues can be generalised to other, memory and non-

¹³ A similar effect was found in our data but is not reported here considering the highly exploratory nature of the analysis (see Chapter IX: General discussion).

memory, operations. Further studies are needed, however, in particular regarding the role of the hippocampus in scene familiarity.

2. *Representational content and the hippocampus long-axis*

We next investigated how the representational specialisation applies to the hippocampus long-axis across the operations measured. As was done in Ross and colleagues (2018), we divided the hippocampus into three equal length segments. Unlike the authors, we found the aHC only to be preferentially engaged in the pattern-completion of scenes as compared with objects. This aHC-specific engagement for scene representations was replicated across all operations studied (table 7.1; except for visual-discrimination where it was also found in the midHC). Those results hardly fit with the proposal that the aHC and pHC are responsible for encoding and retrieval, respectively (Kim, 2015). Rather, this pattern is consistent with a large body of work showing the specific role of the aHC in scene processing (Dalton et al., 2018; Hodgetts et al., 2017; McCormick & Maguire, 2021; Zeidman et al., 2015; Zeidman & Maguire, 2016). More specifically, the activations revealed by whole-brain analyses are consistent with the medial-aHC region identified by Zeidman and Maguire (2016) as responsible for scene construction. In contrast, the pHC showed comparable engagement for scene and object processing irrespective of the operation, which suggests that the overall involvement of the hippocampus for scenes is driven by its anterior portion. This effect is compatible with the broad-to-sharp model of the hippocampus long-axis (Poppenk et al., 2013; see theoretical introduction, chapter V), as scenes can be considered global spatial representations. In contrast, the pHC would process sharp representations, among which the retrieval of details in proper recollection. We explored hippocampal activity in recollection trials and found a posterior>anterior effect regardless of stimulus type, which is consistent with previous studies (Poppenk & Moscovitch, 2011; Robin & Moscovitch, 2017; see also Snytte et al., 2022). The same pattern was observed for strength-signal recognition and visual-discrimination (table 7.1). Complex visual-discrimination has been associated with the pHC in previous studies (A. C. H. Lee & Rudebeck, 2010; Barense, Henson, et al., 2010; Mundy et al., 2013), and does require sharp representations in reason of the high degree of feature overlap between the stimuli to discriminate. In the case of strength-signal recognition, this pattern was unexpected. Interestingly, Poppenk and Moscovitch (2011) found that, although less reliable than recollection, familiarity measures positively correlated with pHC volume as well. Besson and colleagues (2020) also linked the volume of the right hippocampus with familiarity memory in a “discriminative” condition (i.e., high perceptual similarity between targets and lures) in contrast with an “entity” condition (i.e., different-viewpoint recognition). Given the high number of images and their perceptual similarity in the present study, we can hypothesise that sharp representations were also required to dissociate old from new stimuli on the basis of familiar judgements, which would explain the engagement of the pHC. This interpretation differs from a “memory load” interpretation, as it is shared between recognition and visual-discrimination, and is thus independent of the memory versus non-memory nature of the task. Conversely, in studies where stimuli are less perceptually similar,

familiarity judgements can be made on local perceptual features of the images, thus those cannot be regarded as high-dimensional. This account is consistent with the reports that recognition memory for highly-similar stimuli is impaired in case of selective lesion of the hippocampus (Holdstock et al., 2002, 2005; Migo et al., 2009). However, the current protocol was not designed to test this hypothesis, and thus lacks a control condition (in which stimuli would be less similar). Further studies are therefore needed to determine whether the engagement of the pHC in strength-signal recognition depends on perceptual feature overlap. This posterior>anterior pattern was not observed, in contrast, for pattern-completion and strength-signal rejection, in which cases the overall aHC activity was increased by scene processing. This could be explained by a more global processing of scene images in those conditions. Overall, these results support that the representational specialisation of the hippocampus does not apply similarly to each of its segments; and that although further studies are required, the broad-to-sharp account provides a relevant framework to understand this functional organisation.

3. *The perirhinal and parahippocampal cortices*

In this study the PRC is first considered as a control region: if the pattern found in the hippocampus was to be observed in the PRC as well, it could be explained by an overall stronger recruitment of all MTL regions for scene as compared to object processing. The observation of opposite patterns of specialisation in these two structures can be interpreted as a specific representation-dependant organisation. Yet, the PRC is also a ROI *per se*, and its functional specialisation is of interest with regard to the RH predictions. In contrast with the hippocampus, the PRC was more recruited by object than by scene processing. This pattern was found for pattern-completion, strength-signal recognition, visual discrimination, and recollection. As mentioned, this effect differs from the original study, in which no difference in PRC recruitment was observed between scene and object reconstruction. We assume that differences in the content of the scene images could explain this discrepancy. Ross and colleagues used natural pictures of scenes that included objects and hence were more likely to rely on the PRC during recall. In comparison, the scene images that we used were refined to suit the visual-discrimination task, and thus contained minimal object features. Our study also differed regarding the type of task during encoding. Whereas in the original study, participants first completed a categorisation task, encoding in the present study consisted in a complex visual-discrimination task. This task requires in-depth visual processing of the images, which may arguably have enhanced the formation of internal representations of the objects. Thus, visually-discriminating, reconstructing, and recognising these representations fall precisely into the scope of the PRC, that is, representing entities (Bastin et al., 2019; Cowell, 2012; Devlin & Price, 2007; Lacot et al., 2017). Of particular interest is the case of strength-signal recognition. In a dual-process perspective, the PRC should be associated with the process of familiarity in general. By showing that the engagement of the PRC in strength-signal recognition is determined by representational content, and that this pattern is not specific to this operation, the present results challenge this view. Thereby, the conclusion

regarding the PRC is the same as that drawn for the hippocampus: representational content, not the operation, determines its engagement in cognitive processes. Unexpectedly, however, this effect was not found for strength-signal rejection. This is particularly surprising given the role of the PRC in resolving entity-related ambiguity (Kivisaari et al., 2012; A. C. H. Lee, Bandelow, et al., 2006; Mundy et al., 2013; see also Ferko et al., 2022). One possible explanation is that object stimuli in the whole-item condition could be rejected using simple conceptual identification (e.g., “I don’t think I have seen any fork earlier”), due to insufficient perceptual similarity. Although the increased PRC recruitment for object as compared to scene familiarity argues against this view, investigating the role of the PRC in strength-signal rejection as function of representational content and perceptual similarity could be an interesting lead for future research. Finally, even though this region was not concerned by the hypotheses of this work and thus was not included in ROI-based analyses, whole-brain analyses revealed particularly strong activity patterns in the parahippocampal cortex (PHC) for scene processing. This result, observed across all operations investigated, is consistent with the well-documented role of the PHC in the processing of scenes and contextual information (e.g., Litman et al., 2009; Staresina et al., 2011; Pihlajamäki et al., 2004; for reviews, see Aminoff et al., 2013; Davachi, 2006; Ranganath & Ritchey, 2012).

Synthesis

In this study we replicated the results reported by Ross and colleagues concerning the engagement of the hippocampus and PRC in pattern-completion, and extended it to strength-signal recognition, strength-signal rejection, and visual discrimination. However, this pattern was specific to the aHC, whereas no scene specialisation was found in the pHC. Instead, overall enhancement of pHC activity was found in strength-signal recognition, visual discrimination, and recollection. These results are compatible with the broad-to-sharp account of the hippocampus long-axis. Overall, our findings support the representational specialisation of MTL regions across memory and non-memory operations, and highlight that this specialisation interacts with the internal functional organisation of the hippocampus.

Chapter VIII – Representational specialisation and hemispheric lateralisation

In the previous chapter, we evidenced a representational specialisation of MTL regions across memory and visual-perception operations. We also explored the long-axis of the hippocampus, and showed that these results do not apply similarly to each segment. In this chapter we explore another axis of brain organisation: hemispheric lateralisation. Whereas the contribution of left and right MTL regions to memory processing is believed to depend on material type, how representational specialisation varies depending on lateralisation remains little studied. The data from Study 3 are first reanalysed in the aim of exploring the lateralisation of the MTL engagement in scene versus object processing. Subsequently, the visual-discrimination task is applied to patients with unilateral MTL lesions, in order to test the hypothesis that the processing of high-dimensional perceptual representations, outside the memory domain, critically relies on the right MTL specifically.

The results presented in chapter in Study 4 are adapted from an article currently under review in the journal *Hippocampus* under the title: Complex visual discrimination is impaired after right, but not left, anterior temporal lobectomy (Gardette et al.).

A subset of the results was presented in a short communication at the Interdisciplinary congress of the CNRS memory research group (GDR mémoire) in October 2021 in Vers (France) under the title: Les lésions du lobe temporal interne n'affectent-elles que la mémoire ? Étude de la perception visuelle complexe (Gardette et al.).

Contents of chapter VIII

| | |
|--|------------|
| Chapter VIII – Representational specialisation and hemispheric lateralisation | 114 |
| 1. Lateralisation of fMRI activations from Study 3..... | 116 |
| Regions of interest (ROIs) and analyses | 116 |
| Results | 116 |
| Discussion | 121 |
| 2. Visual discrimination in case of unilateral MTL damage: Study 4..... | 123 |
| Introduction..... | 123 |
| Methods | 124 |
| Results | 128 |
| Discussion | 130 |
| Synthesis..... | 132 |

1. Lateralisation of fMRI activations from Study 3

As mentioned in chapter V, there is evidence suggesting that the processing of perceptual high-dimensional representations relies on the right MTL specifically. Here, we reanalysed the data from Study 3 in order to assess this hypothesis by comparing the representational specialisation (i.e., preferential engagement in scene vs object) between the left and right hippocampus and PRC. Functional MRI preprocessing and statistical processing are the same as in the former study. The only difference is in the ROIs definition: whereas each region was analysed in a bilateral manner in Study 3, they are divided into a left and a right ROI in this secondary analysis. For clarity, and because the patient population investigated in study 4 present large MTL lesions (although unilateral), we investigated the hippocampus unitarily instead of dividing it in three segments.

Regions of interest (ROIs) and analyses

The hippocampus and PRC were divided into a left and a right ROI, resulting in height ROIs. Parameter estimates were extracted from those regions using the same procedure as in Study 3. After removing extreme values and checking statistical assumptions, these data were entered into within-subject mixed regressions. The factors included were: stimulus type (i.e., scene, object), side (i.e., left, right), and viewpoint (different, same) in the case of visual-discrimination. To avoid multiple testing, statistical analyses were restricted to the question of whether the effects found in study 3 were specific to one hemisphere. We thus searched for a representational specialisation effect in the left and right hippocampus and PRC ROIs. In the case of visual-discrimination, the effect of viewpoint was also explored.

Results

Visual discrimination

In visual discrimination, an effect of stimulus type was found both in the left, $F(1,49) = 10.11$, $p < .01$, and right hippocampus, $F(1,50) = 68.74$, $p < .001$. Yet, there was a stimulus type \times side interaction, corresponding to a larger effect of stimulus type in the right than in the left hippocampus, $F(1,199) = 31.85$, $p < .001$.

Concerning the PRC, a side × stimulus type interaction was found, $F(1, 193) = 7.1, p < .01$ (figure 8.1.B). The effect of stimulus type, $F(1,48) = 20.28, p < .001$, and stimulus type ×viewpoint interaction, $F(1,48) = 9.48, p < .01$, were found in the right PRC. In contrast, while the effect of stimulus type was also significant in the left PRC, $F(1,48) = 46.46, p < .001$, it was not modulated by viewpoint ($p = .087$).

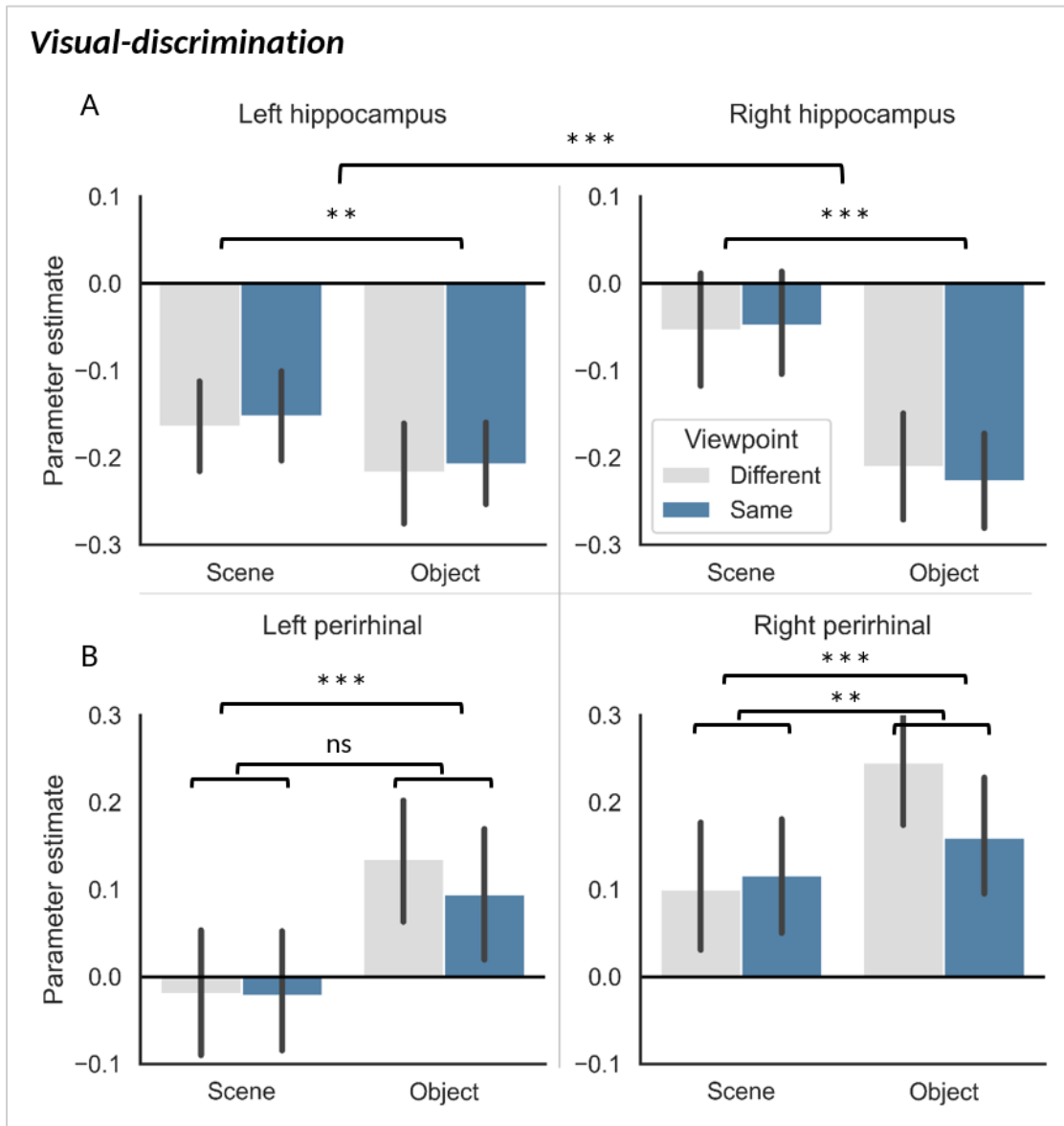


Figure 8.1. Parameter estimate extracted from the matching task as function of region of interest side, stimulus type, and viewpoint. A: left and right hippocampus (means and 95% confidence intervals). B: left and right perirhinal cortex. ***: $p < .001$. **: $p < .01$, *: $p < .05$, ns: Non-significant.

Pattern-completion

Concerning pattern-completion, the effect of stimulus type was significant in the right, $F(1,23) = 4.8, p < .05$, but not left hippocampus ($p = .15$). However, the side × stimulus type interaction was not significant ($p = .46$). In contrast with the hippocampus, the effect of stimulus type was

significant in the left, $F(1,24) = 13.09$, $p < .01$, but not right PRC ($p = .17$, figure 8.2.B). No side \times stimulus type interaction was found in the PRC either ($p = .08$).

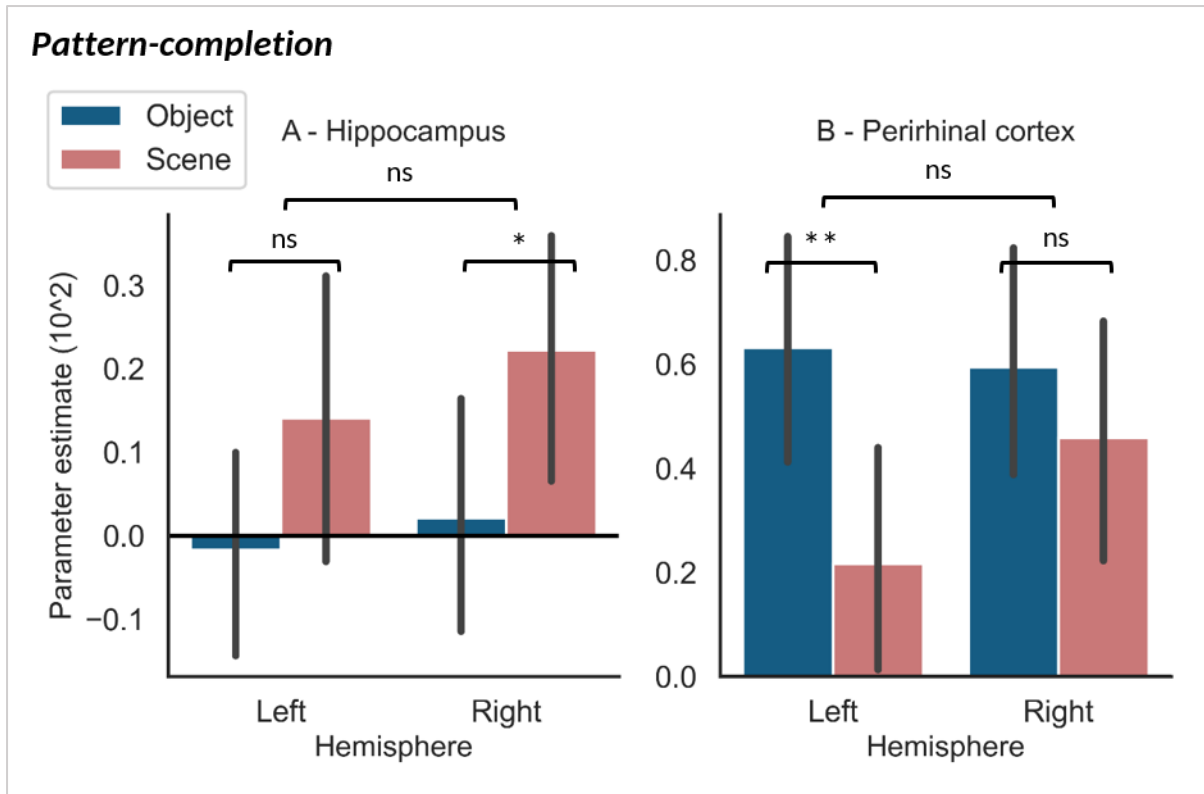


Figure 8.2. Parameter estimate extracted from the patch-cue recognition task for “Rec” responses as function of region of interest side and stimulus type. A: Hippocampus. B: Perirhinal cortex (means and 95% confidence intervals). **: $p < .01$, *: $p < .05$, ns: Non-significant.

Strength-signal recognition

Unlike pattern-completion, no effect of stimulus type was found either in the right ($p = .09$) or left hippocampus ($p = .27$; figure 8.3.A). The side \times stimulus type interaction was not significant ($p = .46$). The effect of stimulus type was significant in the left, $F(1,24) = 9.27$, $p < .01$, but right PRC ($p = .34$; figure 8.3.B). There was no side \times stimulus type interaction in the PRC ($p = .2$).

Strength-signal rejection

In strength-signal rejection, a side \times stimulus type interaction was found in the hippocampus, $F(1,22) = 13.34$, $p < .01$. A significant effect of stimulus type was observed in the right, $F(1,23) = 12.15$, $p < .01$, but not in the left hippocampus ($p = .33$; figure 8.4.A). Consistent with the results of Study 3, no effect of stimulus type was found either in left ($p = .07$), or in the right PRC ($p = .18$; figure 8.4.B).

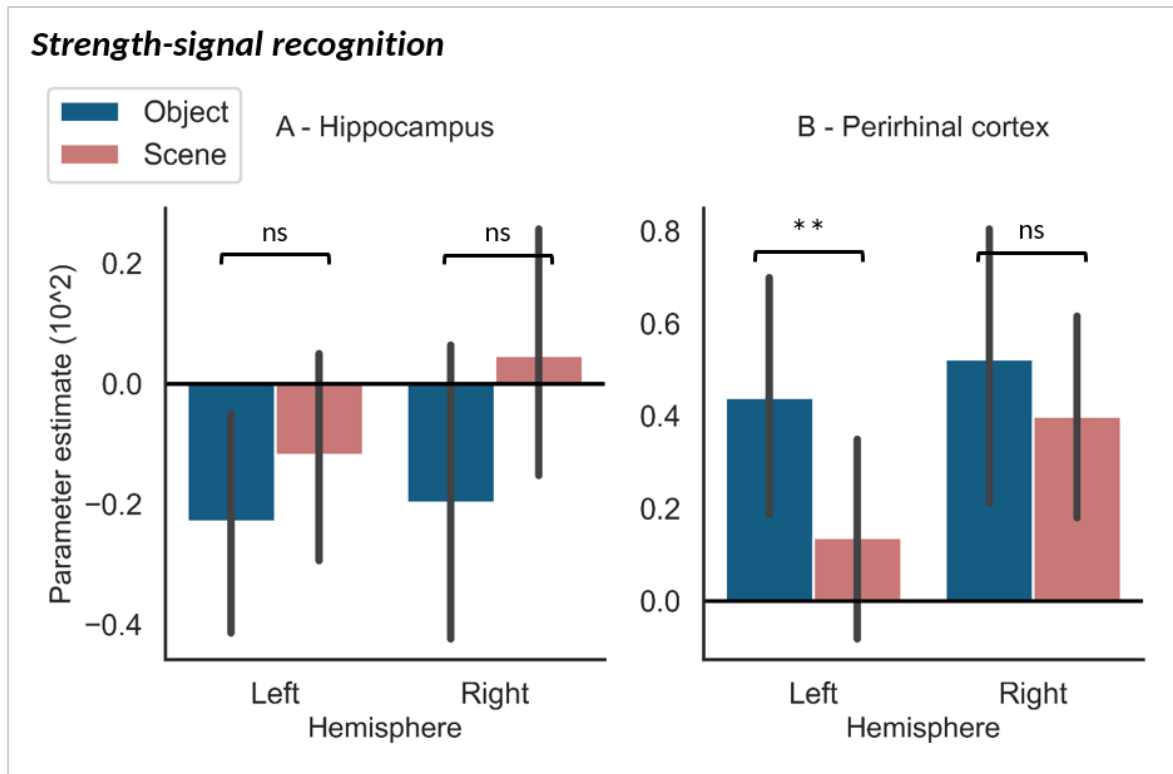


Figure 8.3. Parameter estimate extracted from the whole-item recognition task for “Familiar” responses as function of region of interest side and stimulus type. A: Hippocampus. B: Perirhinal cortex (means and 95% confidence intervals). **: $p < .01$, ns: Non-significant.

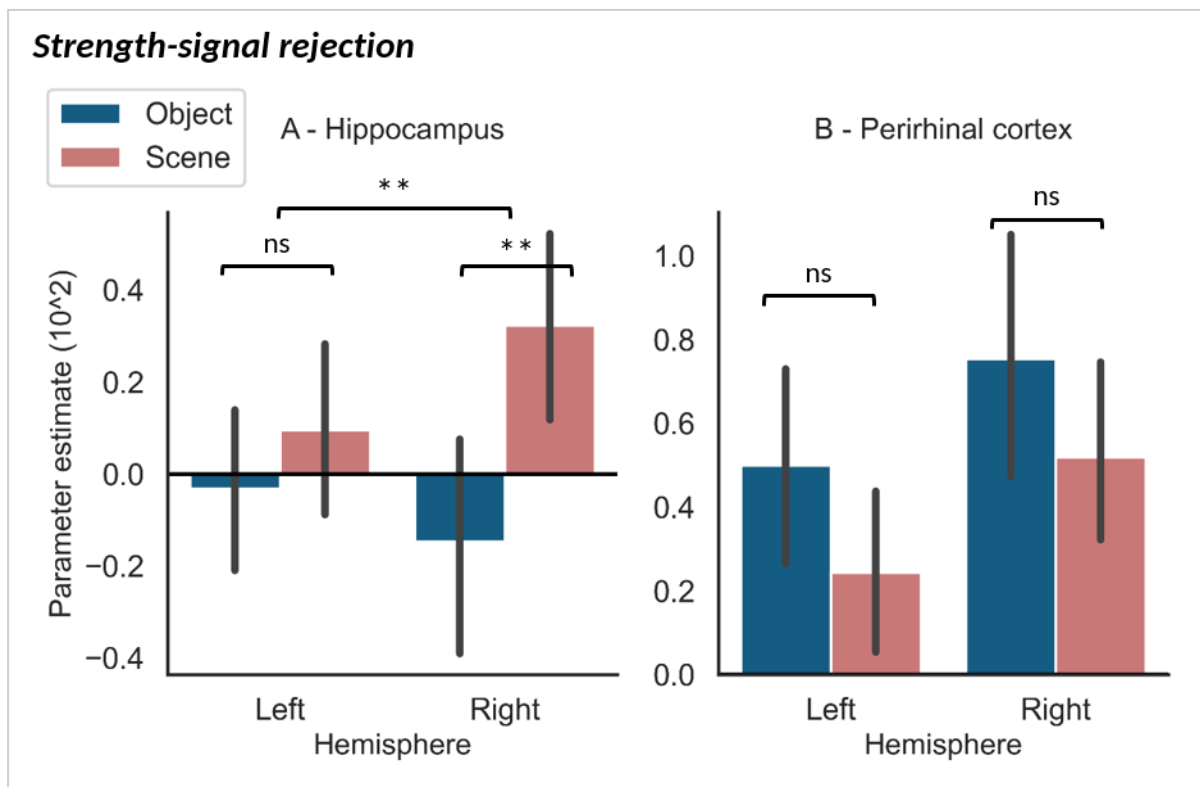


Figure 8.4. Parameter estimate extracted from the whole-item recognition task for “New” responses as function of region of interest side and stimulus type. A: Hippocampus. B: Perirhinal cortex (means and 95% confidence intervals). **: $p < .001$, ns: Non-significant.

Recollection

A side × stimulus type interaction was observed for recollection, $F(1,22) = 4.74, p < .05$. The effect of stimulus type was significant in the right, $F(1,23) = 8.62, p < .01$ (figure 8.5.A). but not in the left hippocampus ($p = .17$). Unlike for the hippocampus, the effect of stimulus type was found in the left, $F(1,24) = 6.67, p < .05$, but not right PRC ($p = .36$; figure 8.5.B). The side × stimulus type interaction was no significant, however ($p = .13$).

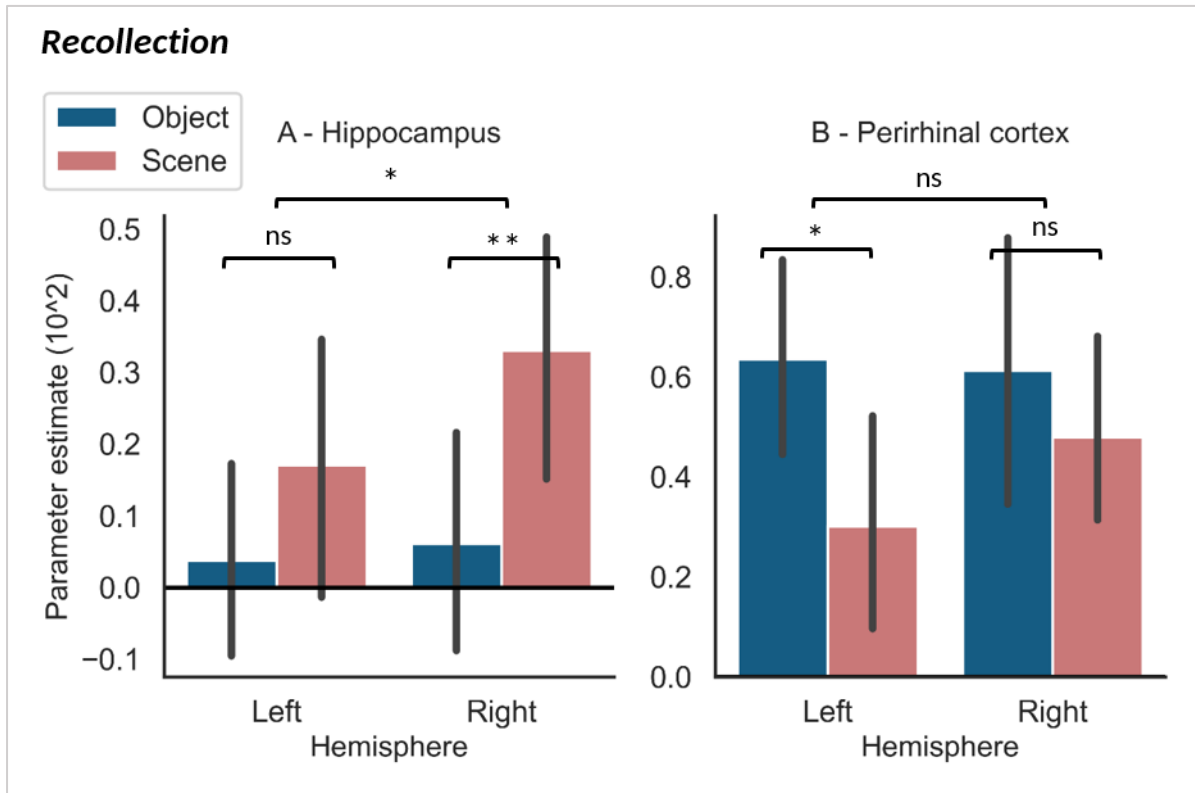


Figure 8.5. Parameter estimate extracted from the whole-item recognition task for “R” responses in the left and right regions of interest. A: Posterior, middle, and anterior hippocampus. B: Perirhinal cortex (means and 95% confidence intervals). **: $p < .001$; *: $p < .05$, ns: Non-significant.

Discussion

Here we reanalysed the data from study 3 in the aim of investigating the lateralisation of the representational specialisation of MTL regions. Having demonstrated that the hippocampus and PRC are preferentially engaged in scene and object processing across perceptual and memory operations, respectively, we focused on determining whether these patterns of specialisation present a hemispheric lateralisation. The hippocampus and PRC ROIs used in study 3 were divided into a left and right ROI, and these effects were searched across hemispheres using the same ROI-based extraction procedure as in the previous study.

Scene specialisation in the hippocampus was mainly right-lateralised across operations. This is consistent with previous investigations of scene construction. In particular, Irish and colleagues (2017) reported that scene construction is impaired in case of lesion to the right but not left hippocampus. The case of patient P01 documented by Mullally, Hassabis, and Maguire (2012), points in the same direction: his scene construction ability was preserved despite massive amnesia, and was supported by residual activity in the right hippocampus. Those studies, however, focused on the construction of fictitious scenes, in order to avoid any memory demand. As mentioned earlier in this work, pattern-completion like retrieval of scenes as measured by patch-cue reconstruction approximates those scene construction tasks, and thus is likely to be supported by the right hippocampus specifically. While we cannot conclude that a cognitive mechanism critically relies on a brain region using fMRI, our results *suggest* that the pattern demonstrated in patients with lesions to the hippocampus is not limited to pattern-completion and imagination, but could be generalised to strength-signal rejection and visual-discrimination of scenes.

Unlike scene processing in the hippocampus, the lateralisation of object specialisation in the PRC varied depending on the operation. A representational specialisation (i.e., object > scene effect) was found in the left, but not right PRC, for all memory operations except strength-signal rejection. In contrast, a representational specialisation was found in both the left and right PRC during visual discrimination. One could argue from this discrepancy that the representational specialisation is not independent of the cognitive function engaged (i.e., memory versus visual perception), an interpretation that would challenge the RH account.

Activity related to object processing in memory operations, however, was comparable between the left and right PRC¹⁴; the absence of difference between object and scene recruitment (i.e., representational specialisation) in the right PRC resulted from increased activity for scene processing as compared to the left PRC. Given the greater semantic distinctiveness of object stimuli, it is possible that conceptual information was relevant to performing the object memory task in addition to perceptual information, whereas only perceptual features contributed to scene memory. Since there is evidence that the PRC

¹⁴ This comparison was not tested statistically, as it was not among our hypotheses, and to avoid multiple testing. However, when exploring the data descriptively, activity related to object processing appears equivalent between the left and right PRC, if not superior in the right PRC.

represents both the perceptual and conceptual aspects of entities (Clarke & Tyler, 2014; Martin et al., 2018), the left PRC could have contributed to object memory, more than to scene memory, through conceptual features. Unlike memory operations, the visual matching task could not be resolved using conceptual features; consistently, a representational specialisation was observed in the right PRC in this task. Moreover, the viewpoint manipulation, which modulates perceptual but not semantic ambiguity (e.g., Barense et al., 2007), influenced activity in the right, but not left PRC. Our results thus suggest that the left and right PRC contribute preferentially to perceptual and conceptual entity disambiguation, respectively. The fact that the increased involvement of the hippocampus for scene processing as compared to objects was mainly right lateralised also argues in favour of this account, given that conceptual features unlikely contributed either to scene visual discrimination or to scene memory.

Overall, these results support the hypothesis that the left and right MTL are involved in different aspects of representational dimensionality. In particular, resolving perceptual ambiguity would rely on right MTL regions, whereas other kinds of features, such as conceptual, would be represented by the left MTL. These data, however, lack a critical demonstration, which is not allowed by functional neuroimaging investigations. Therefore, in study 4 we apply the visual matching task to patients with unilateral MTL lesions, predicting that right, but not left, MTL damage would impair the ability to resolve perceptual ambiguity.

2. Visual discrimination in case of unilateral MTL damage: Study 4

Introduction

Whereas patients with bilateral MTL lesions develop global anterograde amnesia, material-specific impairments are found in patients with unilateral MTL damage. The left MTL has been associated with verbal memory (Baxendale, 1997; Frisk & Milner, 1990; Golby et al., 2001; Kumaran & Maguire, 2007; T. M. C. Lee et al., 2002; Rocchetta & Milner, 1993), sequence learning (Igloi et al., 2010; Lehn et al., 2009; Schendan et al., 2003), and autobiographical recall (Burgess et al., 2001; Maguire & Mummery, 1999; Stern et al., 1996). In contrast, right MTL regions are preferentially involved in the visual (Jones-Gotman, 1986; C.-H. Lee et al., 2016; Spiers, Burgess, et al., 2001) and spatial aspects of memory (Maguire et al., 1996, 1997, 1998; Worsley et al., 2001). The study of hemispheric specialisation of MTL functions has focused primarily on memory. In contrast, representation-dependant perceptual impairments in case of MTL damage were mainly reported in patients with bilateral lesions (Aly et al., 2013; Barense et al., 2005, 2007; A. C. H. Lee, Buckley, et al., 2005; A. C. H. Lee, Bussey, et al., 2005). Consequently, the hemispheric lateralisation of these functions remains largely unknown. As exposed in chapter V, there is evidence suggesting that complex perceptual representations may preferentially rely on the right MTL both at the level of entities (Besson et al., 2020; see also Pollmann et al., 2014) and scenes (Irish et al., 2017; Mullally, Hassabis, et al., 2012; Barense, Henson, et al., 2010; Hodgetts et al., 2016). The reanalysis of Study 3 data presented earlier in this chapter is consistent with this account. One interpretation of these results is that conceptual features contributed to object memory, whereas perceptual features contributed to both object and scene memory operations. Therefore, right MTL regions specifically would be required to process representations made high-dimensional by perceptual ambiguity. To demonstrate that resolving entity and scene perceptual ambiguity critically relies on right MTL regions, however, functional neuroimaging is not sufficient.

The aim of the present study was to assess this hypothesis by investigating patients with unilateral MTL lesions. Because visual-discrimination is not subject to biases such as the contribution of conceptual features and compensatory strategies (e.g., verbalisation in visual-memory tasks), we chose to use an adapted version of the matching task used in Study 3¹⁵. To ensure that a visual discrimination/matching task requires high-dimensional representations, perceptual ambiguity is a critical methodological characteristic (Barense et al., 2005, 2007). Therefore, we manipulated the degree of feature overlap by adding a “building” condition to the stimulus type variable. Similar to objects, buildings were acontextual; yet they were more visually complex, and so presented a higher degree of perceptual overlap between targets and lures (see materials: General section). The matching task thus included three stimulus types (i.e., objects, buildings, and scenes) and two viewpoint conditions (i.e., same and different).

¹⁵ Investigating *both* visual discrimination *and* memory for scenes and objects would have been interesting; but the choice of tasks applied to the patient population was also constrained by the available evaluation time.

Patients who underwent anterior temporal cortectomy for drug-resistant right temporal lobe epilepsy (RTLE) and left temporal lobe epilepsy (LTLE), as well as control subjects, were recruited. We expected RTLE, but not LTLE, to impair visual discrimination, and this impairment to be exacerbated by feature ambiguity and presentation viewpoint.

Methods

Participants

Twenty patients who underwent surgery for drug-resistant epilepsy and 38 healthy control participants were tested. Of the 20 patients, 8 had RTLE, whereas 12 had LTLE. They were tested on average 25.5 months after the surgery and presented no other medical or psychiatric conditions. All patients underwent anterior temporal lobectomy according to the standardised approach (Boling, 2018, Spencer, et al., 1984; figure 8.6). Anatomical magnetic resonance imaging data were available for 17 patients. A segmentation of using the Vol2brain procedure (Manjon et al., 2022) confirmed that surgery led to vast unilateral MTL lesions in all patients (these data are summarised in figure 8.7). At the time of the experiment, 14 patients took antiepileptic drugs (5 RTLE and 9 LTLE), and 6 patients still experienced seizures (2 RTLE and 4 LTLE). Low-level visual perceptual and verbal abilities were in the normal range, as measured by the Wechsler Adult Intelligence Scale, and no difference between RTLE and LTLE patients was found on these measures (Wechsler, 2008, figure 8.8). Control participants presented no neurological or psychiatric conditions and normal or correct-to-normal vision. Demographic characteristics, neuropsychological scores, and group comparisons are summarised in Table 8.1 and figure 8.8.

Procedure

Patients were tested in the context of a neuropsychological examination either at the University Hospital of Grenoble or at the University Hospital of Saint-Étienne (France) and gave their written informed consent (MR004 ethics framework). The study was conducted in accordance with the Declaration of Helsinki. Control participants were recruited and tested at Grenoble or Chambéry universities (France). The study with controls was approved by the local ethics committee (CER_2021_15), and participants gave their written informed consent before participating. Both patients and controls underwent neuropsychological tests before performing the experimental task. Control participants were first screened for any global cognitive impairment with the Mini-Mental State Examination (Kalafat et al., 2003). Moreover, to rule out any potential memory or executive difficulty, we chose tests that are administered to the patients during clinical routine (Brissart et al., 2019, see appendices C3 and C4): the fourth Wechsler Memory Scale (Wechsler, 2009) and the Trail Making Test (TMT; Mitrushina et al., 2005). The experimental task lasted between 15-20 min depending on response speed. The overall examination of control subjects lasted about 2 h. Demographic and neuropsychological data are summarised in Table 8.1.

Experimental task and material

The visual-matching task, inspired by previous studies (Barens et al., 2005, 2007, 2010; Hodgetts et al., 2017; Lee, Buckley, et al., 2005; Lee, Bussey, et al., 2005), was similar to that used in Study 3. In each trial, three images were displayed simultaneously on the screen, one positioned above the other two until the participant answered. Participants were instructed to indicate which of the lower images (i.e., the target and lure) matched the image at the top (i.e., the reference). The position of the correct response was selected randomly in each trial. Unlike in Study 3, trials lasted a maximum of 12 s, and two subsequent trials were separated by a fixation cross presented at the centre of the screen for 1500, 2000, or 2500 ms (randomly determined to maintain attention). There were 15 trials per condition (i.e., 90 trials), grouped into 18 blocks of 5 trials of the same condition. Two blocks were separated by a self-paced break. Before performing the experimental task, participants underwent a training session to ensure that they correctly understood the instructions and that they familiarised themselves with the task. They were first presented with one trial of each experimental condition with no time limit, and feedback was given on each response's accuracy. They then performed another series of training trials, one for each experimental condition, but under the same conditions as the experimental task (i.e., trials lasted 12 s maximum, and no feedback was given). Both the experimental and training sessions were run with OpenSesame (Mathôt et al., 2012; version 3.3: <https://osdoc.cogsci.nl/>). The 270 used in this study stimuli were chosen from the material set designed for this work (see Materials: General). Based on pilot data, the 15 trials per condition were chosen among the most succeeded trials. Each image appeared only once in the experiment.

Analyses

Statistical analyses were performed with R. Accuracy (i.e., percentages of correct responses per experimental condition) and response times (RT) were analysed. Groups were analysed as a between-subject variable (i.e., control participants, RTLE, and LTLE), whereas stimulus type (i.e., scenes, buildings, and objects) and viewpoint (i.e., same vs. different) were analysed as within-subject variables. Because the data and sample size violated the general linear model assumptions, non-parametric statistical tests were used.

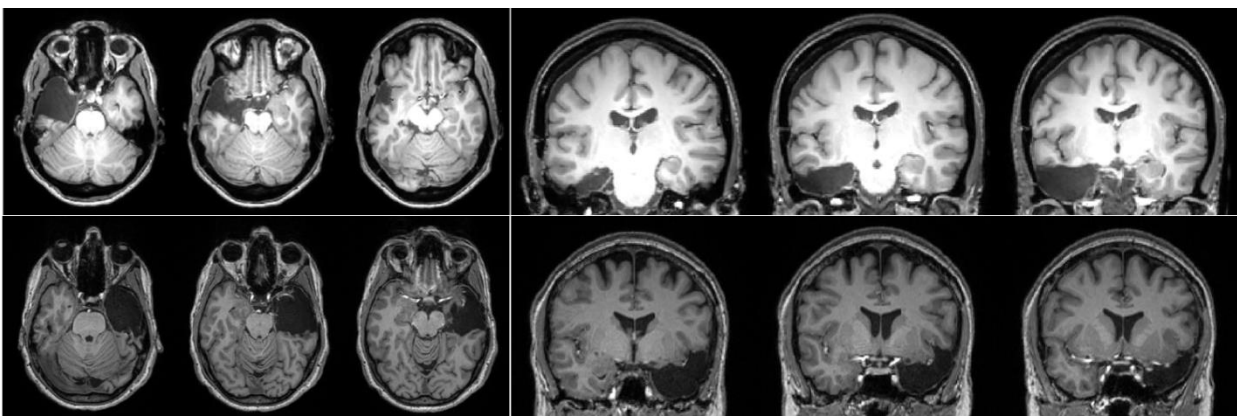


Fig. 8.6. Structural magnetic resonance imaging from two representative patients with left (top panels) and right (lower panels) anterior temporal cortectomy, displayed in the axial (left panels) and coronal axes (right panels).

Table 8.1. Neuropsychological measures and demographic variables in LTLE patients, RTLE patients, and control participants.

| | LTLE patients | RTLE patients | HC participants | <i>p-value</i> | |
|--------------------------------|----------------|----------------|-----------------|--------------------------|---------|
| | | | | LTLE/HC | RTLE/HC |
| <i>Demographic data</i> | | | | | |
| Gender (F:M) | 6:6 | 4:4 | 26:12 | n.s. | n.s. |
| Age | 38.92 (10.14) | 45.53 (6.27) | 39.34 (8.37) | n.s. | n.s. |
| Delay from surgery | 26.44 (14.63) | 26.57 (15.92) | / | <i>LTLE / RTLE: n.s.</i> | |
| <i>Neuropsychological data</i> | | | | | |
| AMI | 95.66 (18.81) | 98.88 (12.40) | 116.81 (11.78) | ** | * |
| VMI | 97.58 (13.55) | 82.38 (11.13) | 103.23 (14.4) | n.s. | ** |
| IMI | 96.75 (15.93) | 89.63 (14.75) | 110.57 (14.83) | * | ** |
| DMI | 92.83 (18.56) | 86.63 (9.13) | 110.57 (11.93) | * | ** |
| VWMI | 105.83 (15.22) | 88.12 (16.5) | 106.55 (11.96) | n.s. | * |
| VCI | 100.27 (9.77) | 102.57 (15.93) | / | <i>LTLE / RTLE: n.s.</i> | |
| PRI | 103.63 (12.12) | 98.0 (11.83) | / | <i>LTLE / RTLE: n.s.</i> | |
| TMT-A | 31.23 (13.32) | 29.75 (8.14) | 26.25 (13.31) | n.s. | n.s. |
| TMT-B | 61.25 (27.56) | 84.53 (36.02) | 55.04 (26.61) | n.s. | n.s. |
| TMT B-A | 30.36 (17.33) | 54.74 (36.75) | 28.79 (18.27) | n.s. | n.s. |
| MMSE | / | / | 29.71 (0.61) | / | / |

LTLE: left temporal lobe epilepsy; RTLE: right temporal lobe epilepsy; HC: healthy controls; F: female; M: male; n.s.: not significant; AMI: auditory memory index; VMI: visual memory index; IMI: immediate memory index; DMI: delayed memory index; VWMI: visual working memory index (Wechsler, 2009); VCI: verbal comprehension index; PRI: perceptual reasoning index (Wechsler, 2008); TMT: Trail-Making Test (Mitrushina et al., 2005); MMSE: Mini-Mental Statement Examination (Kalafat et al., 2003); LTLE/HC: comparison between LTLE patients and healthy controls; RTLE/HC: comparison between RTLE patients and healthy controls. **: < .01; * < .05. Values represent means and standard deviations.

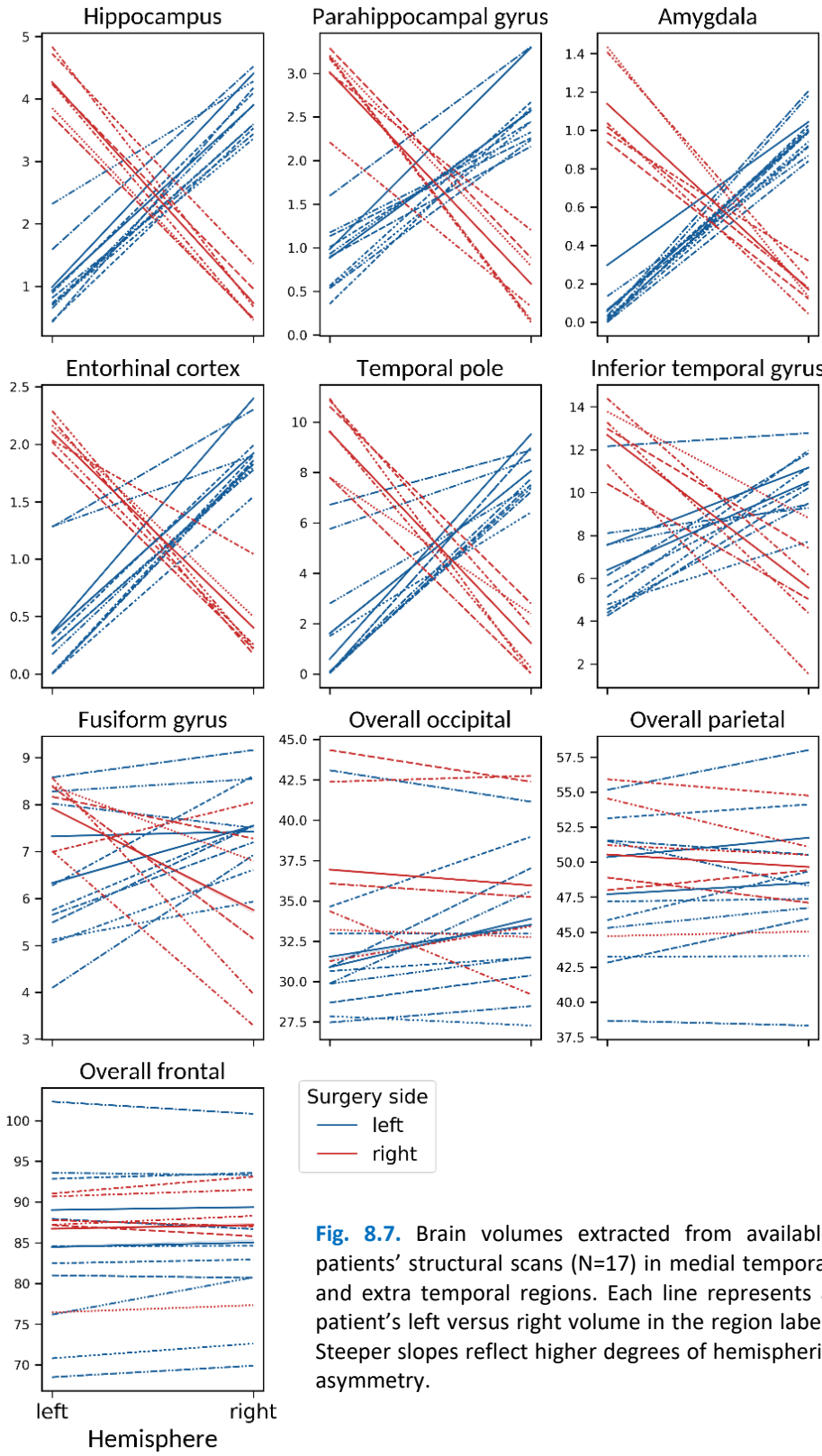


Fig. 8.7. Brain volumes extracted from available patients' structural scans (N=17) in medial temporal and extra temporal regions. Each line represents a patient's left versus right volume in the region label. Steeper slopes reflect higher degrees of hemispheric asymmetry.

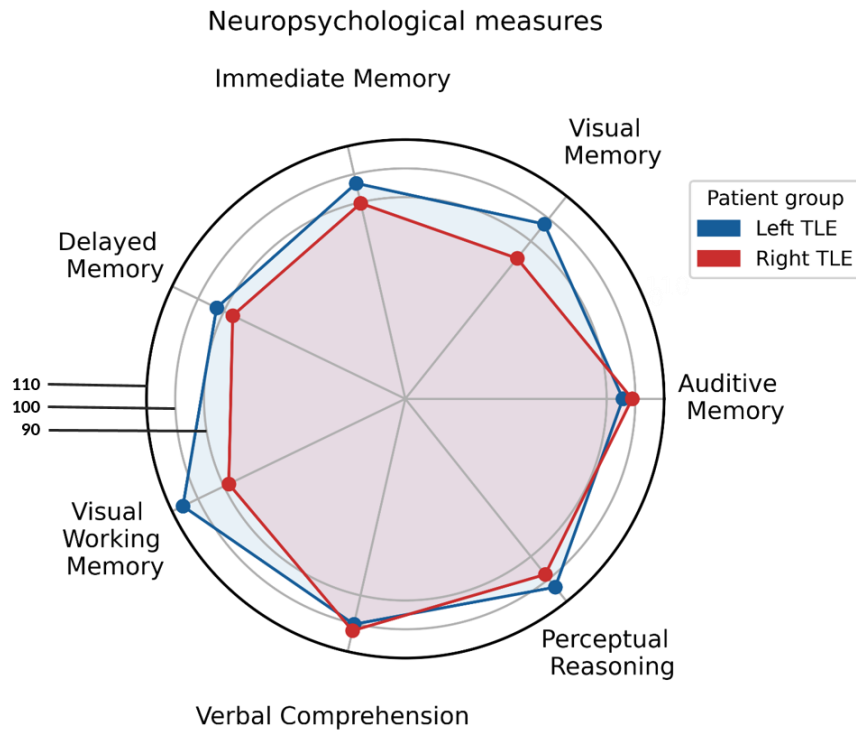


Figure 8.8. Mean values for the main neuropsychological measures in both groups of patients. Visual memory was lower in patients with RTLE whereas auditive (i.e., verbal) memory was comparable between the groups. Intellectual ability, including perceptual reasoning, was also closely matched. TLE: temporal lobe epilepsy.

Results

Accuracy comparisons versus chance

Control subjects and LTLE patients performed significantly above chance level in all task conditions (all $p < .05$). In contrast, RTLE patients' accuracy did not exceed chance level in the scene-different ($M = 48.3$; $SD = 14.5$; $p = .6156$) and building-different ($M = 57.5$; $SD = 15.9$; $p = .292$) conditions, whereas it did in all other conditions (all $p < .05$).

Control participants

Considering control participants only, Friedman's tests revealed significant main effects of Stimulus type [$\chi^2(2) = 47.87$; $p < .001$; effect size: $w = .63$; figure 8.9] and of viewpoint, with higher accuracy for the same viewpoint compared with different viewpoint trials [$\chi^2(2) = 34.1$; $p < .001$, $w = .898$]. A significant interaction between Stimulus type and viewpoint was also found [$\chi^2(2) = 37.69$; $p < .001$; $w = .496$]. The simple effect of Stimulus type was significant in the different viewpoint condition [$\chi^2(2) = 48.27$; $p < .001$; $w = .635$], but not in the same viewpoint condition [$\chi^2(2) = 4.46$; $p = .107$; $w = .058$]. Post-hoc comparisons revealed that in the different viewpoint condition, participants performed better in the object than in the building condition [paired Wilcoxon $W = 14.5$; $p < .001$; $r = .819$], and better in the building than in the scene condition [$W = 392$; $p < .01$; $r = .447$]. Accordingly, the effect of viewpoint

was greater in the scene than in the building condition [$W = 498; p < .01; r = .428$], and greater in the building than in the object condition [$W = 45.5; p < .001; r = .7$].

RT consistently varied depending on Stimulus type [$\chi^2(2) = 58.9; p < .001; w = .775$; figure 8.10]. Participants responded faster in the object than in the building condition [$W = 741; p < .001; r = .872$], and faster in the building than in the scene condition [$W = 191; p < .01; r = .422$]. RT were also shorter in the same than in the different condition [$W = 204; p < .001; r = .617$]. A significant Stimulus type \times Viewpoint interaction on RT was observed [$\chi^2(2) = 33.1; p < .001; w = .435$]. The effect of viewpoint on RT was greater in the scene than in the building condition [$W = 160; p < .01; r = .495$], and greater in the building than in the object condition [$W = 608; p < .001; r = .559$].

Group effects

The Kruskal-Wallis test revealed a main effect of group on overall accuracy [$\chi^2(2) = 11.3; p < .01; \eta^2 = .16$; figure 8.9]. Specifically, RTLE patients had lower accuracy rates than did control subjects (Games-Howell test, $p < .05$) whereas LTLE patients did not ($p = .643$). A trend for lower overall accuracy in RTLE than LTLE was also observed ($p = .053$). There was neither a significant Group \times Stimulus type, nor Group \times Viewpoint, nor Group \times Stimulus type \times Viewpoint interaction for accuracy (all $p > .1$). A main effect of group was also observed on overall RT [$\chi^2(2) = 8.9; p < .05; \eta^2 = .11$, figure 8.10]. Post-hoc comparisons revealed that RTLE patients had longer overall RT than control subjects did ($p < .05$), whereas the overall RT of LTLE patients did not differ significantly from that of controls ($p = .694$) and RTLE patients ($p = .376$). There was a Group \times Stimulus type \times Viewpoint three-way interaction [$\chi^2(2) = 8.52; p <$

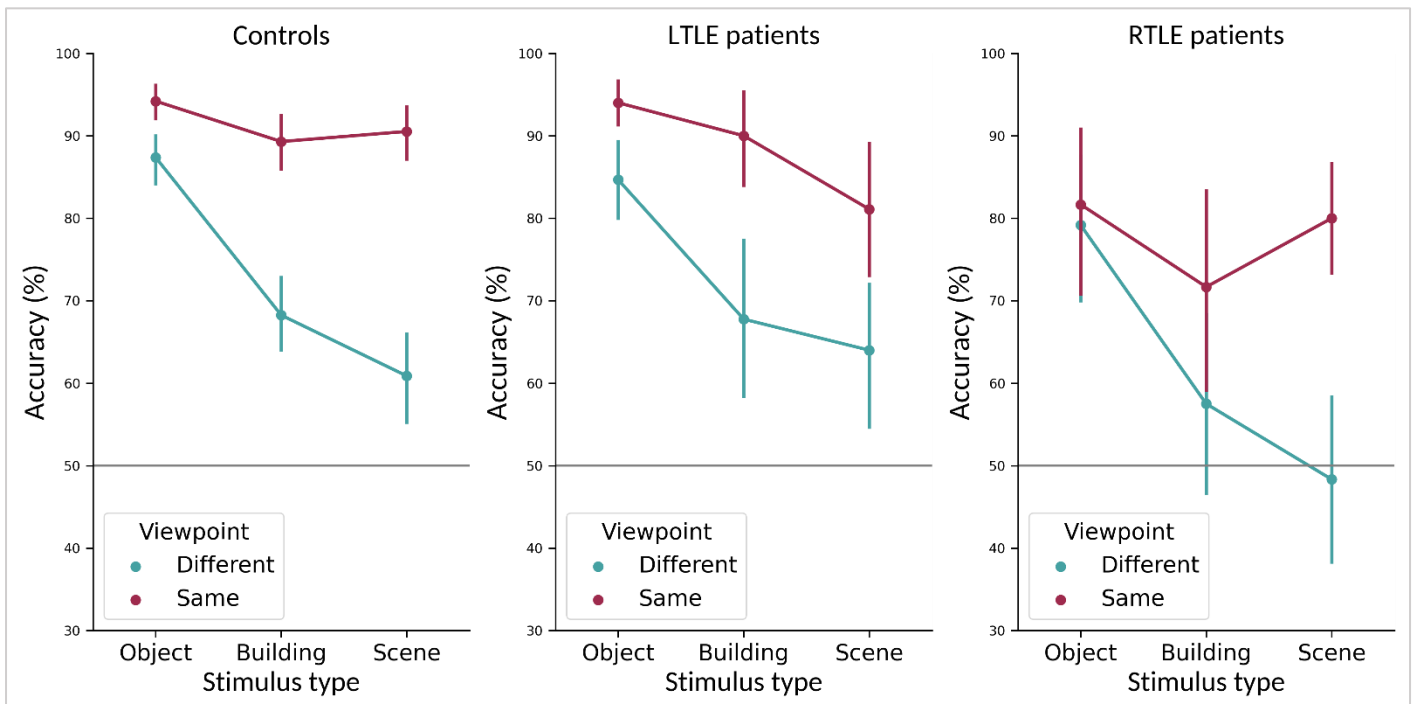


Figure 8.9. Mean accuracy in all task conditions for the controls (left), LTLE (middle), and RTLE patient groups (right) as a function of stimulus type and viewpoint. Error bars represent 95% confidence intervals. LTLE: left temporal lobe epilepsy; RTLE: right temporal lobe epilepsy. Horizontal lines mark chance level (i.e., 50%).

.05, $\eta^2 = .116$]. Specifically, the Stimulus type \times Viewpoint interaction observed in control participants was not found in LTLE ($p = .494$) and RTLE patients ($p = .949$).

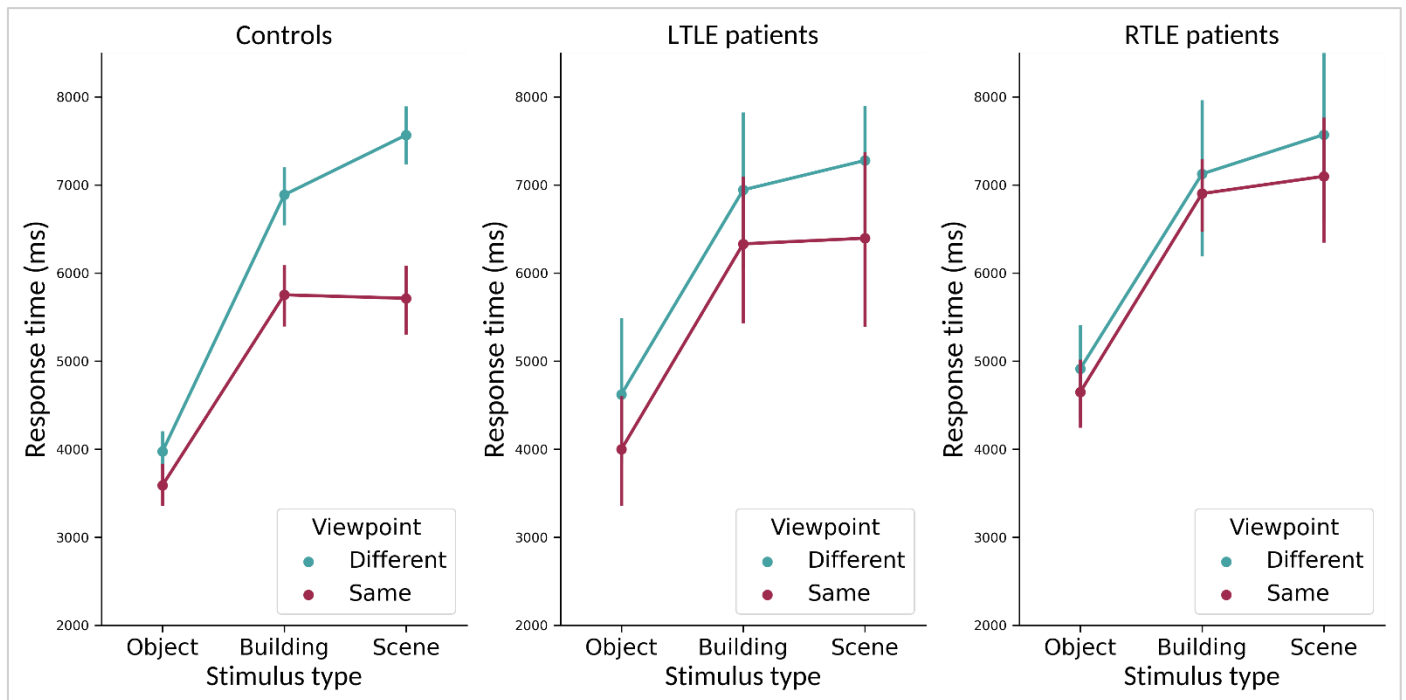


Figure 8.10. Mean response times (milliseconds) in all task conditions for the controls (left), LTLE patient groups (middle), and RTLE patient groups (right) as a function of material type and viewpoint. Error bars represent 95% confidence intervals. LTLE: left temporal lobe epilepsy; RTLE: right temporal lobe epilepsy.

Discussion

In the present study, we assessed the hypothesis that right, but not left, MTL regions are crucial to complex visual-discrimination, a paradigm that has previously been used in patients with bilateral lesions. In this purpose, we investigated patients with either left or right anterior temporal resection for drug-resistant epilepsy, as well as matched controls.

Visual-discrimination impairments in patients with MTL lesions are exacerbated by feature ambiguity (Barens et al., 2005, 2007) and viewpoint manipulation (Lee, Buckley, et al., 2005, 2006; see also Barens et al., 2010; Devlin & Price, 2007). We therefore manipulated these two factors, expecting that they would contribute to evidencing high-order visual deficits. In control subjects, accuracy was above chance level in all conditions and was modulated by stimulus type in the different viewpoint condition only. This suggests that although control participants succeeded in all conditions, the viewpoint manipulation efficiently prevented the use of low-level perceptual cues to resolve the task, thus revealing the effect of perceptual ambiguity. Accuracy and RT of LTLE patients were comparable to those of controls, and they consistently performed above chance level in all task conditions. Taken together, these results suggest that damage limited to the left MTL does not affect the ability to resolve visual-discrimination tasks, even in presence of high perceptual ambiguity.

Unlike LTLE patients, RTLE patients had both poorer overall accuracy and longer response times than control participants. Specifically, they failed to resolve the task in the scene-different and building-different conditions. This deficit is unlikely to be explained by low-level perceptual abilities, since RTLE patients succeeded with the task both when feature ambiguity was minimal (i.e., object conditions) and when the presentation viewpoint was not manipulated (i.e., same viewpoint conditions), and their visual reasoning index was in the normal range and not different from that of LTLE patients (figure 8.8). Importantly, these findings argue in favour of a specific role of the right MTL in representing complex visual stimuli even when the task implies no memory demand. Previously reported impairments in bilateral MTL patients in similarly designed studies may thus be explained mainly by the damage to right MTL regions (Barense et al., 2005, 2007; A. C. H. Lee, Buckley, et al., 2005; A. C. H. Lee, Bussey, et al., 2005).

Notably, the impairment of RTLE patients was exacerbated both in the scene and building conditions. Although both conditions present a high degree of visual complexity, scene stimuli differ from building stimuli in that they are spatially contextualised. Building stimuli are thus considered *complex entities*, whereas scene stimuli are considered proper *spatial scenes*. There is considerable evidence showing the role of the hippocampus in representing spatial scenes in memory (Hassabis, Kumaran, Vann, et al., 2007; Ross et al., 2018; K. J. Taylor et al., 2007; Zeidman & Maguire, 2016), imagination (Hassabis, Kumaran, & Maguire, 2007; Hassabis, Kumaran, Vann, et al., 2007; Zeidman & Maguire, 2016), and visual perception (Barense, Henson, et al., 2010; Hodgetts et al., 2016, 2017; A. C. H. Lee et al., 2012; McCormick et al., 2017; Zeidman et al., 2015). In contrast, entity representation is believed to rely on the PRC and the antero-lateral ERC (Barense et al., 2011; Besson et al., 2020; Erez et al., 2016; Lawrence et al., 2020; Martin et al., 2018). Both of these structures are impacted by standard anterior temporal cortex resection (Olivier et al., 2012; Boling, 2018; figure 8.7), which prevents from identifying the impairment that results from the specific lesion of each of these regions in the present study. It is only by thinking our results in the light of the previously-evidence specific roles of the hippocampus and PRC in representing scenes and entities, respectively, that such conclusions can be drawn. Therefore, our results argue for a specific role of right MTL regions in resolving perceptual ambiguity, but call for further research to ascertain whether scene and entity visual discrimination exclusively rely on the right hippocampus and PRC, respectively. These questions could be answered by using the presented protocol in case studies of patients with selective unilateral lesions of these regions.

In conclusion, the processing of representations made high-dimensional by perceptual characteristics appears to be the domain of the right MTL. As they support a hemispheric lateralisation of the previously-documented representational specialisation of MTL areas, these results also emphasise the question of the high-dimensional representations processed by the left MTL. Those regions might represent other kinds of representations, such as verbal or conceptual (Bruffaerts et al., 2013; Clarke & Tyler, 2014; Martin et al., 2018; Warren et al., 2016). Left unilateral MTL lesions would therefore impair the ability to resolve feature

ambiguity situations for this class of representations. This hypothesis is further discussed in the general discussion section.

Synthesis

In this chapter, we investigated the hemispheric lateralisation of the representational specialisation of MTL regions. First, a reanalysis of the data from study 3 suggested that the perceptual aspect of high-dimensional representations may be supported by right MTL regions preferentially. In study 4 we then tested this hypothesis by applying a visual-discrimination task to patients with unilateral MTL surgery for epilepsy. Impairments in this task were found in case of right, but not left, MTL damage. Taken together, these results support that representational dimensionality is modulated by hemispheric specialisation, and opens the way to the investigations how the RH principles apply to different kinds of representations.

Chapter IX – General discussion

Contents of chapter IX

| | |
|---|------------|
| Chapter IX – General discussion | 133 |
| 1. Summary of thesis objectives and main results..... | 134 |
| 2. Recollection, reconstruction, and the patch-cue paradigm | 134 |
| Dissociating the operation from the representation | 134 |
| Where is recollection in the hippocampus? | 135 |
| 3. The MTL processes representations across operations..... | 137 |
| Representational specialisation of the hippocampus and PRC across operations..... | 137 |
| Where is familiarity in the MTL? | 139 |
| 4. Future perspectives: different kinds of dimensionality along two brain axes? | 140 |
| Broad and sharp scene representations in the hippocampus long-axis..... | 140 |
| Different kinds of high-dimensional representations | 142 |
| 5. Conclusion | 144 |

1. Summary of thesis objectives and main results

In this thesis work, we explored the predictions of the RH model concerning the functional organisation of the MTL. This view proposes to decompose cognitive processes into representations and operations, and predicts that representations are the key factor explaining the specialisation of these regions. Accordingly, similar MTL regions would be involved in any operation performed on the same type of representation, whereas different regions would be recruited by different representations even for a same operation. The dimensionality of a representation would determine “where” in the VVS-MTL hierarchy it is processed (Cowell et al., 2019). If this proposal leads to testable predictions, it also raises new questions. One of these questions is how representational dimensionality applies to the hippocampus long-axis, and how the evidence concerning its internal organisation can fit in with the RH principles. The broad-to-sharp model explains this organisation in terms of “grain of resolution” of the representation processed, rather than by the operation performed by hippocampus subfields (Poppenk et al., 2013).

In a seminal study, Ross and colleagues (2018) have decomposed the process of recollection, showing that it engages the hippocampus in reason of the high-dimensional representation it involves rather than by the operation of pattern-completion. Taking the methodological questions raised by this study as a starting point, we first showed that the representation and operation composing recollection can indeed be dissociated using a patch-cue reconstruction paradigm. Then, combining this procedure with fMRI, we found that the preferential engagement of the hippocampus in the pattern-completion of scenes compared to that of objects is limited to its anterior segment. Importantly, this pattern of hippocampus activity was reproduced across memory and non-memory operations. The opposite representational specialisation was observed in the PRC. In addition to supporting the RH model, these results highlight the fact that different kinds of high-dimensional representations require different hippocampus segments. Besides the hippocampus long-axis, representational dimensionality may also vary depending on hemispheric specialisation. Our results suggest that the processing of representations made high-dimensional by the manipulation of perceptual variables depends on the right MTL specifically.

2. Recollection, reconstruction, and the patch-cue paradigm

Dissociating the operation from the representation

The first aim of this thesis was to assess the hypothesis that the representation involved in recollection determines the engagement of the hippocampus in this process, rather than the operation. According to the RH view, the operation involved is a pattern-completion like retrieval, and the representation is high-dimensional since it implies a spatial/temporal context. The patch-cue paradigm was designed in order to dissociate these two components. It would thus be possible to manipulate representational dimensionality while keeping the

operation constant, that is, measuring pattern-completion of high- and low-dimensional representations. In this paradigm, the visual reconstruction of previously encountered images is used as a proxy for pattern-completion, while representational dimensionality is manipulated through the complexity of these images: scenes versus objects. Measuring the engagement of MTL regions in visual reconstruction of scenes and objects using fMRI thereby allows to test the predictions of the RH view.

Considering that in this apparatus, reconstructing a scene and reconstructing an object rely on a same operation, comes with the assumption that they constitute a same cognitive mechanism. In study 2 we investigated whether memory representations contributed to the visual reconstruction of both object and scene images by evaluating the precision of (re)-constructions as function of prior exposures. We found no evidence for stronger influence of exposure for scenes than for objects; indeed, the effect was rather the opposite. In absence of brain activity measure in this study, we cannot conclude that the computation of pattern-completion is not modulated by stimulus type. Yet, these findings support that any effect of representational dimensionality on brain activity observed in our paradigm would not result from non-equivalent contributions of memory representations between the two types of stimuli. In study 3 we used this paradigm combined with fMRI in healthy young participants to attempt replicating the results observed by Ross and colleagues: the involvement of the hippocampus in reconstruction was specific to scenes (Ross et al., 2018). We did replicate this finding, although not using the same material set, which reinforces the original demonstration.

Where is recollection in the hippocampus?

The results from study 3, however, did not match those of Ross et al. when analysing the hippocampus long-axis. In particular, the scene specialisation pattern was specific to the anterior segment of the hippocampus, whereas in the original study it was also found in the middle and posterior segments. Several models were proposed to explain the functional specialisation of the aHC/pHC, for instance in terms of encoding/retrieval (Kim, 2015; Lepage et al., 1998), context/spatial processing (Nadel et al., 2013), or broad/sharp representations (Poppenk et al., 2013). The results of Ross et al. do not appear to fit in any of these models, as it suggests a similar functional specialisation of the three hippocampus segments. One possible explanation is the confusion between visual reconstruction and recollection.

Visual reconstruction of scenes is a means of approximating recollection. Yet, recollection is not limited to the reconstruction of a perceptual pattern, but includes other components such as the feeling of auto-noetic consciousness associated with mental time travel (Tulving, 1989). As exposed in chapter VI, the instructions used in the original study may have been confusing in this regard. In study 1 we explored the occurrence of proper recollection among reconstructions using a justified remember/know paradigm. The results showed that visual reconstruction can occur in absence of proper recollection, but that they can also be confounded, as some recollections did occur during visual reconstructions. This

stresses the importance of dissociating these two kinds of cognitive mechanisms in the instructions. In particular, we claim that using the terms “reconstruct the image” is better suited for measuring visual reconstruction, whereas the term “to remember” (*se remémorer* in French) biases towards proper recollection. In the original study, the distinction between these types of instructions was unclear, as the term “remember” was used to measure visual reconstruction.

Reconstruction is hence (at least partially) separable from proper recollection. We therefore built two independent versions of the recognition task: one measuring reconstruction from partial cues, the other measuring proper recollection and familiarity with complete stimuli. The aHC only was preferentially recruited by the pattern-completion of scenes compared with that of objects. As discussed in chapter VII, these results are consistent with the numerous studies that evidenced a specific engagement of the anterior-medial hippocampus in scene processing (for review, see Zeidman & Maguire, 2016). Poppenk, Evensmoen, Moscovitch, and Nadel proposed a model of the hippocampus long-axis in which the main characteristic of a given cognitive process is the “grain” of resolution of the representation involved (Poppenk et al., 2013). In this account, termed here *broad-to-sharp*, scenes can be regarded as global spatial representations, and so are likely to recruit broad representations in the aHC. Our results directly support this account against the competing hypothesis that the aHC and pHC are responsible for pattern-completion and pattern-separation, respectively, which would not predict any difference in aHC engagement between scene and object reconstruction. In line with the broad-to-sharp model of the hippocampus, recollection has been associated with the pHC specifically (Poppenk & Moscovitch, 2011). This link is thought to rely on the retrieval of contextual details (Robin & Moscovitch, 2017; Snytte et al., 2022), which are considered sharp representations. Consistent with previous studies, we found “remember” responses in the whole-item R/K task to be associated with an overall increase in pHC activity; but pHC recruitment was again independent of stimulus type. Considering that proper recollection can happen both when prompted by a scene and by an object image, these results are in agreement with the broad-to-sharp model.

Scenes are usually considered high-dimensional in reason of their spatial associative content, and have been widely associated with the hippocampus (reviews in Graham et al., 2010; Maguire & Mullally, 2013). In the case of visual reconstruction, scene reconstruction therefore relies on the hippocampus, and more specifically on the aHC, in reason of its global spatial resolution. Proper recollection also implies a high-dimensional representation given the associative details retrieved, but rather taps into the pHC specialisation as a fine-grained representation. Taken together, these results show that although scene reconstruction and proper recollection both recruit high-dimensional representations with respect to the RH predictions, those representations differ in their degree of resolution. Further characterising one of the intermediate-level components (i.e., representations) thereby reveals two specific ways by which a higher-level component (i.e., recollection) can be mapped onto the hippocampus (Cowell et al., 2019). We thus argue that the concept of *resolution* proposed by

the broad-to-sharp model allows to specify more finely the dimensionality of a given representation, and hence completes of the RH view (see section 4).

3. The MTL processes representations across operations

Representational specialisation of the hippocampus and PRC across operations

In study 3 we extended the result found for pattern-completion to other operations. This is one essential prediction of the RH model: representational dimensionality should determine the (VVS and) MTL regions engaged in a given process, independently of the operation. Crucially, the aHC was engaged in scene processing in all operations investigated, which strongly argues in favour of this view. Yet, the assumption that a *same* hippocampal region is engaged in scene representation independently of the operation performed remained to be tested. Similar to Zeidman et al. (2015), we performed an exploratory conjunction analysis between the four conditions for the Scene > Object contrast, hence directly assessing this hypothesis (Friston et al., 2005, see appendix B5 for full details of the analysis procedure and results). This analysis revealed a significant activation of the right medial aHC, meaning that this specific region was consistently activated by all tasks performed on scenes as compared to objects. Moreover, the observed peak coordinates corresponded to the region previously identified by Zeidman and Maguire as responsible for scene construction (2016; figure 9.1). The role of this region in scene construction is well-known (Zeidman et al., 2015; Dalton et al., 2018; for review, see Zeidman & Maguire, 2016). Yet, our results support that the specialisation of the medial aHC is independent of the constructive nature of the task, since strength-signal operations, unlike pattern-completion, do not imply a (*re*)-*constructive* component. This adds to previous studies on scene perception (Zeidman et al., 2015) and scene discrimination (Hodgetts et al., 2017) in demonstrating that the medial aHC *represents* scenes independently of the nature of the operation performed on it.

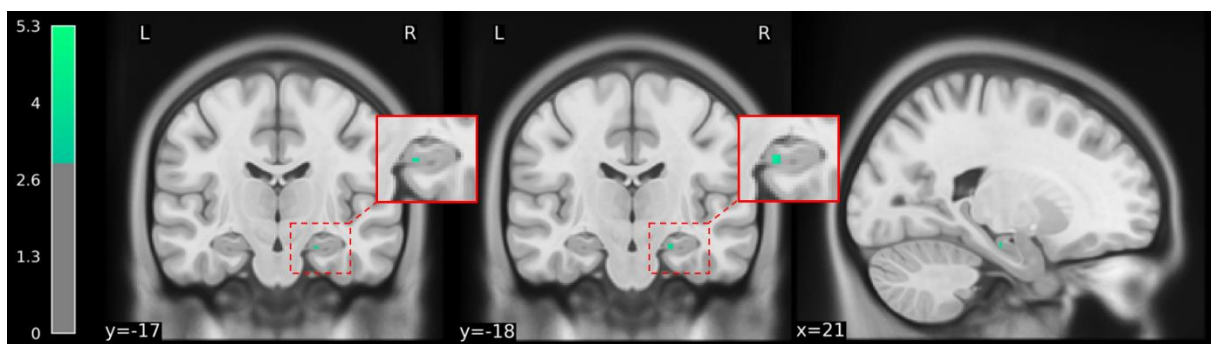


Figure 9.1. Hippocampal region identified by the conjunction analysis: this region was activated by the Scene>Object contrast independently of the operation (i.e., in all tasks investigated). Here no mask was applied but the slices were chosen to display the hippocampal region specifically. Activations are projected on the icbm T1 template in MNI space with a threshold $T = 3$ (this cluster was found at $p < .001$ uncorrected, $T = 3.78$). See appendix B5 for detailed analysis procedure and results. Peak coordinates 21, -18, -18.

Unlike the aHC, the pHC responded indifferently to scene and object processing; rather, an increase in overall pHC activity was found in the conditions that required sharp

representations. Yet, whereas the scene-specific role of the aHC was shown by a comparison between the scene and object conditions, any sharpness-specific interpretation of the patterns found in the pHC in study 3 should be taken cautiously since it is not drawn from an experimental manipulation. In other words, only differences in long-axis activity patterns between tasks can be explored. As discussed above, the pHC supports recollection when assessed through the retrieval of contextual details (Poppenk & Moscovitch, 2011; Snytte et al., 2022). Several studies have linked the pHC with sharp-representation processing outside the memory domain (Aly et al., 2013; Barense, Henson, et al., 2010; Dalton et al., 2018; McCormick et al., 2021). Thinking our results in the light of this evidence drives towards a broad-to-sharp interpretation of the hippocampus long-axis organisation. We thus argue that the role of the pHC is larger than recollection, and extends to any cognitive process that requires sharp representations (Poppenk et al., 2013). Importantly, this account also explains the diversity of cognitive domains in which hippocampal patients are impaired when stimuli present a high degree of perceptual ambiguity (Aly et al., 2013; Holdstock et al., 2002, 2005; Kirwan et al., 2012; A. C. H. Lee, Bussey, et al., 2005; Migo et al., 2009).

In the PRC, an object-specific pattern was found, and was reproduced across all operations except strength-signal rejection. Complementary to the scene specialisation evidenced in the aHC, this opposite effect argues in favour of a representation-based organisation of the MTL (figure 9.2). Specifically it (1) shows that the role of the PRC in entity representation is independent of the operation performed (Devlin & Price, 2007; Ferko et al., 2022; Kivisaari et al., 2012; Staresina et al., 2011), and (2) suggests that operations such as pattern-completion can happen anywhere in the VVS-MTL hierarchy depending on the dimensionality of the representation (Cowell et al., 2019). Yet, neuroimaging results do not tell us the conditions in which the integrity of a region is required. We may thus ask: does the lesser engagement of the hippocampus, and stronger engagement of the PRC, in object reconstruction mean that only the latter is critical to performing this task? Furthermore, can

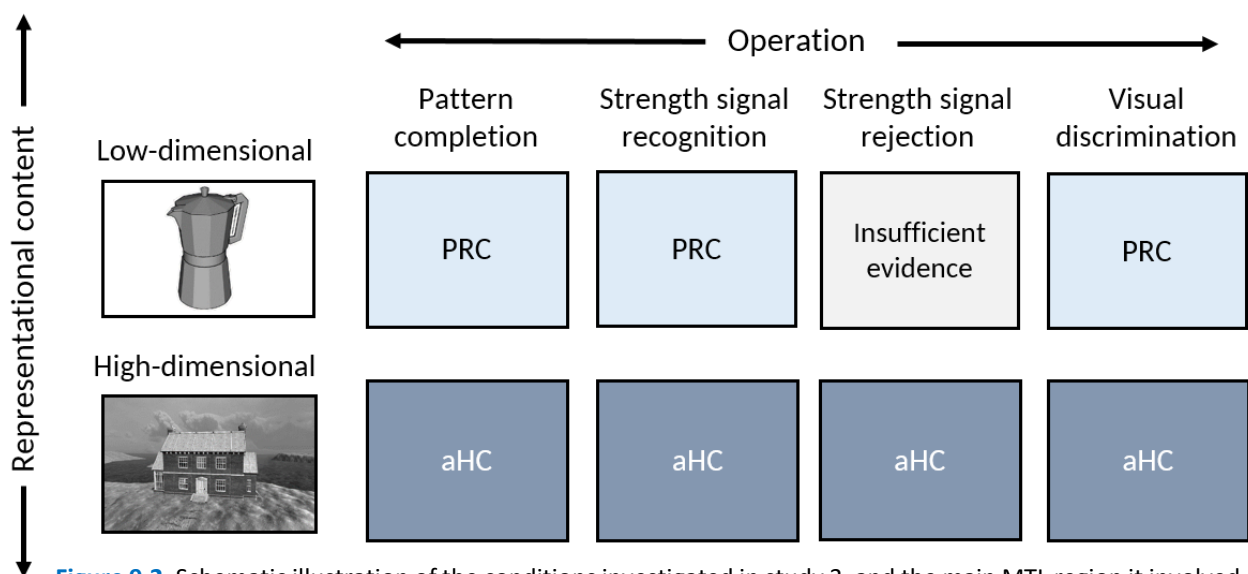


Figure 9.2. Schematic illustration of the conditions investigated in study 3, and the main MTL region it involved. PRC: perirhinal cortex, aHC: anterior hippocampus.

pattern-completion of representations of lower-dimensionality than objects be performed in case of lesions that include both the hippocampus and PRC? Such predictions can be drawn from the RH model, and require to be tested experimentally. Applying an adapted version of this protocol to patients with selective lesions to different VVS-MTL regions while manipulating representational dimensionality would be informative. Among the operations studied, the case of strength-signal recognition is particularly interesting, as it sheds new light on a long-lasting debate: what MTL region(s) contribute to familiarity memory?

Where is familiarity in the MTL?

In a dual-process account of the MTL, recollection is associated with the hippocampus, whereas the PRC is believed to be responsible for familiarity (Aggleton & Brown, 2006; Diana et al., 2006). According to the RH view, the representation involved in familiarity determines the brain regions it relies on. In contrast, the operation involved, termed strength-signal recognition, could happen anywhere in the VVS-MTL hierarchy (Cowell et al., 2019).

In a dual-process account, a confusion between memory process and operation is often made: when measuring the familiarity component of recognition memory without controlling the representations involved, operation and representational dimensionality are confounded. In the present work, by decoupling the representation from the operation involved in familiarity, that is, comparing strength-signal recognition of scenes and objects, we showed a preferential engagement of the PRC in object familiarity. This result challenges any process-based account, according to which the PRC should have responded to familiarity generally, and independently of representational content. Rather, it is consistent with its specific role in *entity familiarity* (Besson et al., 2020), and more largely *entity representation*.

Reciprocally, we reported hippocampal recruitment for scene familiarity compared to object familiarity. The region of the hippocampus recruited in scene familiarity was the same as for all operations investigated: the medial aHC (confirmed by the conjunction analysis, figure 9.1). Yet, the pattern of results appeared weaker in familiarity memory in ROI-based analyses. Strength-signal recognition of high-dimensional representations may be tricky to measure, especially through neuroimaging since (1) confidence can be confounded with processes in the R/K procedure; (2) familiarity judgements can sometimes be made on low-level perceptual features, thus biasing representational dimensionality in certain trials, and (3) strength-signal recognition is a fast operation, which makes it harder to detect using techniques with a low temporal resolution such as fMRI. Several studies that investigated this question in patients with isolated lesions of the hippocampus reported recognition impairments for scene stimuli (Bird et al., 2007; K. J. Taylor et al., 2007), including when dissociating recollection from familiarity (Cipolotti et al., 2006; see also Kirwan et al., 2010). Furthermore, priming, a less controlled operation than familiarity, is impaired for scenes and configurations in case of damage to the hippocampus (Chun & Phelps, 1999; Ryan et al., 2000). Remember/know paradigms may thus not be the most appropriate apparatus to explore this question in neuroimaging. Building a fast, block-based, recognition task of different classes of

stimuli would be an interesting lead for future research. Similar to recollection, strength-signal recognition was accompanied with increased pHC activity, irrespective of the representation. As discussed earlier, the proposal that sharp representations were required to discriminate old from new stimuli via familiarity is consistent with studies showing that recognition memory performance relies on hippocampus integrity when targets and lures present a high degree of perceptual ambiguity (Kirwan et al., 2012; S. M. Stark et al., 2019). In line with the predictions of the RH and broad-to-sharp models of the MTL and hippocampus, we thus propose two ways by which the hippocampus can play a role in familiarity. These two situations, scene representation in the aHC and sharp representations in the pHC, are the same as for recollection, consistent with an operation-independent view of the MTL (Cowell et al., 2019). While which of the aHC and pHC will be involved in familiarity memory heavily depends on *how* it is evaluated, in both cases high-dimensional representations are recruited in reason of perceptual characteristics of the material. This observation stresses the need for a more detailed account of the features that contribute to representational dimensionality.

4. Future perspectives: different kinds of dimensionality along two brain axes?

Broad and sharp scene representations in the hippocampus long-axis

In the literature on scene processing, numerous studies have focused on the *spatial coherence* of scenes, also termed *layout* (Hassabis & Maguire, 2007; McCormick et al., 2017). Consequently, the material used in these studies is particularly suited for evaluating this aspect of scene-based cognition (examples in figure 9.3.C). Based on previous studies

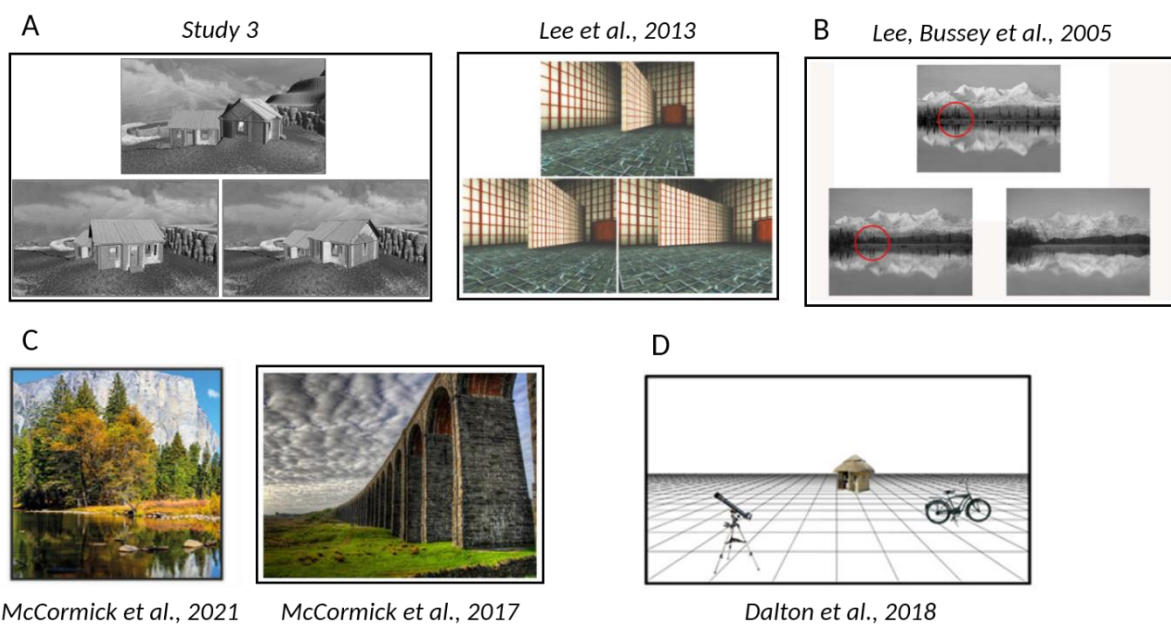


Figure 9.3. Different types of scene stimuli. A: Stimuli used in study 3 of the present work, and those used by Lee et al., 2013. B: Stimuli used by Lee, Bussey, et al., 2005 (the figure is from Lee et al., 2012). C: Examples of images from McCormick et al., 2017; 2021; D: Example of 3-dimensional array and objects from Dalton et al., 2018.

(Barens, Henson, et al., 2010; A. C. H. Lee, Buckley, et al., 2005; A. C. H. Lee et al., 2013), the stimuli used in the present work were built in a comparable manner (figure 9.3.A). By putting the emphasis on scene spatial coherence, this kind of material may be specifically prone to recruiting aHC-dependant global spatial representations. In line with this account, Dalton et al. (2018) reported medial aHC engagement when participants imagined 3-dimensional grids with 3 objects positioned on it, which isolates the spatial coherence of scene processing from the perceptual details (figure 9.3.D). As illustrated in figure 9.3.B, a different type of scenes that has been used could arguably be relabelled *landscape*. Visually processing those stimuli, however, does rely on the hippocampus as well (e.g., A. C. H. Lee, Bussey, et al., 2005). In contrast with the above-mentioned, this type of scenes may be more suited for engaging the pHC through sharp perceptual representations.

In addition to material variables, task variables can also modulate the segment of the hippocampus engaged in scene processing. For instance, Barens and colleagues (2010) reported that manipulating the presentation viewpoint modulates the scene versus object effect in the right pHC activity specifically. Although it is not presented in this thesis, we found a trending similar effect in our data¹⁶. Using the same images in both conditions, McCormick et al. (2021) showed that searching for differences in the layout and in the colour of a scene preferentially engaged the anterior and posterior portions of the hippocampus, respectively. They concluded that the pHC guides online scene perception whereas the aHC constructs spatially-coherent internal representations of the surrounding environment. Interestingly, this account proposes that different aspects of the same environment are processed simultaneously by the aHC and pHC. However, it does not take into consideration the role of the hippocampus in processes unrelated to scene-based cognition, such as how the pHC supports recollection, or how the aHC supports semantic gist retrieval (Poppenk et al., 2013; Robin & Moscovitch, 2017). Moreover, there is evidence that the hippocampus flexibly integrates information from multiple inputs, the diversity of which largely extends beyond purely spatial features (Aly & Turk-Browne, 2018). It is possible, therefore, that different kinds of broad and sharp representations can be extracted from the external or internal environment or stimuli depending on the task at hand. In the case of spatial navigation, this will correspond to global spatial scene coherence and the precise location of elements in it; but in other cases, such as episodic memory retrieval, the global/gist representation of the event and sharp/contextual-details will be processed as broad and sharp representations, respectively. As shown by McCormick and colleagues, it is possible to modulate the resolution of the representations required through material or task manipulations, thus revealing differences in functional specialisation within the hippocampus.

¹⁶ We found a trend for segment \times side \times viewpoint interaction, corresponding to an effect of viewpoint in the right pHC only, which is reported in the associated publication. The stimulus type \times viewpoint interaction, however, was found only when controlling for behavioural performance; considering the highly exploratory nature of this analysis, it is not presented here.

Finally, although in most studies the hippocampus is divided into a posterior and an anterior segment, other procedures have been proposed. In the present work we chose a 3-segments division in a replication perspective (Ross et al., 2018). Interestingly, not all the patterns of activation observed in the midHC were equivalent to that of the pHC. While the present work was not designed to distinguish between these two accounts, this observation could be interpreted as supporting a 3-segments fractionation (for similar observations, see Hannula et al., 2013). Taking this question a step further, Strange and colleagues (2014) suggested that the functional organisation of the hippocampus could follow a continuous gradient. Recent evidence showed that representation resolution is mapped continuously along the hippocampus long-axis (Brunec et al., 2018), hence opening a promising avenue for future research.

Different kinds of high-dimensional representations

According to the definition proposed by Cowell, Barense, and Sadil (2019), representational dimensionality is not limited to the perceptual aspects of a representation, but is determined by various kinds of features. The majority of the evidence that contributed to the development of the RH model came from the domain of visual perception and the modulation of perceptual variables such as ambiguity (e.g., Murray & Bussey, 1999). The questions explored in the present thesis were in line with this body of research, and hence were addressed within the same experimental framework. While investigating several kinds of features was beyond the scope of our experimental contributions, we sought to test the hypothesis that this kind of tasks – that imply high-dimensional representations in reason of perceptual properties of the material and/or task manipulations – present a hemispheric specialisation. Previous studies (see chapters V and VIII) suggested that these tasks would rely on the right MTL specifically. The lateralisation of fMRI activity found in study 3 pointed in the same direction. As mentioned, however, it is possible that conceptual information contributed more to object memory than to scene memory. The observed lateralisation of the PRC object specialisation during memory operations would then have been biased, which constitutes a potential limitation of Study 3. Visual-discrimination, in contrast, does not present this bias, since performing this task exclusively demands to process the stimuli perceptually. Yet the results from this task in study 3 could also be interpreted in terms of memory encoding: the stronger engagement of the hippocampus for scenes as compared to objects could result from a stronger involvement in scene encoding. Visual-perception tasks have been widely used in previous studies to investigate the representational specialisation of MTL regions in patients with brain damage, as the performance does not rely on memory (Graham et al., 2010). We therefore chose to apply this task to patients with unilateral MTL lesions in study 4, and showed that right but not left MTL damage resulted in visual-discrimination impairments in case of high perceptual ambiguity. In addition to supporting a right-lateralisation of perceptual high-dimensional representations, this result argues against the interpretation of Study 3 results in terms of mere memory encoding.

The main limitations of study 4 results come with the population investigated and the sample size. First, patients with epilepsy exhibit reorganisation patterns of neurocognitive networks through brain plasticity, which can lead to atypical lateralisation of cognitive functions such as memory and language (Baciu & Perrone-Bertolotti, 2015; Banjac et al., 2021; Labudda et al., 2012; Li et al., 2017). Replicating this study with larger patient groups would allow more confidence on the generalisability of the results. In addition, the patients underwent standard anterior lobe cortectomy, the extent of which prevents from drawing inferences on the specific role of left and right MTL subregions. The vast majority of similar studies were conducted in patients with more selective, but bilateral, damage. Accordingly, the specific kind of visual representation processed by different MTL subregions is well established. In contrast, limited information is available concerning the lateralisation of these functions. In this context, and since patients with more selective lesions could not be recruited in the course of this thesis, we chose to test the prediction that visual-discrimination impairments would appear in the case of right-lateralised MTL resection only. Consequently, our experimental contribution is to show that right but not left MTL damage impairs complex visual-discrimination *overall*, while the well-known roles of the hippocampus and PRC in discriminating scenes and entities, respectively, allow to infer that the damage to those structures in the right hemisphere is responsible for the observed impairments. This evidence hence calls for further studies. In particular, studying patients with selective *and* unilateral lesions would be the appropriate framework to supplement those results.

In the original definition given by Cowell et al., verbal material can recruit high-dimensional representations in reason of their semantic/associative character. Indeed, there is evidence that hippocampal damage impairs certain aspects of language processing (Duff & Brown-Schmidt, 2012; Hilverman & Duff, 2021), creative thinking (Duff et al., 2013; Warren et al., 2016), and semantic memory (Klooster et al., 2020; Klooster & Duff, 2015; for review, see Duff et al., 2020). These impairments were consistently observed in conditions where information must be manipulated and/or integrated in a flexible manner, which could be considered situations requiring non-perceptual high-dimensional representations. Similarly, there is evidence that the PRC contributes to resolving entity-related conceptual ambiguity (Barese, Rogers, et al., 2010; Bruffaerts et al., 2013). A recent study by Martin and colleagues (2018) further suggested that the left PRC integrates conceptual *and* perceptual aspects of objects (see also Bruffaerts et al., 2013). Having shown that high-dimensional representations related to perceptual features critically rely on right MTL regions, we will now investigate the type of representations that presents the reverse pattern of hemispheric specialisation. In line with our results and previous studies, we hypothesise that left, but not right, MTL lesions will impair the ability to resolve conceptual ambiguity. If testing this assumption was beyond the scope of this thesis, we plan to address this question in the near future.

5. Conclusion

Being at the crossroad between neuropsychology and cognitive neuroscience, this thesis addressed the general objective of mapping the correspondence between human behaviour and brain areas. By assuming that the appropriate level of analysis to this question is representations and operations rather than cognitive processes, we positioned ourselves more generally within the representational hypothesis. Overall, we found that representational specialisation was independent of the operations, thereby providing further support for this general framework. Specifying the determinants of the MTL representational organisation in more details also opens interesting avenues for future research.

Our work supports that considering the resolution of the representations provides a finer characterisation of its dimensionality. The internal organisation of the hippocampus seems to follow a continuous anteroposterior gradient where information is represented depending on resolution sharpness. Conceiving the hippocampus internal organisation as a continuum, a phenomenon known from the animal literature but relatively novel to the field of human neuroscience, leads to assume the existence of intermediate levels of resolution, rather than a dichotomy between broad and sharp representations (Strange et al., 2014). In most current studies the experimental framework does not allow to unveil such intermediate levels. Because a dichotomous aHC/pHC functional dissociation is often assumed, the methodological procedure and level of analysis are driven by this postulate. In a concluding comment, Brunec and colleagues (2018) empathised that further studies are required to assess whether the manipulation of the representational demand of the task would result in modifications of “signal granularity”, a marker of representation resolution. In future investigations the paradigm will therefore need to be adapted in order to study the hippocampus long-axis specialisation in its full complexity. Another level of investigation opens when considering the modulation of this long-axis organisation by hemispheric lateralisation. Our work and previous studies suggested that representational specialisation assessed with visual-spatial material is independent of left MTL regions, which would process different types of high-dimensional representations such as verbal or conceptual. We might then ask how to conceptualise, and operationalise, resolution sharpness for this class of representations. These avenues of research, together with studying the kinds of features contributing to entity representation that critically rely on the left PRC, are among those we intend to pursue in future work.

In addition to the leads for future fundamental research, our work is also of interest from a clinical research perspective. Clarifying the functional organisation of the MTL helps to better understand and predict the cognitive changes associated with the pathologies that affect these regions. By objectifying non-memory impairments in patients who underwent right anterior temporal cortectomy, our findings contribute to shedding light on an area of cognitive dysfunction that can have a significant impact on the patients’ daily life. It is therefore essential to replicate these results, and to overcome the sample size limitation by

recruiting larger groups. More generally, a growing body of research has begun to take into account the representational specialisation of these regions when testing patients with neurological conditions, and in particular those with mild cognitive impairment due to early neuroprogressive diseases. With this research emerge new ways of evaluating the integrity of these regions, which, in turn, provide promising leads for the early detection of such pathologies. Generalising the representational specialisation across operations, our work further supports that representations, rather than processes, are the appropriate level of investigation to evaluate the integrity of MTL regions, hence contributing to shape such encouraging perspectives.

Appendices

| | |
|--|------------|
| Appendices A: Studies 1 & 2 supplementary material | 147 |
| 1. Appendix A1: Illustrations used in study 1 | 147 |
| Whole-item condition | 147 |
| Patch-cue condition | 148 |
| 2. Appendix A2: Illustration used in Study 2 | 149 |
| Appendices B: Study 3 supplementary material..... | 150 |
| 1. Appendix B1: Matching task whole-brain analysis | 150 |
| Visualisation of activations on a 3D template..... | 150 |
| Activated regions..... | 150 |
| 2. Appendix B2: Pattern-completion whole-brain analysis | 152 |
| Visualisation of activations..... | 152 |
| Activated regions..... | 152 |
| 3. Appendix B3: Strength-signal recognition whole-brain analysis | 155 |
| Visualisation of activations..... | 155 |
| Activated regions..... | 155 |
| 4. Appendix B4: Strength-signal rejection whole-brain analysis | 157 |
| Visualisation of activations..... | 157 |
| Activated regions..... | 157 |
| 5. Appendix B5: Exploratory conjunction analysis | 159 |
| Visualisation of resulting activations | 161 |
| Activated regions..... | 162 |
| Appendices C: Neuropsychological tests used in Studies 3 and 4..... | 164 |
| 1. Appendix C1: Mini mental state examination (MMSE)..... | 164 |
| 2. Appendix C2: Trail-making test | 166 |
| 3. Appendix C3: Example of Wechsler memory scale (MEM-IV) profile summary..... | 169 |
| 4. Appendix C4: Example of neuropsychological examination | 170 |

Appendices A: Studies 1 & 2 supplementary material

1. Appendix A1: Illustrations used in study 1

Whole-item condition

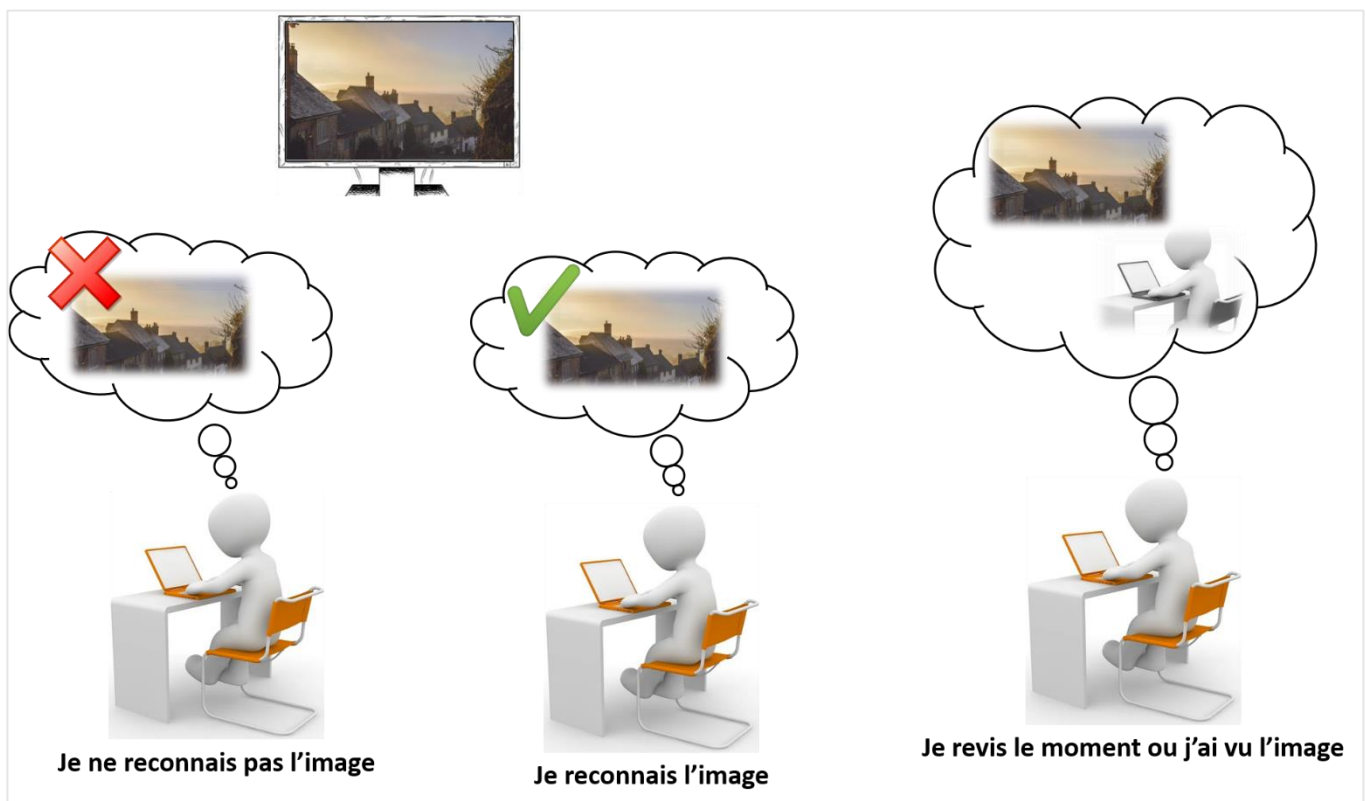


Figure A1.1. Figure used in the “whole-item” condition in Study 1 to illustrate the three response options: “new” (left), “familiar” (centre), and “remember” (right). French instructions translated from left to right: “I do not recognise the image”; “I recognise the image”, and “I relive the moment I saw the image”.

Patch-cue condition

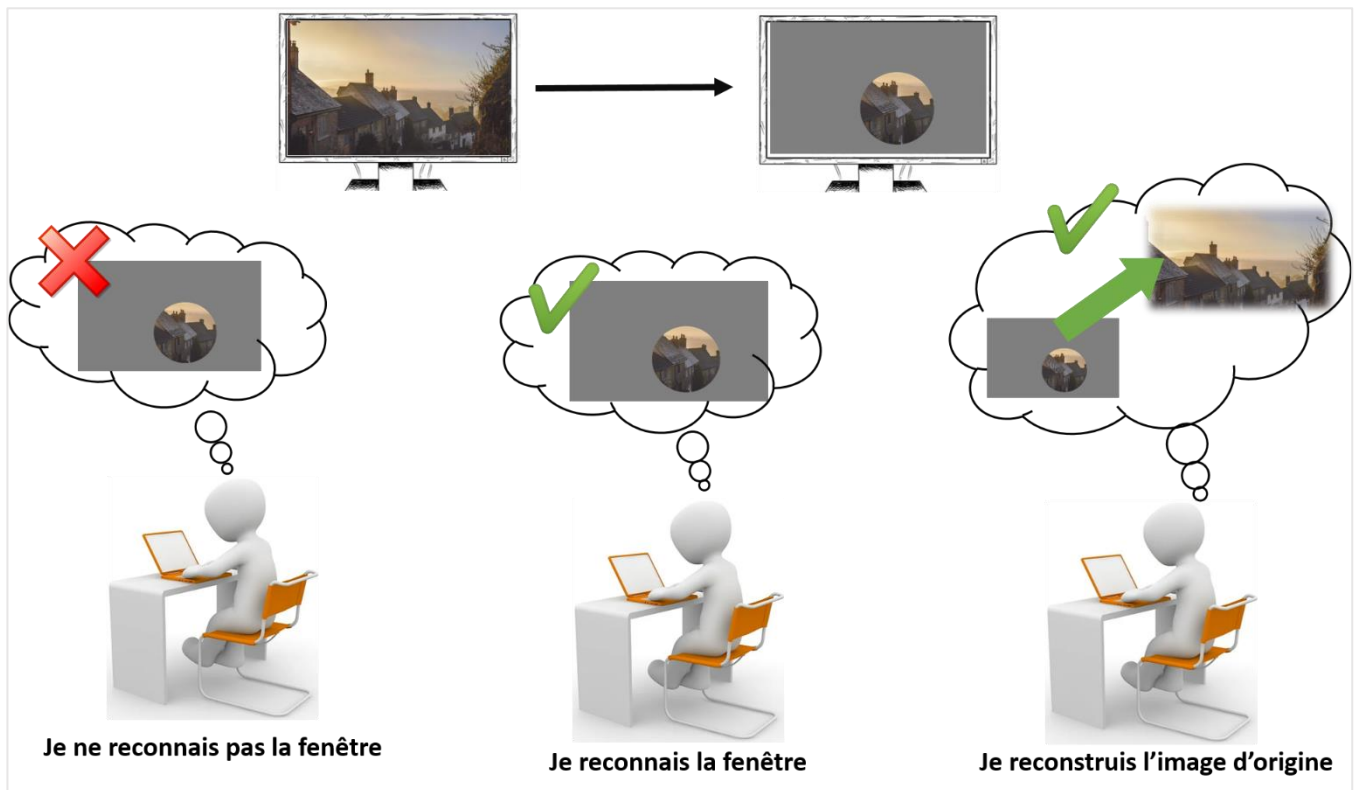


Figure A1.2. Figure used in the “Patch-cue” condition in Study 1 to illustrate the three response options: “new patch” (left), “patch familiar” (centre), and “reconstruction” (right). French instructions translated from left to right: “I do not recognise the patch”; “I recognise the patch”, and “I reconstruct the original image”.

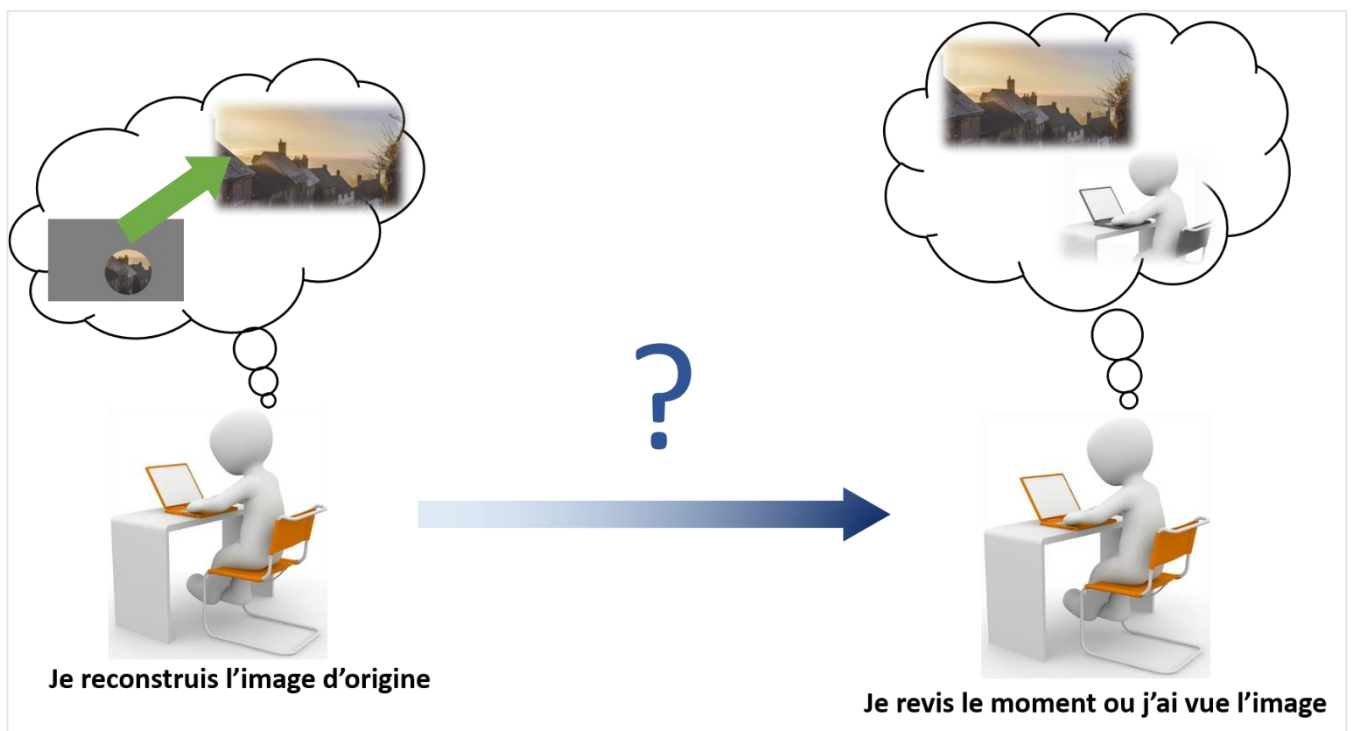


Figure A1.3. Figure used in the “Patch-cue” condition in Study 1 to illustrate the “remember” question following reconstruction responses. French instructions translated, left: “I reconstruct the original image”, right: “I relive the moment I saw the image”.

2. Appendix A2: Illustration used in Study 2

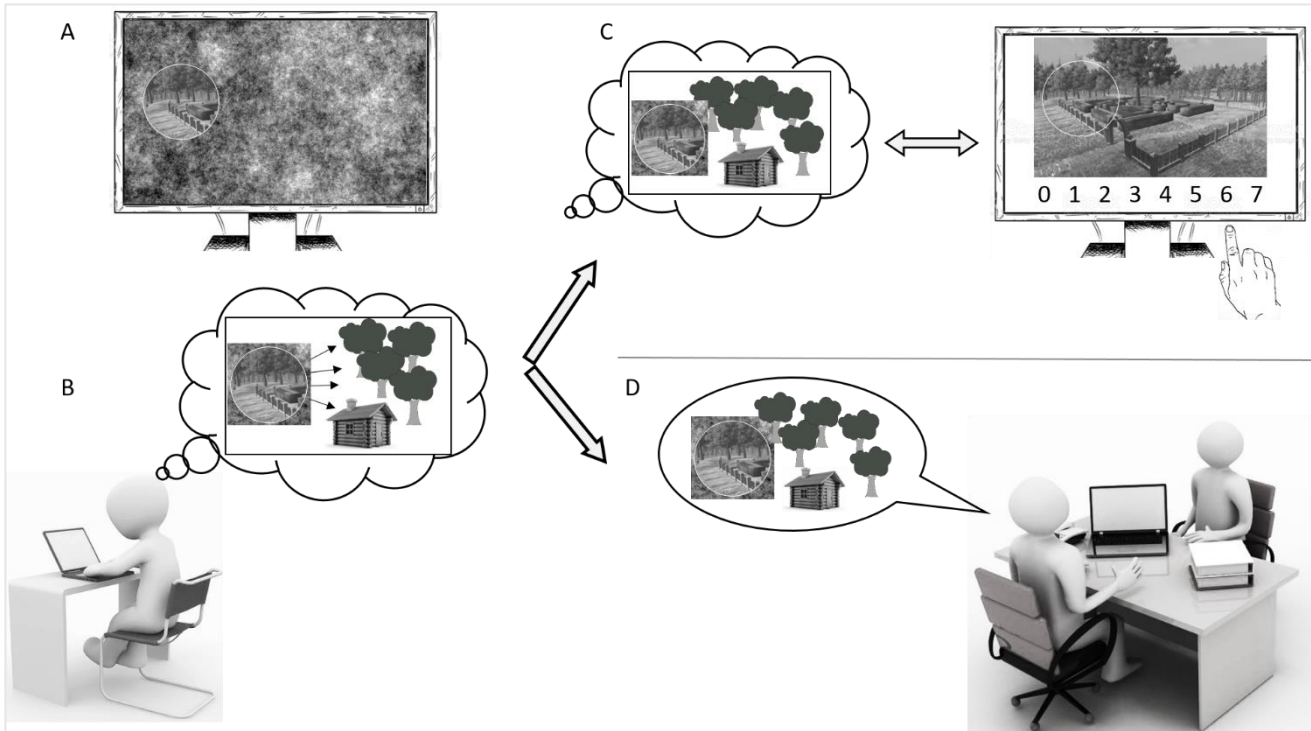


Figure A2.1. Figure used to illustrate the instructions in Study 2. A: Example of patch stimulus. B: Schematic drawing illustrating the visual (re)-construction step. C: Explanation of the similarity judgement task: the subject is instructed to rate the similarity between the imagined image (i.e., in the imagination bubble) and the whole image displayed on screen from 0 to 7. D: Explanation of the verbal description task: the subject is instructed to describe the imagined image to the experimenter. Letters were added for figure description purposes, in the original form of the figure, only the arrows were present to illustrate the sequence between drawings B and C/D.

Appendices B: Study 3 supplementary material

In study 3, whole-brain analyses were presented to complete ROI-based analyses. The main goal was to specify more finely the location within the hippocampus of significant differences in activity resulting from the Scene > Object contrast. Full details of the results from this contrast for each task is therefore presented here (appendices B1 to B4). Because they do not answer this question and for clarity, the results from the reversed contrast (i.e., Object>Scene) are not presented here. Finally, the procedure and results of the conjunction analysis performed on these data (appendix B5).

1. Appendix B1: Matching task whole-brain analysis

Visualisation of activations on a 3D template

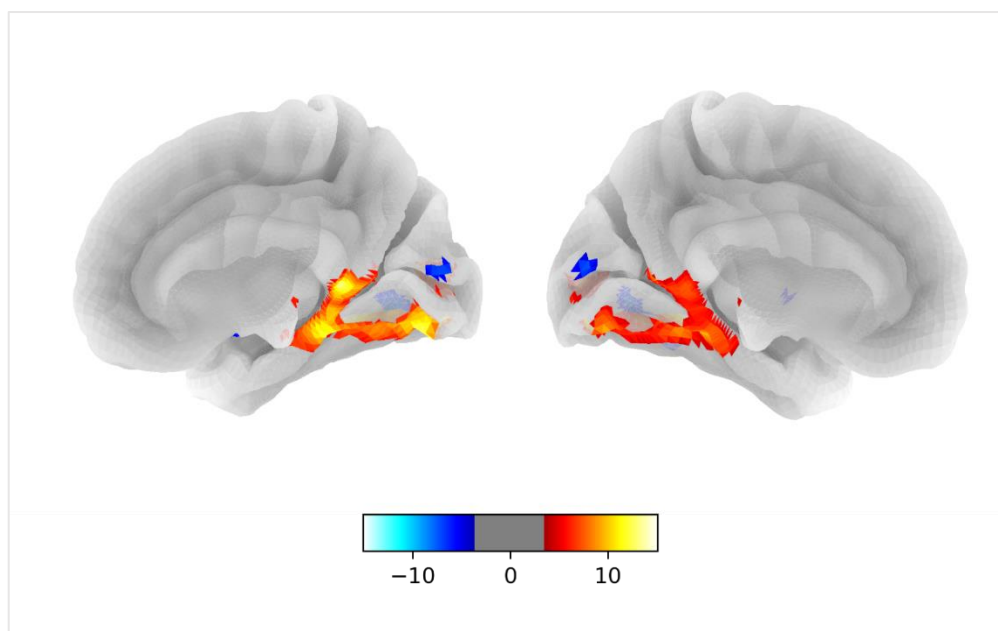


Figure B1.1. Activations resulting from the [Scene > Object] contrast in the matching task, projected on a 3D template, presented from the medial view. A threshold $T = 3.5$ was applied. Note that in this representation, the right hemisphere is presented on the left and the left hemisphere is presented on the right. Transparency is set to 80% so that some activation clusters slightly appear through the surface.

Activated regions

Table B1. Activated regions for the Scene > Object contrast in the matching task ($p < .001$ uncorrected). For each peak, the number of voxels (k), the T value, the coordinates (x, z, y, in mm), and AAL3 label (Tzourio-Mazoyer et al., 2002) are given. In case of unidentified region (i.e., unknown label > 60%), the label “unknown” is given.

| K | T | x | y | z | AAL |
|-------|--------|-----|-------|-------|-----------------------------|
| 17706 | 15.116 | -24 | -45 | -7.5 | left_Parahippocampal_gyrus |
| | 14.806 | 30 | -39 | -10.5 | right_Parahippocampal_gyrus |
| | 12.620 | 15 | -82.5 | -10.5 | right_Lingual_gyrus |

| | | | | | |
|-----|-------|-------|-------|-------|----------------------------------|
| 268 | 7.082 | 3 | -28.5 | -1.5 | unknown |
| | 4.772 | 6 | -18 | -4.5 | unknown |
| | 4.710 | -3 | -33 | -4.5 | unknown |
| 1 | 6.878 | 16.5 | -12 | -21 | right_Parahippocampal_gyrus |
| 33 | 5.450 | 1.5 | -57 | -25.5 | Vermis_lobule_IV |
| 11 | 5.231 | -10.5 | -43.5 | -16.5 | left_Cerebellum_lobule_IV |
| 6 | 5.131 | -12 | 0 | 0 | left_Lenticular_nucleus/Pallidum |
| 8 | 4.830 | 49.5 | -52.5 | 10.5 | right_Middle_Temporal_gyrus |
| 33 | 4.828 | -1.5 | -48 | -19.5 | Vermis_lobule_III |
| 26 | 4.809 | 31.5 | 22.5 | -7.5 | right_Inferior_Frontal_gyrus |
| 10 | 4.808 | 34.5 | -9 | -7.5 | right_Lenticular_nucleus/Putamen |
| 40 | 4.607 | -31.5 | 25.5 | -6 | left_Inferior_Frontal_gyrus |
| 6 | 4.553 | -3 | -28.5 | -15 | unknown |
| 3 | 4.324 | -24 | -21 | -7.5 | unknown/left_Hippocampus |
| 6 | 4.263 | 12 | -34.5 | -27 | unknown |
| 8 | 4.227 | 3 | -27 | -12 | unknown |
| 12 | 4.187 | -19.5 | -31.5 | 4.5 | left_anterior_Pulvinar |
| 2 | 4.024 | 9 | -57 | -13.5 | right_Cerebellum_lobule_IV |
| 5 | 3.973 | 42 | 21 | -9 | right_Insula |
| 4 | 3.965 | -4.5 | -22.5 | -19.5 | unknown |
| 13 | 3.927 | 51 | -6 | -18 | right_Middle_Temporal_gyrus |
| 8 | 3.910 | -37.5 | 15 | -1.5 | left_Insula |
| 3 | 3.860 | -25.5 | -51 | -22.5 | left_Cerebellum_lobule_IV |
| 2 | 3.846 | 12 | 7.5 | -3 | unknown/right_Nucleus_Accumbens |
| 4 | 3.820 | -34.5 | 12 | -22.5 | left_Temporal_pole |
| 3 | 3.802 | -3 | -36 | -24 | unknown |
| 1 | 3.778 | -25.5 | -30 | 3 | unknown/left_Hippocampus |
| 5 | 3.777 | 28.5 | -28.5 | 0 | unknown/right_Hippocampus |
| 9 | 3.750 | -13.5 | -12 | 4.5 | left_Ventral_lateral |
| 1 | 3.715 | -12 | -64.5 | -22.5 | left_Cerebellum_lobule_IV |
| 5 | 3.713 | -1.5 | -19.5 | -19.5 | unknown |
| 3 | 3.707 | 22.5 | -30 | 7.5 | right_medial_Pulvinar |
| 7 | 3.700 | 4.5 | -36 | -19.5 | right_Locus_Coeruleus |
| 2 | 3.683 | 37.5 | -66 | -24 | right_Cerebellum_crus_I |
| 2 | 3.616 | -22.5 | -51 | -27 | left_Cerebellum_lobule_IV |
| 2 | 3.594 | -16.5 | -10.5 | -21 | left_Hippocampus |
| 4 | 3.591 | -36 | 21 | -15 | left_Inferior_Frontal_gyrus |
| 2 | 3.578 | 45 | 16.5 | -4.5 | right_Insula |
| 2 | 3.576 | 4.5 | -34.5 | -28.5 | unknown |
| 4 | 3.556 | -7.5 | -16.5 | -12 | left_Substantia_nigra |
| 3 | 3.549 | 52.5 | -7.5 | -13.5 | right_Superior_Temporal_gyrus |
| 1 | 3.523 | -15 | -31.5 | -30 | unknown |
| 1 | 3.514 | 21 | -25.5 | -3 | unknown/right_Hippocampus |
| 2 | 3.500 | -37.5 | -54 | -27 | left_Cerebellum_crus_I |
| 2 | 3.498 | -9 | -66 | -22.5 | left_Cerebellum_lobule_IV |
| 3 | 3.480 | 39 | 10.5 | -21 | right_Temporal_pole |
| 1 | 3.464 | 37.5 | -60 | -25.5 | right_Cerebellum_crus_I |

| | | | | | |
|---|-------|-------|-------|-------|--|
| 1 | 3.454 | -36 | -55.5 | -25.5 | left_Cerebellum_lobule_IV |
| 1 | 3.443 | -45 | -75 | 12 | left_Middle_Occipital_gyrus |
| 3 | 3.431 | -16.5 | -3 | 1.5 | left_Lenticular_nucleus/Pallidum |
| 1 | 3.428 | 46.5 | 18 | -6 | unknown/right_Insula |
| 1 | 3.407 | -31.5 | 19.5 | -6 | left_Insula |
| 1 | 3.384 | -7.5 | -24 | 3 | unknown/left_Mediodorsal_magnocellular |
| 1 | 3.373 | 52.5 | -6 | -9 | right_Superior_Temporal_gyrus |
| 2 | 3.372 | 19.5 | -28.5 | 9 | right_medial_Pulvinar |
| 1 | 3.363 | 0 | -6 | -4.5 | unknown |
| 2 | 3.356 | 3 | -19.5 | -7.5 | unknown/right_red_Nucleus |
| 1 | 3.346 | -12 | -18 | -7.5 | unknown |
| 2 | 3.342 | -3 | -36 | -16.5 | unknown |
| 2 | 3.340 | 13.5 | -63 | -24 | right_Cerebellum_lobule_VI |
| 1 | 3.312 | 12 | -16.5 | -6 | unknown/right_red_Nucleus |
| 1 | 3.311 | -13.5 | -73.5 | 6 | left_Calcarine_fissure |
| 1 | 3.302 | -4.5 | -9 | 3 | unknown/left_Mediodorsal_magnocellular |
| 1 | 3.302 | 3 | -64.5 | 1.5 | unknown/right_Lingual_gyrus |
| 1 | 3.281 | -19.5 | -12 | -9 | unkonw/left_Hippocampus |

2. Appendix B2: Pattern-completion whole-brain analysis

Visualisation of activations

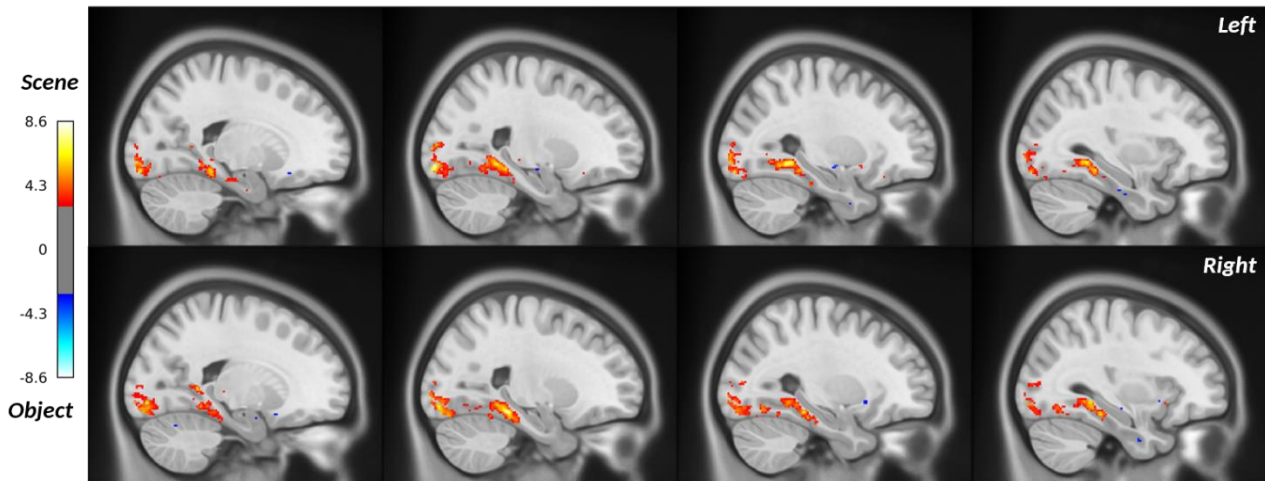


Figure B2.1. Activations resulting from the [Scene > Object] contrast in pattern-completion trials (i.e., correct “Rec” responses in the patch-cue paradigm), projected on the icbm template displayed in sagittal slices in the left and right hemispheres (MNI x coordinates from left to right: -20, -24, -28, -32 and opposite). A threshold $T = 3$ was applied.

Activated regions

Table B2. Activated regions for the Scene > Object contrast in pattern-completion trials (i.e., correct “Rec” responses in the patch-cue paradigm) ($p < .001$ uncorrected). For each peak, the number of voxels (k), the T value, the coordinates (x, z, y , in mm), and AAL3 label (Tzourio-Mazoyer et al., 2002) are given. In case of unidentified region (i.e., unknown label > 60%), the label “unknown” is given.

| K | T | x | y | z | AAL |
|-----|-------|-------|-------|-------|---------------------------------|
| 647 | 8.632 | 25.5 | -45 | -7.5 | right_Parahippocampal_gyrus |
| | 7.996 | 24 | -37.5 | -13.5 | right_Parahippocampal_gyrus |
| | 5.773 | 31.5 | -40.5 | -10.5 | right_Fusyform_gyrus |
| 480 | 8.175 | -25.5 | -94.5 | -9 | left_Inferior_Occipital_gyrus |
| | 6.384 | -30 | -88.5 | -15 | left_Lingual_gyrus |
| | 5.396 | -12 | -94.5 | -9 | left_Inferior_Occipital_gyrus |
| 558 | 8.104 | -28.5 | -48 | -7.5 | left_Lingual_gyrus |
| | 6.626 | -18 | -37.5 | -13.5 | left_Parahippocampal_gyrus |
| | 6.019 | -30 | -39 | -13.5 | left_Parahippocampal_gyrus |
| 278 | 7.709 | 16.5 | -48 | 3 | right_Precuneus |
| | 6.935 | 9 | -43.5 | 3 | right_Posterior_Cingulate_gyrus |
| 581 | 7.107 | 21 | -87 | -7.5 | right_Lingual_gyrus |
| | 6.284 | 15 | -97.5 | -6 | right_Calcarine_fissure |
| | 5.705 | 33 | -90 | -9 | right_Inferior_Occipital_gyrus |
| 116 | 7.027 | -16.5 | -51 | 4.5 | left_Precuneus |
| | 5.191 | -7.5 | -43.5 | 6 | left_Posterior_Cingulate_gyrus |
| | 5.078 | -10.5 | -55.5 | 7.5 | left_Calcarine_fissure |
| 53 | 6.925 | -27 | -91.5 | 7.5 | left_Middle_Occipital_gyrus |
| 58 | 5.269 | 28.5 | -66 | -13.5 | right_Fusyform_gyrus |
| 23 | 5.156 | 37.5 | -79.5 | 9 | right_Middle_Occipital_gyrus |
| 7 | 4.906 | 24 | -49.5 | -18 | right_Cerebellum_IV |
| 7 | 4.778 | 27 | -24 | -22.5 | right_Parahippocampal_gyrus |
| 18 | 4.703 | -18 | -22.5 | -19.5 | left_Hippocampus |
| 24 | 4.696 | 33 | -88.5 | 7.5 | right_Middle_Occipital_gyrus |
| 8 | 4.691 | -31.5 | -82.5 | -19.5 | left_Fusyform_gyrus |
| 4 | 4.321 | -22.5 | -31.5 | -21 | left_Parahippocampal_gyrus |
| 3 | 4.298 | -30 | 9 | -9 | unknown |
| 6 | 4.297 | -10.5 | -22.5 | -24 | unknown |
| 6 | 4.263 | 27 | -93 | 9 | right_Middle_Occipital_gyrus |
| 7 | 4.261 | -18 | -36 | -4.5 | left_Hippocampus |
| 2 | 4.205 | -4.5 | -75 | -24 | left_Cerebellum_IV |
| 5 | 4.204 | 42 | 18 | -9 | right_Insula |
| 2 | 4.129 | -13.5 | -42 | -10.5 | left_Lingual_gyrus |
| 1 | 4.071 | -16.5 | -31.5 | -12 | left_Hippocampus |
| 4 | 4.069 | 28.5 | -55.5 | -16.5 | right_Cerebellum_IV |
| 5 | 4.049 | -28.5 | -30 | -24 | left_Parahippocampal_gyrus |
| 1 | 3.939 | 1.5 | -30 | -25.5 | unknown |
| 2 | 3.884 | -25.5 | -85.5 | -18 | left_Lingual_gyrus |
| 1 | 3.882 | 21 | -27 | 1.5 | right_Medial_Geniculate |
| 1 | 3.881 | -22.5 | -25.5 | -27 | left_Parahippocampal_gyrus |
| 2 | 3.864 | 1.5 | -49.5 | -19.5 | Vermis |
| 1 | 3.845 | -10.5 | -34.5 | -9 | unknown |
| 1 | 3.844 | 27 | -10.5 | -28.5 | right_Parahippocampal_gyrus |
| 3 | 3.784 | 31.5 | -52.5 | -10.5 | right_Fusyform_gyrus |
| 2 | 3.784 | -33 | -84 | 7.5 | left_Middle_Occipital_gyrus |
| 6 | 3.746 | 18 | -94.5 | 6 | right_Calcarine_fissure |

| | | | | | |
|---|-------|-------|-------|-------|--------------------------------|
| 1 | 3.732 | 25.5 | -16.5 | 0 | unknown |
| 2 | 3.731 | -25.5 | -79.5 | -10.5 | left_Fusyform_gyrus |
| 1 | 3.691 | -10.5 | -46.5 | 0 | left_Precuneus |
| 1 | 3.676 | 31.5 | 19.5 | -9 | right_Insula |
| 1 | 3.663 | -25.5 | -52.5 | -15 | left_Fusyform_gyrus |
| 1 | 3.625 | 36 | 16.5 | -7.5 | right_Insula |
| 1 | 3.622 | -10.5 | -15 | -1.5 | left_Ventral_lateral |
| 1 | 3.617 | 18 | -79.5 | -12 | right_Lingual_gyrus |
| 1 | 3.616 | 3 | 0 | -4.5 | unknown |
| 4 | 3.577 | 33 | -91.5 | -4.5 | right_Inferior_Occipital_gyrus |
| 1 | 3.548 | -7.5 | -33 | -31.5 | unknown |
| 1 | 3.543 | 28.5 | -76.5 | -10.5 | right_Fusyform_gyrus |
| 1 | 3.534 | -34.5 | 0 | -6 | left_Insula |
| 1 | 3.523 | -51 | -25.5 | -12 | left_Middle_Temporal_gyrus |
| 1 | 3.514 | -1.5 | -31.5 | -18 | unknown |
| 1 | 3.512 | 18 | -28.5 | 3 | right_medial_Pulvinar |
| 1 | 3.490 | -30 | -30 | -19.5 | left_Parahippocampal_gyrus |
| 1 | 3.487 | 1.5 | -1.5 | -6 | unknown |
| 1 | 3.473 | -33 | -91.5 | -10.5 | left_Inferior_Occipital_gyrus |
| 2 | 3.467 | -37.5 | -82.5 | -15 | left_Inferior_Occipital_gyrus |
| 1 | 3.460 | -18 | -57 | -15 | left_Cerebellum_IV |
| 1 | 3.457 | 51 | -30 | 1.5 | right_Superior_temporal_gyrus |

3. Appendix B3: Strength-signal recognition whole-brain analysis

Visualisation of activations

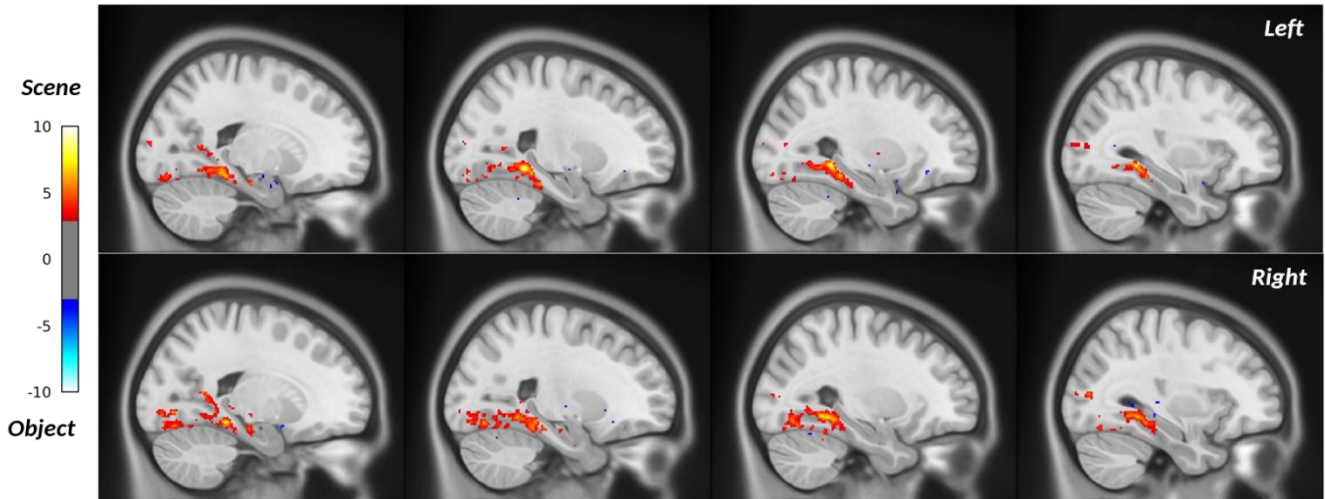


Figure B3.1. Activations resulting from the [Scene > Object] contrast in strength-signal recognition trials (i.e., correct “familiar” responses in the whole-item paradigm), projected on the icbm template displayed in sagittal slices in the left and right hemispheres (MNI x coordinates from left to right: -20, -24, -28, -32 and opposite). A threshold $T = 3$ was applied.

Activated regions

Table B3. Activated regions for the Scene > Object contrast in strength-signal recognition trials (i.e., correct “familiar” responses in the whole-item paradigm) ($p < .001$ uncorrected). For each peak, the number of voxels (k), the T value, the coordinates (x, z, y, in mm), and AAL3 label (Tzourio-Mazoyer et al., 2002) are given. In case of unidentified region (i.e., unknown label > 60%), the label “unknown” is given.

| K | T | x | y | z | AAL |
|------|-------|-------|-------|-------|------------------------------|
| 1010 | 10.02 | -25.5 | -43.5 | -7.5 | left_Parahippocmapal_gyrus |
| | 7.94 | -9 | -51 | 4.5 | left_Precuneus |
| | 7.34 | -25.5 | -37.5 | -13.5 | left_Parahippocmapal_gyrus |
| 709 | 8.55 | 28.5 | -51 | -7.5 | right_Lingual_gyrus |
| | 7.92 | 15 | -37.5 | -12 | right_Lingual_gyrus |
| | 7.18 | 30 | -40.5 | -9 | right_Parahippocmapal_gyrus |
| 312 | 7.46 | 10.5 | -48 | 3 | right_Precuneus |
| | 6.90 | 12 | -52.5 | 10.5 | right_Precuneus |
| | 4.75 | 19.5 | -51 | 4.5 | right_Calcarine_fissure |
| 20 | 6.64 | 19.5 | -78 | -4.5 | right_Lingual_gyrus |
| 35 | 6.59 | 21 | -19.5 | -18 | right_Parahippocmapal_gyrus |
| 34 | 6.38 | 33 | -79.5 | 10.5 | right_Middle_Occipital_gyrus |
| 452 | 6.24 | 25.5 | -73.5 | -12 | right_Lingual_gyrus |
| | 6.07 | 13.5 | -82.5 | -12 | right_Lingual_gyrus |
| | 5.49 | 22.5 | -85.5 | -6 | right_Fusyform_gyrus |

| | | | | | |
|-----|------|-------|-------|-------|--------------------------------|
| 158 | 5.47 | -13.5 | -84 | -15 | left_Lingual_gyrus |
| | 4.95 | -21 | -87 | -16.5 | left_Lingual_gyrus |
| 15 | 5.33 | -19.5 | -18 | -19.5 | left_Hippocampus |
| 29 | 5.17 | -34.5 | -90 | 10.5 | left_Middle_Occipital_gyrus |
| 5 | 4.60 | 19.5 | -45 | -4.5 | right_Lingual_gyrus |
| 1 | 4.57 | -15 | -6 | 1.5 | unknown |
| 4 | 4.54 | -24 | -67.5 | -7.5 | left_Fusyform_gyrus |
| 16 | 4.50 | 27 | -57 | -16.5 | right_Cerebellum_IV |
| 6 | 4.48 | 15 | -78 | 6 | right_Calcarine_fissure |
| 9 | 4.44 | -25.5 | -78 | 10.5 | unknown |
| 9 | 4.36 | 27 | -48 | -19.5 | right_Cerebellum_IV |
| 5 | 4.33 | -19.5 | -94.5 | 10.5 | left_Middle_Occipital_gyrus |
| 1 | 4.28 | 19.5 | -18 | -6 | unknown |
| 5 | 4.21 | 28.5 | -78 | -18 | right_Cerebellum_IV |
| 2 | 4.21 | -7.5 | -82.5 | 0 | left_Calcarine_fissure |
| 4 | 4.19 | -13.5 | -94.5 | -1.5 | left_Calcarine_fissure |
| 2 | 4.14 | 25.5 | -49.5 | -16.5 | right_Calcarine_fissure |
| 26 | 4.13 | -12 | -78 | -7.5 | left_Lingual_gyrus |
| 15 | 4.13 | -22.5 | -75 | -13.5 | left_Fusyform_gyrus |
| 2 | 4.13 | 43.5 | -27 | 3 | unknown |
| 15 | 4.11 | 39 | -79.5 | 12 | right_Middle_Occipital_gyrus |
| 4 | 4.08 | 46.5 | -6 | -10.5 | right_Superior_temporal_gyrus |
| 7 | 4.08 | 13.5 | -73.5 | -6 | right_Lingual_gyrus |
| 2 | 4.07 | 7.5 | 19.5 | -12 | right_Olfactory_cortex |
| 3 | 4.04 | 34.5 | -73.5 | 10.5 | unknown |
| 10 | 4.01 | -27 | -88.5 | -13.5 | left_Lingual_gyrus |
| 2 | 3.96 | -24 | -70.5 | -10.5 | left_Fusyform_gyrus |
| 1 | 3.93 | 48 | 16.5 | -15 | right_Temporal_pole |
| 1 | 3.87 | -16.5 | -97.5 | 10.5 | left_Middle_Occipital_gyrus |
| 1 | 3.86 | 30 | -88.5 | 9 | right_Middle_Occipital_gyrus |
| 2 | 3.85 | 25.5 | -93 | -4.5 | right_Inferior_Occipital_gyrus |
| 3 | 3.83 | 6 | -78 | -6 | right_Lingual_gyrus |
| 1 | 3.81 | 3 | 19.5 | -4.5 | right_Olfactory_cortex |
| 2 | 3.80 | 42 | 7.5 | -13.5 | right_Insula |
| 2 | 3.79 | -1.5 | -31.5 | -3 | unknown |
| 3 | 3.78 | 42 | 12 | -13.5 | right_Insula |
| 1 | 3.76 | 6 | -39 | 6 | unknown |
| 8 | 3.72 | 10.5 | -78 | -9 | right_Lingual_gyrus |
| 1 | 3.71 | 43.5 | -37.5 | -10.5 | unknown |
| 3 | 3.70 | -6 | -34.5 | -6 | unknown |
| 2 | 3.69 | 19.5 | -33 | -1.5 | unknown |
| 1 | 3.68 | 18 | -15 | -19.5 | right_Hippocampus |
| 1 | 3.65 | -22.5 | -90 | 12 | left_Middle_Occipital_gyrus |
| 2 | 3.64 | 10.5 | -85.5 | -3 | right_Calcarine_fissure |
| 1 | 3.62 | 24 | -45 | 4.5 | right_Precuneus |
| 2 | 3.61 | 16.5 | -91.5 | -1.5 | right_Calcarine_fissure |

| | | | | | |
|---|------|-------|-------|-------|-----------------------------|
| 2 | 3.60 | -27 | -70.5 | -18 | left_Fusyform_gyrus |
| 2 | 3.59 | -30 | -88.5 | 7.5 | left_Middle_Occipital_gyrus |
| 1 | 3.58 | 33 | -43.5 | -19.5 | right_Fusyform_gyrus |
| 1 | 3.57 | -10.5 | -87 | 0 | left_Calcarine_fissure |
| 1 | 3.55 | -28.5 | -79.5 | -16.5 | left_Fusyform_gyrus |
| 1 | 3.54 | 9 | -72 | -4.5 | right_Lingual_gyrus |
| 1 | 3.52 | -3 | -19.5 | -7.5 | unknown |
| 3 | 3.52 | -30 | -93 | 10.5 | left_Middle_Occipital_gyrus |
| 2 | 3.51 | 12 | -85.5 | 1.5 | right_Calcarine_fissure |
| 1 | 3.51 | 34.5 | -55.5 | -4.5 | unknown |
| 1 | 3.50 | 18 | -16.5 | -22.5 | right_Parahippocmapal_gyrus |
| 1 | 3.50 | -31.5 | -81 | 9 | left_Middle_Occipital_gyrus |
| 1 | 3.50 | -1.5 | -4.5 | 3 | unknown |
| 1 | 3.46 | -13.5 | 18 | -12 | unknown |
| 1 | 3.46 | -9 | -12 | -7.5 | unknown |
| 1 | 3.45 | 34.5 | 10.5 | -13.5 | right_Insula |

4. Appendix B4: Strength-signal rejection whole-brain analysis

Visualisation of activations

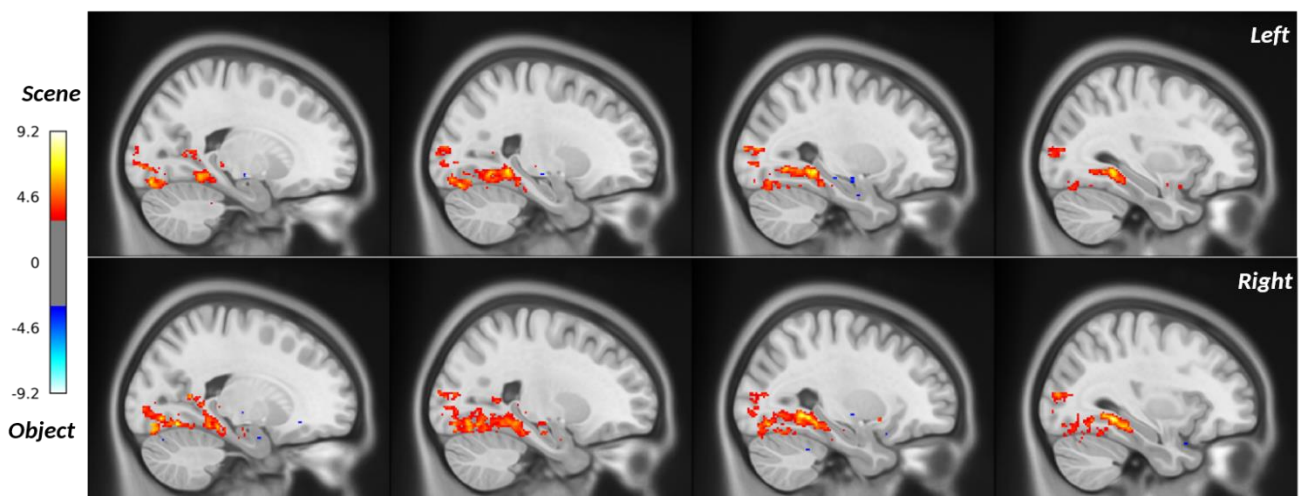


Figure B4.1. Activations resulting from the [Scene > Object] contrast in strength-signal rejection trials (i.e., correct “New” responses in the whole-item paradigm), projected on the icbm template displayed in sagittal slices in the left and right hemispheres (MNI x coordinates from left to right: -20, -24, -28, -32 and opposite). A threshold $T = 3$ was applied.

Activated regions

Table B4. Activated regions for the Scene > Object contrast in strength-signal rejection trials (i.e., correct “New” responses in the whole-item paradigm) ($p < .001$ uncorrected). For each peak, the number of voxels (k), the T value, the coordinates (x, z, y , in mm), and AAL3 label (Tzourio-Mazoyer et al., 2002) are given. In case of unidentified region (i.e., unknown label > 60%), the label “unknown” is given.

| K | T | x | y | z | AAL |
|------|------|-------|-------|-------|---------------------------------|
| 2467 | 9.20 | 31.5 | -43.5 | -7.5 | right_Parahippocampal_gyrus |
| | 8.07 | 15 | -82.5 | -9 | right_Lingual_gyrus |
| | 7.82 | 21 | -64.5 | -12 | right_Fusyform_gyrus |
| 840 | 7.39 | -28.5 | -40.5 | -7.5 | left_Parahippocampal_gyrus |
| | 6.45 | -27 | -52.5 | -7.5 | left_Fusyform_gyrus |
| | 6.37 | -28.5 | -61.5 | -4.5 | left_Lingual_gyrus |
| 498 | 7.22 | -21 | -85.5 | -13.5 | left_Fusyform_gyrus |
| | 5.96 | -13.5 | -88.5 | -13.5 | left_Lingual_gyrus |
| | 5.59 | -24 | -75 | -13.5 | left_Fusyform_gyrus |
| 172 | 6.85 | -15 | -58.5 | 9 | left_Calcarine_fissure |
| | 4.94 | -9 | -48 | 1.5 | left_Calcarine_fissure |
| | 3.82 | -22.5 | -55.5 | 7.5 | left_Calcarine_fissure |
| 304 | 6.67 | 16.5 | -55.5 | 10.5 | right_Calcarine_fissure |
| | 6.06 | 15 | -46.5 | 6 | right_Precuneus |
| | 5.19 | 22.5 | -51 | 6 | right_Calcarine_fissure |
| 449 | 6.31 | -9 | -94.5 | 0 | left_Calcarine_fissure |
| | 5.58 | -18 | -91.5 | -1.5 | left_Middle_Occipital_gyrus |
| | 4.92 | -15 | -79.5 | -6 | left_Lingual_gyrus |
| 184 | 6.16 | -30 | -84 | 10.5 | left_Middle_Occipital_gyrus |
| | 5.53 | -28.5 | -93 | 10.5 | left_Middle_Occipital_gyrus |
| | 5.22 | -34.5 | -90 | 4.5 | left_Middle_Occipital_gyrus |
| 200 | 5.62 | 34.5 | -79.5 | 12 | right_Middle_Occipital_gyrus |
| | 5.42 | 25.5 | -84 | 10.5 | right_Middle_Occipital_gyrus |
| | 4.54 | 25.5 | -94.5 | 12 | right_Superior_Occipital_gyrus |
| 15 | 5.09 | 22.5 | -16.5 | -19.5 | right_Hippocampus |
| 1 | 5.08 | 21 | -90 | -10.5 | right_Lingual_gyrus |
| 8 | 5.06 | 4.5 | -31.5 | -3 | unknown |
| 4 | 5.01 | 18 | -18 | -22.5 | right_Parahippocampal_gyrus |
| 7 | 4.72 | 12 | -60 | 1.5 | right_Lingual_gyrus |
| 5 | 4.69 | -48 | 4.5 | -28.5 | left_Middle_Occipital_gyrus |
| 11 | 4.56 | -24 | -78 | -9 | left_Fusyform_gyrus |
| 5 | 4.54 | 28.5 | 9 | -7.5 | left_lenticular_nucleus/putamen |
| 2 | 4.54 | 12 | -40.5 | -33 | unknown |
| 1 | 4.50 | -15 | -33 | -12 | left_Parahippocampal_gyrus |
| 1 | 4.47 | 25.5 | -4.5 | -25.5 | right_Hippocampus |
| 1 | 4.38 | -19.5 | -31.5 | -1.5 | left_lateral_Geniculate |
| 2 | 4.36 | -37.5 | -57 | -27 | left_Cerebellum |
| 1 | 4.33 | -1.5 | -16.5 | 4.5 | unknown |
| 1 | 4.24 | 24 | -15 | -10.5 | unknown |
| 7 | 4.15 | 4.5 | -39 | -21 | unknown |
| 3 | 4.08 | 24 | -55.5 | -4.5 | right_Lingual_gyrus |
| 2 | 4.07 | -33 | -69 | -10.5 | left_Fusyform_gyrus |
| 4 | 4.04 | -30 | -61.5 | -18 | left_Fusyform_gyrus |
| 3 | 4.02 | 21 | -10.5 | 1.5 | unknown |
| 8 | 4.00 | 6 | -21 | -4.5 | unknown |
| 2 | 3.98 | -10.5 | 1.5 | 1.5 | left_lenticular_nucleus/putamen |

| | | | | | |
|---|------|-------|-------|-------|--------------------------------|
| 1 | 3.98 | 12 | -39 | -13.5 | right_Cerebellum_III |
| 7 | 3.93 | 31.5 | -52.5 | -18 | right_Fusyform_gyrus |
| 2 | 3.88 | -24 | -70.5 | -10.5 | left_Fusyform_gyrus |
| 2 | 3.84 | 21 | -33 | 1.5 | right_medial_Pulvinar |
| 2 | 3.74 | -1.5 | -16.5 | -3 | unknown |
| 1 | 3.74 | -25.5 | -66 | 1.5 | unknown |
| 4 | 3.73 | -7.5 | -12 | -10.5 | unknown |
| 1 | 3.72 | 31.5 | -48 | -16.5 | right_Fusyform_gyrus |
| 2 | 3.71 | 22.5 | -21 | -15 | right_Hippocampus |
| 1 | 3.69 | 33 | -4.5 | -21 | unknown |
| 2 | 3.67 | -13.5 | -22.5 | 1.5 | unknown |
| 1 | 3.65 | -36 | -87 | 10.5 | left_Middle_Occipital_gyrus |
| 1 | 3.64 | -19.5 | -52.5 | 3 | left_Precuneus |
| 1 | 3.63 | -33 | 13.5 | -6 | left_Insula |
| 1 | 3.62 | 33 | -88.5 | 6 | right_Middle_Occipital_gyrus |
| 1 | 3.58 | -13.5 | -45 | -12 | left_Lingual_gyrus |
| 1 | 3.58 | 4.5 | -22.5 | -27 | unknown |
| 1 | 3.56 | 24 | -18 | -12 | right_Hippocampus |
| 2 | 3.56 | 37.5 | -45 | -9 | right_Fusyform_gyrus |
| 1 | 3.56 | 13.5 | -66 | -19.5 | right_Cerebellum_VI |
| 1 | 3.54 | 15 | -25.5 | -6 | unknown |
| 1 | 3.54 | 24 | -3 | -24 | right_Amygdala |
| 1 | 3.53 | -39 | -19.5 | -1.5 | left_Superior_Temporal_gyrus |
| 2 | 3.53 | -3 | -45 | 6 | left_posterior_Cingulate_gyrus |
| 1 | 3.53 | -7.5 | -63 | -7.5 | left_Lingual_gyrus |
| 1 | 3.52 | -18 | -46.5 | -3 | left_Precuneus |
| 1 | 3.51 | 4.5 | 24 | -13.5 | right_superior_Frontal_gyrus |
| 1 | 3.50 | -31.5 | 7.5 | -18 | left_Insula |
| 1 | 3.49 | 16.5 | -82.5 | 9 | right_Calcarine_fissure |
| 1 | 3.49 | 15 | -64.5 | -18 | right_Cerebellum_VI |
| 1 | 3.47 | 3 | -57 | 9 | right_Precuneus |
| 1 | 3.47 | 51 | 0 | -24 | right_Middle_Occipital_gyrus |
| 1 | 3.47 | 16.5 | -97.5 | 13.5 | right_Cuneus |
| 1 | 3.46 | -12 | -75 | -22.5 | left_Cerebellum_VI |
| 1 | 3.46 | 36 | -73.5 | -18 | right_Fusyform_gyrus |
| 1 | 3.45 | -13.5 | -85.5 | 4.5 | left_Superior_Occipital_gyrus |

5. Appendix B5: Exploratory conjunction analysis

Native ROI-based analyses revealed aHC specialisation for scene processing across the four operations investigated. Normalised whole-brain analyses completed these data by showing that in each case, the medial anterior region of the hippocampus specifically responded to the comparison between scene and object. To test whether a same region presented the same specialisation for scene processing across operations, we performed an additional conjunction analysis (for a similar approach, see Zeidman et al., 2015). This analysis is to a between-

subjects F-test corresponding to a logical AND between the results of the [Scene > Object] contrast in the different conditions (as opposed to global null hypothesis testing, Friston et al., 2005; Nichols et al., 2005). We included normalised data from the matching, pattern-completion, strength-signal recognition, and rejection conditions. For theoretical reasons, recollection trials were not included. This analysis revealed a limited set of regions that included the bilateral parahippocampal cortex and fusiform, and the right hippocampus. These results are summarised in table B5 and illustrated in figure B5.1. Of particular interest is the activated region in the right hippocampus. This corresponds to the medial anterior region previously documented by Zeidman and Maguire (2016) as being responsible for scene construction (figure B5.2, MNI coordinates: 21, -18, -18). The conjunction analysis computed with the reverse contrast (i.e., [Object > Scene]) revealed only one cluster, located in the left inferior temporal gyrus (peak coordinates -48, -58, -15), and is not detailed here.

Visualisation of resulting activations

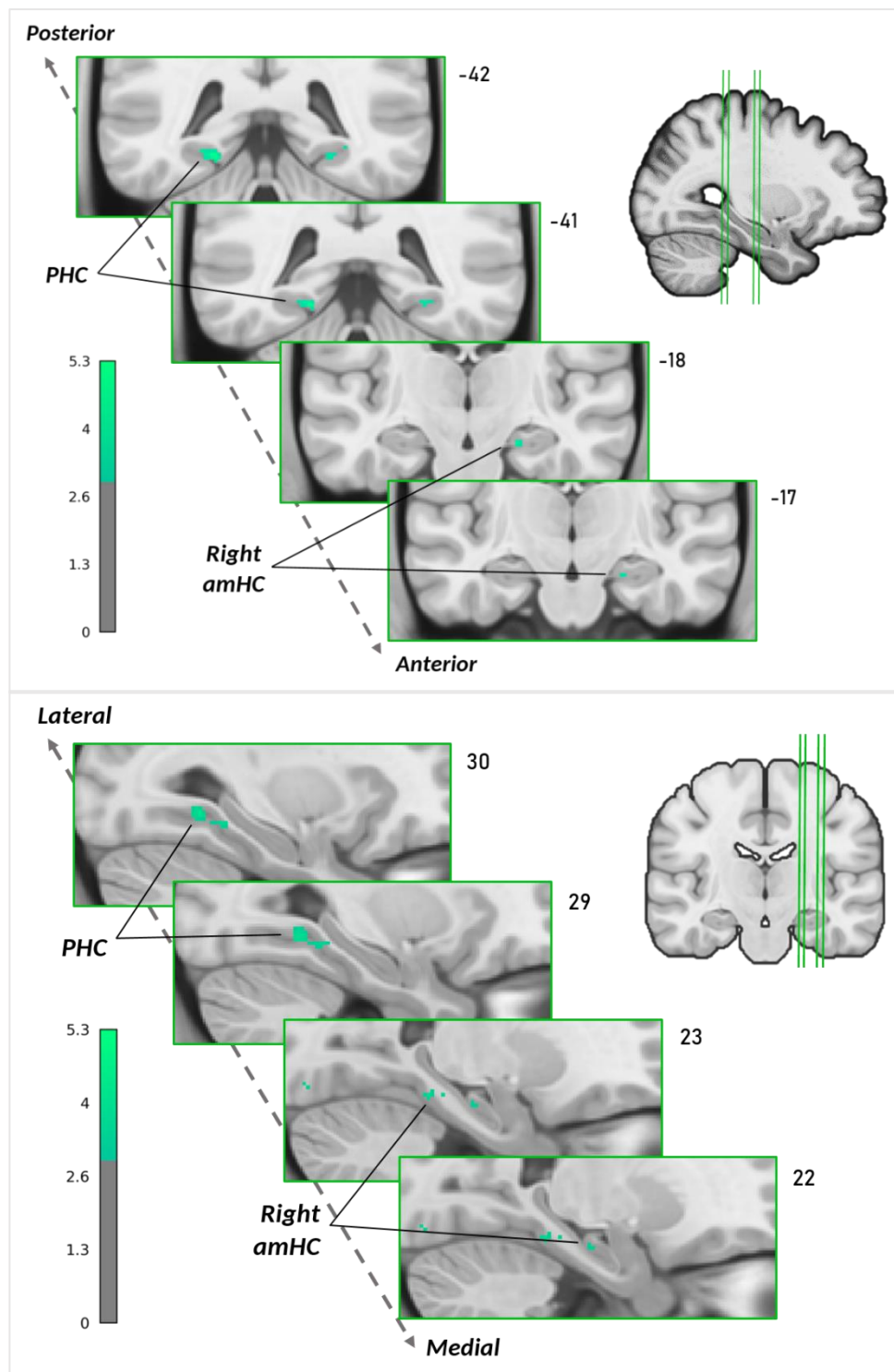


Figure B5.1. Activations resulting from the conjunction analysis testing the [Scene > Object] contrast in the four operations, projected on the icbm template. Coronal (top panel) and sagittal (lower panel) slices are selected to present the posterior parahippocampal gyrus and anterior hippocampus (see table B5). A threshold $T = 3$ was applied. PHC: Parahippocampal cortex, amHC: anterior-medial hippocampus.

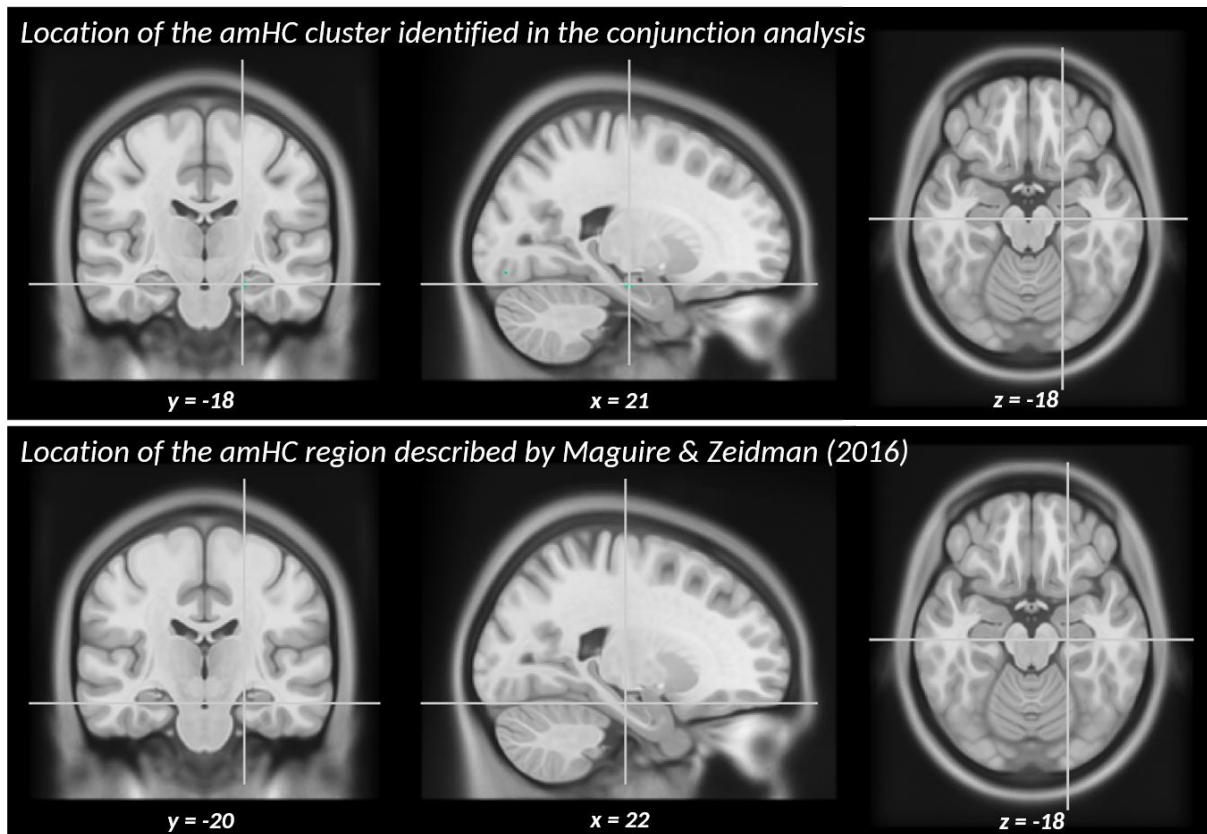


Figure B5.2. Location of the hippocampal region identified by the conjunction analysis compared with that documented by Zeidman & Maguire (2016). Coordinates of the peak activation (MNI): 21, -18, -18; coordinates reported by Zeidman & Maguire: 22, -20, -18. amHC: anterior medial hippocampus.

Activated regions

Table B5. Activated regions resulting from the conjunction analysis testing the Scene > Object contrast in the four operations ($p < .001$ uncorrected). For each peak, the number of voxels (k), the T value, the coordinates (x, z, y, in mm), and AAL3 label (Tzourio-Mazoyer et al., 2002) are given.

| K | T | x | y | z | AAL |
|----------|-------------|-----------|------------|------------|---------------------------------|
| 82 | 5.29 | -21 | -42 | -12 | left_Parahippocampal_gyrus |
| | 3.30 | -25.5 | -49.5 | -4.5 | left_Lingual_gyrus |
| 14 | 4.27 | 24 | -36 | -15 | right_Parahippocampal_gyrus |
| 81 | 4.19 | 33 | -37.5 | -12 | right_Parahippocampal_gyrus |
| | 4.04 | 30 | -48 | -6 | right_Lingual_gyrus |
| 19 | 3.99 | 13.5 | -48 | 3 | right_Precuneus |
| 2 | 3.84 | -24 | -34.5 | -21 | left_Fusiform_gyrus |
| 7 | 3.78 | 21 | -18 | -18 | right_Hippocampus |
| 7 | 3.75 | 7.5 | -46.5 | 4.5 | right_Posterior_cingulate_gyrus |
| 5 | 3.68 | -31.5 | -37.5 | -13.5 | left_Parahippocampal_gyrus |
| 7 | 3.67 | 24 | -85.5 | -12 | right_Fusiform_gyrus |
| 1 | 3.47 | 22.5 | -30 | -15 | right_Parahippocampal_gyrus |
| 3 | 3.39 | -13.5 | -94.5 | -3 | left_Calcarine_fissure |

| | | | | | |
|---|------|------|-------|------|--------------------------------|
| 1 | 3.34 | -9 | -51 | 1.5 | left_Calcarine_fissure |
| 1 | 3.26 | 34.5 | -42 | -7.5 | right_Parahippocampal_gyrus |
| 1 | 3.23 | 24 | -93 | -3 | right_Inferior_Occipital_gyrus |
| 1 | 3.21 | -9 | -57 | 7.5 | left_Calcarine_fissure |
| 1 | 3.18 | 27 | -43.5 | -4.5 | right_Parahippocampal_gyrus |

Appendices C: Neuropsychological tests used in Studies 3 and 4

1. Appendix C1: Mini mental state examination (MMSE)

| | |
|--|----------------------|
| MINI MENTAL STATE EXAMINATION (M.M.S.E) | Etiquette du patient |
| Date : | |
| Évalué(e) par : | |
| Niveau socio-culturel | |

ORIENTATION

Je vais vous poser quelques questions pour apprécier comment fonctionne votre mémoire. Les unes sont très simples, les autres un peu moins. Vous devez répondre du mieux que vous pouvez.

Quelle est la date complète d'aujourd'hui ?

⇒ Si la réponse est incorrecte ou incomplète, posez les questions restées sans réponse, dans l'ordre suivant :

- | | | | | | |
|----------------------------------|--------|--|--|------------------------------|--------|
| 1. en quelle année sommes-nous ? | !0ou1! | | | 4. Quel jour du mois ? | !0ou1! |
| 2. en quelle saison ? | ! ! ! | | | 5. Quel jour de la semaine ? | ! ! ! |
| 3. en quel mois ? | ! ! ! | | | | |
- ⇒ Je vais vous poser maintenant quelques questions sur l'endroit où nous nous trouvons.
- | | |
|--|-------|
| 6. Quel est le nom de l'Hôpital où nous sommes ? | ! ! ! |
| 7. Dans quelle ville se trouve-t-il ? | ! ! ! |
| 8. Quel est le nom du département dans lequel est située cette ville ? | ! ! ! |
| 9. Dans quelle province ou région est situé ce département ? | ! ! ! |
| 10. A quel étage sommes-nous ici ? | ! ! ! |

APPRENTISSAGE

⇒ Je vais vous dire 3 mots ; je voudrais que vous me les répétiez et que vous essayiez de les retenir car je vous les demanderai tout à l'heure.

- | | | | | | |
|------------|----|---------|----|-----------|-------|
| 11. Cigare | | [citron | | [fauteuil | ! ! ! |
| 12. fleur | ou | [clé | ou | [tulipe | ! ! ! |
| 13. porte | | [ballon | | [canard | ! ! ! |

Répéter les 3 mots.

ATTENTION ET CALCUL

- ⇒ Voulez-vous compter à partir de 100 en retirant 7 à chaque fois ?
- | | | |
|--|--------|-------|
| | 14. 93 | ! ! ! |
| | 15. 86 | ! ! ! |
| | 16. 79 | ! ! ! |
| | 17. 72 | ! ! ! |
| | 18. 65 | ! ! ! |
- ⇒ Pour tous les sujets, même pour ceux qui ont obtenu le maximum de points, demander : « voulez-vous épeler le mot MONDE à l'envers » : E D N O M.

APPEL

⇒ Pouvez-vous me dire quels étaient les 3 mots que je vous ai demandé de répéter et de retenir tout à l'heure ?

- | | | | | | |
|------------|----|---------|----|-----------|-------|
| 19. Cigare | | [citron | | [fauteuil | ! ! ! |
| 20. fleur | ou | [clé | ou | [tulipe | ! ! ! |
| 21. porte | | [ballon | | [canard | ! ! ! |

LANGAGE

- | | | | | | |
|--|--------------------|--|--|--|-------|
| 22. quel est le nom de cet objet? | Montrer un crayon. | | | | ! ! ! |
| 23. Quel est le nom de cet objet | Montrer une montre | | | | ! ! ! |
| 24. Écoutez bien et répétez après moi : « PAS DE MAIS, DE SI, NI DE ET » | | | | | ! ! ! |
- ⇒ Poser une feuille de papier sur le bureau, la montrer au sujet en lui disant : « écoutez bien et faites ce que je vais vous dire » (consignes à formuler en une seule fois) :
- | | | | | | |
|---|--|--|--|--|-------|
| 25. prenez cette feuille de papier avec la main droite. | | | | | ! ! ! |
| 26. Pliez-la en deux. | | | | | ! ! ! |
| 27. et jetez-la par terre ». | | | | | ! ! ! |
- ⇒ Tendre au sujet une feuille de papier sur laquelle est écrit en gros caractères : « FERMEZ LES YEUX » et dire au sujet :
- | | | | | | |
|---------------------------------|--|--|--|--|-------|
| 28. «faites ce qui est écrit ». | | | | | ! ! ! |
|---------------------------------|--|--|--|--|-------|
- ⇒ Tendre au sujet une feuille de papier et un stylo en disant :
- | | | | | | |
|---|--|--|--|--|-------|
| 29. voulez-vous m'écrire une phrase, ce que vous voulez, mais une phrase entière. » | | | | | ! ! ! |
|---|--|--|--|--|-------|

PRAXIES CONSTRUCTIVES.

- ⇒ Tendre au sujet une feuille de papier et lui demander :
- | | | | | | |
|---|--|--|--|--|-------|
| 30. « Voulez-vous recopier ce dessin ». | | | | | ! ! ! |
|---|--|--|--|--|-------|



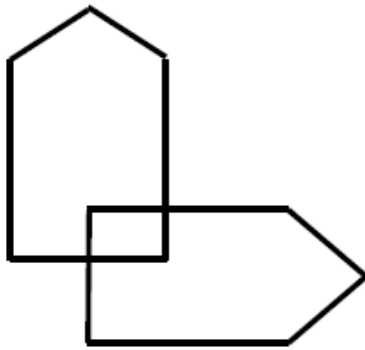
SCORE TOTAL (0 à 30) ! ! !

FERMEZ LES YEUX

Phrase :

.....
.....
.....

Recopier le dessin :

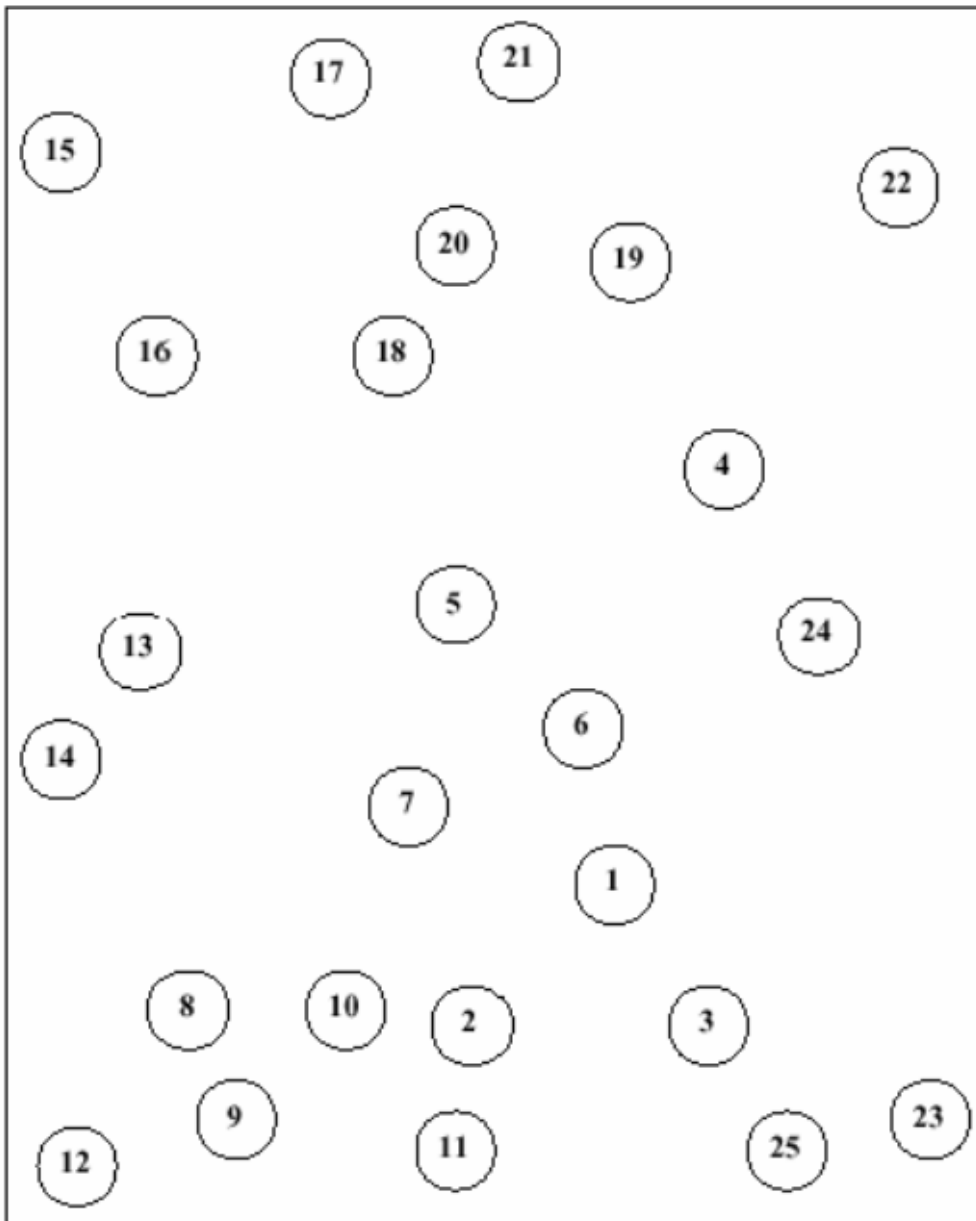


2. Appendix C2: Trail-making test (TMT)

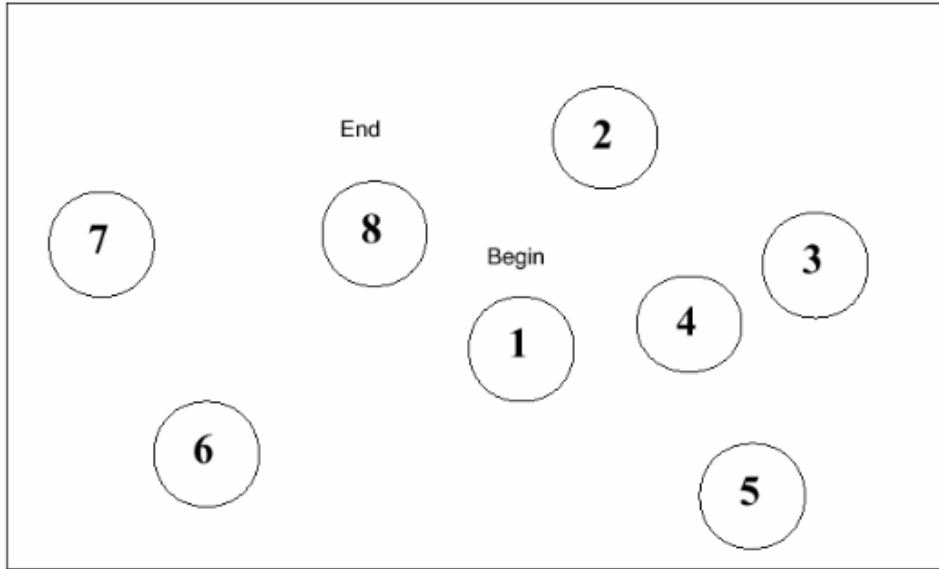
Trail Making Test Part A

Patient's Name: _____

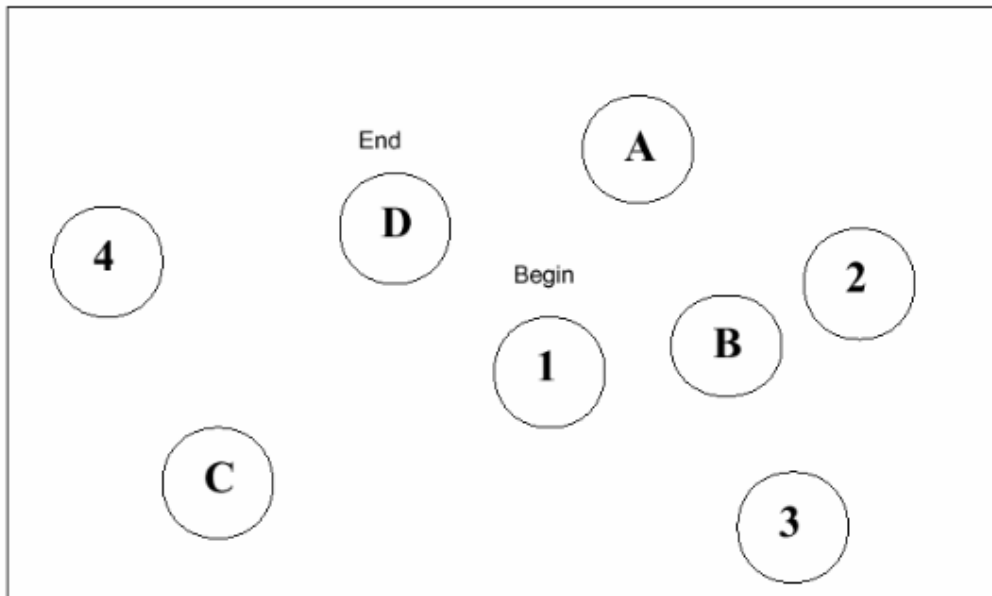
Date: _____



Trail Making Test Part A – SAMPLE



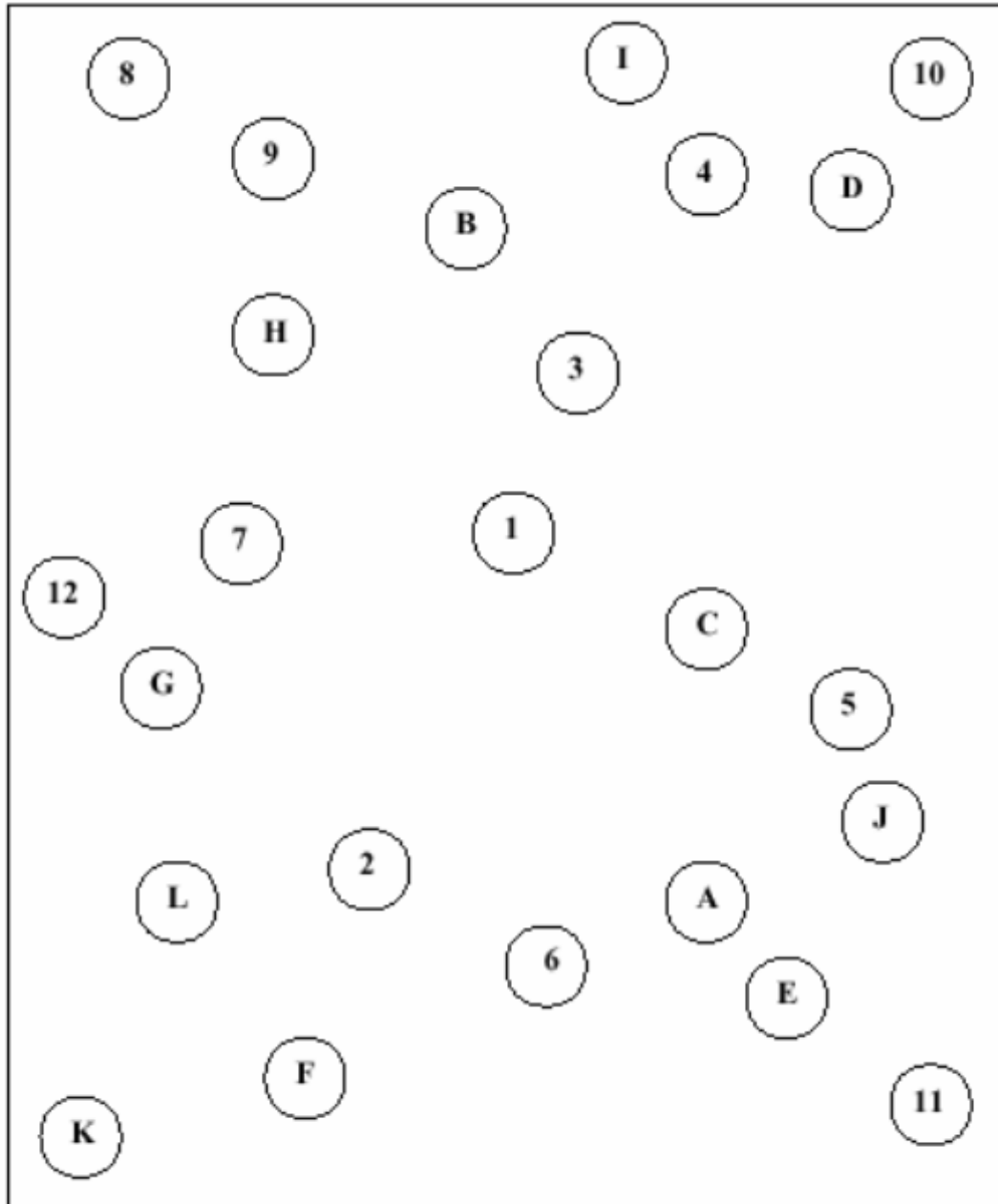
Trail Making Test Part B – SAMPLE




Trail Making Test Part B

Patient's Name: _____

Date: _____



3. Appendix C3: Example of Wechsler memory scale (MEM-IV) profile summary



MEM-IV

Echelle Clinique de Mémoire de Wechsler
4^e édition

Batterie Adultes (16 à 69 ans)
Cahier d'administration

Nom du sujet : _____

Nom du psychologue : _____

Calcul de l'âge du sujet

| | | |
|-------|------|------|
| Année | Mois | Jour |
| | | |

Date d'administration : _____

Date de naissance : _____

Age : _____

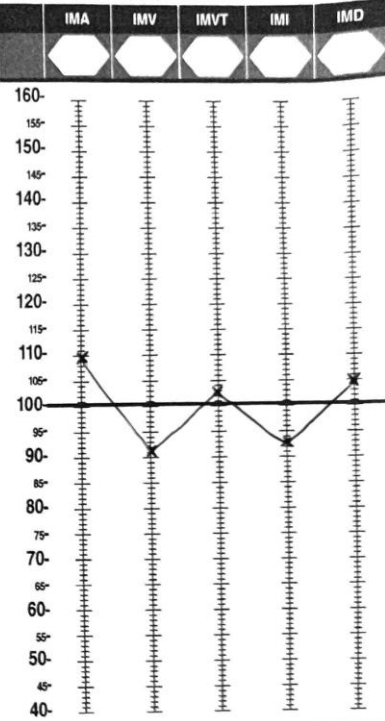
Conversion des notes brutes en notes standard

| Subtests | Notes brutes | Notes standard | | | | |
|--------------------------|--------------|----------------|----|----|----|----|
| Mémoire Logique I | 34 | 12 | | | 12 | |
| Mémoire Logique II | 29 | 13 | | | | 13 |
| Mots Couplés I | 36 | 10 | | | 10 | |
| Mots Couplés II | 13 | 12 | | | | 12 |
| Dessins I | 63 | | 8 | | 8 | |
| Dessins II | 59 | | 10 | | | 10 |
| Reproduction Visuelle I | 34 | | 8 | | 8 | |
| Reproduction Visuelle II | 29 | | 10 | | | 10 |
| Addition Spatiale | 13 | | | 9 | | |
| Mémoire de Symboles | 30 | | | 12 | | |

Conversion des sommes des notes standard en notes d'indice

| | Mémoire Auditive (IMA) | Mémoire Visuelle (IMV) | Mémoire Visuelle de Travail (IMVT) | Mémoire Immédiate (IMI) | Mémoire Différée (IMD) |
|------------------------------------|------------------------|------------------------|------------------------------------|-------------------------|------------------------|
| Somme des notes standard | 47 | 36 | 21 | 38 | 45 |
| Note d'indice | 110 | 91 | 102 | 93 | 105 |
| Rang percentile | | | | | |
| Intervalle de confiance 90% ou 95% | | | | | |

Profil des notes d'indice



Profil des notes standard

| | Mémoire Auditive | | | | Mémoire Visuelle | | | | Mémoire Visuelle de Travail | | |
|----|------------------|-------|------|-------|------------------|-------|------|-------|-----------------------------|----|----|
| | ML I | ML II | MC I | MC II | DE I | DE II | RV I | RV II | AS | MS | |
| 19 | • | • | • | • | • | • | • | • | • | • | 19 |
| 18 | • | • | • | • | • | • | • | • | • | • | 18 |
| 17 | • | • | • | • | • | • | • | • | • | • | 17 |
| 16 | • | • | • | • | • | • | • | • | • | • | 16 |
| 15 | • | • | • | • | • | • | • | • | • | • | 15 |
| 14 | • | • | • | • | • | • | • | • | • | • | 14 |
| 13 | • | • | • | • | • | • | • | • | • | • | 13 |
| 12 | • | • | • | • | • | • | • | • | • | • | 12 |
| 11 | • | • | • | • | • | • | • | • | • | • | 11 |
| 10 | • | • | • | • | • | • | • | • | • | • | 10 |
| 9 | • | • | • | • | • | • | • | • | • | • | 9 |
| 8 | • | • | • | • | • | • | • | • | • | • | 8 |
| 7 | • | • | • | • | • | • | • | • | • | • | 7 |
| 6 | • | • | • | • | • | • | • | • | • | • | 6 |
| 5 | • | • | • | • | • | • | • | • | • | • | 5 |
| 4 | • | • | • | • | • | • | • | • | • | • | 4 |
| 3 | • | • | • | • | • | • | • | • | • | • | 3 |
| 2 | • | • | • | • | • | • | • | • | • | • | 2 |
| 1 | • | • | • | • | • | • | • | • | • | • | 1 |

| Subtests | Abréviation |
|---------------------------------|-------------|
| Mémoire Logique I | ML I |
| Mémoire Logique II | ML II |
| Mots Couplés I | MC I |
| Mots Couplés II | MC II |
| Dessins I | DE I |
| Dessins II | DE II |
| Reproduction Visuelle I | RV I |
| Reproduction Visuelle II | RV II |
| Addition Spatiale | AS |
| Mémoire de Symboles | MS |
| Examen cognitif rapide du sujet | ECRS |

4. Appendix C4: Example of neuropsychological examination

Subject ■ - LEFT

Epreuves utilisées pour l'évaluation post-chirurgicale

Niveau scolaire BAC – crises généralisées dans l'enfance puis crises partielles à partir de 20ans

Épilepsie temporale gauche opérée en avril 2020 : lobectomie temporale gauche incluant néocortex temporal basal jusqu'à E, noyau amygdalien, hippocampe antérieur et postérieur et gyrus parahippocampique

Niveau

| | | |
|-------------------|-------|------------------|
| Wais-IV | | |
| Information : | 8/19 | |
| Vocabulaire : | 11/19 | |
| Similitude : | 13/19 | |
| | | ICV : 100 (50ct) |
| Puzzles visuels : | 10/19 | |
| Cubes : | 11/19 | |
| Matrices : | 10/19 | IRP : 104 (61ct) |

Différence ICV/IRP : 4 (seuil critique à 8.50)

Mémoire

MEM IV – Mémoire verbale

Mémoire logique I : 10/19
 Mémoire logique II : 9/19
 Reconnaissance histoires : 23/30 (26-50ct)
 Paires de mots I : 7/19
 Paires de mots II : 8/19 (maximum)
 Reconnaissance : 38/40 (26-50ct)

Indice de mémoire auditive (IMA) : 88 (21ct)

MEM IV – Mémoire visuelle

Reproduction visuelle I : 9/19
 Reproduction visuelle II : 7/19
 Reconnaissance visuelle : 7/7 (>75ct)

Rappel de dessins I : 4/19 (8 & 4)

Rappel de dessins II : 7/19 (8 & 9)
 Reconnaissance : 16/24 (51-75ct)

Indice de mémoire visuelle (IMV) : 79 (8ct)

Différence IMA/IMV : 9 (seuil critique à 10.17)

Indice de mémoire immédiate (IMI) : 76 (5ct)

Indice de mémoire différée (IMD) : 79 (7ct)

MCT/MDT

Empan de chiffres : 5 Empan envers : 5
 Empan croissant : 5
 Mémoire des chiffres : 8/19

Additions spatiales : 12/19
 Mémoire de symboles : 12/19
 Indice de mémoire visuelle de travail : 111 (77ct)

Différence IMV-IMVT : 32* (seuil critique à 10.17) ; 0,4%

Fonctions exécutives et langage

TMT A : 60,95 (10-25ct)
 TMT B : 73,12 (<5ct) ; 1 erreur (5ct)
 B-A : 22,17 (75ct)

Stroop (Grafix) :
 Dénomination : 62,57 (25ct)
 Lecture : 53,41 (<5ct)
 Interférence : 100,36 (25-50ct)
 I-D : 37,79 (50-75ct)

Code : 9/19

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