Prior-knowledge Effects on Associative Memory Processing

by

Zhong Xu Liu

A thesis submitted in conformity with the requirements for the degree of Doctor of Philosophy
Graduate Department of Applied Psychology and Human Development
Ontario Institute for Study in Education
University of Toronto

© Copyright by Zhong Xu Liu 2015
Abstract

Forming new associations is a fundamental process in building our knowledge system and creating episodic memories. How prior-knowledge influences acquisition of novel associations has not been thoroughly investigated. Based on recent cognitive neuroscience literature on multiple-component memory processing, I hypothesize that prior-knowledge can trigger additional evaluative, semantic, or episodic processes, supported by the ventral medial prefrontal cortex (vmPFC), anterior temporal pole regions (aTPL), and hippocampus (HPC), respectively, to facilitate new associative learning. To test this hypothesis, I first developed a face-house associative memory task in Experiment 1, in which famous faces were used to elicit multiple-component prior-knowledge, such as social emotional, semantic, and episodic memories. Using this task, I found that recollection-based, not familiarity-based, associative memory was indeed facilitated by this type of prior-knowledge. Then, I used this task in two fMRI studies to examine how prior-knowledge could affect brain activity during associative encoding (Experiment 2) and post-encoding rests (Experiment 3). Consistent with my hypotheses, in Experiment 2, I found that the vmPFC and HPC, as well as the parahippocampal place area (PPA) and fusiform face area (FFA), showed stronger activation when famous, compared to nonfamous, faces were involved. Importantly, the vmPFC, aTPL, and HPC also exhibited stronger activation when famous faces elicited stronger prior emotions and memories. Experiment 3 showed that HPC
connectivity with FFA and vmPFC during rest was stronger following encoding of associations with famous than non-famous faces. Post-encoding connectivity between the HPC and FFA, and between the aTPL and PPA/FFA, also predicted later associative, but not item, memory, only in the famous condition. These results indicate that when prior-knowledge is involved, the HPC, vmPFC, and aTPL, which support prior episodic, social-evaluative, and semantic memories, respectively, continue to interact with each other and the posterior perceptual brain regions (e.g., the PPA and FFA) during the post-encoding rest to facilitate off-line processing of the newly formed memory and enhance it. Taken together, these findings support my hypotheses that prior-knowledge reconfigures memory processing among different brain systems, by triggering additional evaluative, semantic, or episodic processes, to facilitate new associative memory formation during both encoding phase and post-encoding rests.
Acknowledgments

First, I would like to thank my supervisor, Dr. Morris Moscovitch, for his generous help and support during the past several years. I feel so lucky to have the opportunity to work with him. For me, as well as all other trainees in his lab, Morris is not only a role model of a great scientist, but also a best friend and a genuinely kind person.

I would also like to thank my supervision committee members, Dr. Cheryl Grady and Dr. Kang Lee, for their guidance on my dissertation research. Their expertise in neuroimaging experimental design and data analyses, as well as their insights during this research project, were extremely important for the completion of my dissertation.

Also, I would like to take the opportunity to thank my defense committee member Dr. Lila Davachi from the New York University, and Dr. Bradley Buchsbaum and Dr. Andy Lee from the University of Toronto for their insightful questions and suggestions during my defense, which pushed me to think more deeply and broadly about my research question and will be very helpful for my next step of research.

I am also particularly grateful to Marilyne Ziegler, the program manager and research officer of Morris' lab, and Nick Hoang, the lab manager of Morris' lab, for their generous help and support in all aspects of my research, and for their friendship, kindness, and encouragement.

I would also like to thank Dr. Rosemary Tannock from my home department at Ontario Institute for Study in Education (OISE) for her guidance and support during my second research project on working memory training effects in adults with Attention Deficit Hyperactivity Disorder (ADHD).

Dr. Marc Lewis, my Master's thesis supervisor who left Canada after the first year of my Ph.D., continues to be encouraging and supportive to me, which I really appreciate.

My friend and colleague Dr. Steven Woltering also deserves a special thank you for all his generosity and positivity towards me (and himself) during the past several years. He agreed that I can use his face picture for task illustration in this thesis (e.g., see Page 21), although he thought that his picture would look much better in the famous, rather than, the nonfamous condition.
There is no doubt that my lab mates are the ones with whom I interacted the most during the past several years. I benefit tremendously from working or interacting with them. Therefore, I would like to sincerely thank all the graduate students and post-doc fellows in Morris' lab during my study, including Jordan Poppenk, Marnie Hirshhorn, Signy Sheldon, Marie St-Laurent, Raluca Petrican, Kristoffer Romero, Cornelia McCormick (from Dr. Mary Pat McAndrews' lab), Jessica Robin, Buddhika Bellana, Kyra Mc Kelvey, Iva Kristl Brunec, Caspian Sawczak, Yoav Kessler, Yunjo Lee, Susan Vandermorris, Jason Ozubko, Melanie Sekeres, and Talya Sadeh. I would also like to thank my colleagues and friends in Dr. Rosemary Tannock's lab and Dr. Marc Lewis' lab at OISE, including Kathryn Hum, Monica Janus, Victoria Lishak, Soyeon Kim, Alan Rokeach, Daniel Glizer, and Karizma Mawjee.

During my study, I received financial support from a Natural Sciences and Engineering Research Council of Canada (NSERC) Post-Doctoral Scholarship, the Quebec government (Ministère de l'éducation), OISE, and my supervisor Dr. Morris Moscovitch's NSREC Grant A8347. This grant also supported the dissertation research project. I am extremely grateful for all the support and hope my contributions prove worthy of it.

Last but not least, I would like to thank my family members, including my father Huai Laiang Liu, my mother Guimei Bie, my wife Yanning Li, and our daughters Mona, Rena, and Selina, for their love, encouragement, and support. Particularly, I need to thank my wife Yanning for her being so supportive and encouraging. Without her support, I definitely would not have been able to complete my Ph.D. study. Therefore, this thesis also belongs to her.
# Table of Contents

Table of Contents ........................................................................................................................... vi  
List of Tables ................................................................................................................................. ix  
List of Figures ................................................................................................................................. x  
Chapter 1 General Introduction ...................................................................................................... 1  
  1.1 Prior-knowledge effects on associative memory processing at the behavioral level........ 3  
  1.2 Prior-knowledge effects on new memory encoding at the brain level......................... 6  
  1.3 Prior-knowledge effects on post-encoding brain activity........................................... 11  
  1.4 Overview of the current study............................................................................... 14  
Chapter 2 Study 1: Prior-knowledge Enhances Recollection of Associative Memory .......... 17  
  2.1 Introduction..................................................................................................................... 17  
  2.2 Method .......................................................................................................................... 19  
    2.2.1 Participants............................................................................................................. 19  
    2.2.2 Stimulus materials............................................................................................... 19  
    2.2.3 Procedure ............................................................................................................ 20  
  2.3 Results ......................................................................................................................... 23  
    2.3.1 Easy/difficult ratings for encoding trials.............................................................. 23  
    2.3.2 Single face and house recognition .................................................................... 24  
    2.3.3 Associative identification............................................................................... 26  
    2.3.4 Associative reinstatement ............................................................................. 28  
    2.3.5 Correlations among different memory measures.......................................... 31  
  2.4 Discussion ...................................................................................................................... 33  
    2.4.1 Prior-knowledge effects on face/house item memory ........................................ 33  
    2.4.2 Prior-knowledge effects on associative identification ...................................... 34  
    2.4.3 Prior-knowledge effects on associative reinstatement ..................................... 36  
    2.4.4 Relationship between different memory measures ....................................... 37  
    2.4.5 Conclusion ......................................................................................................... 38  
  2.5 Appendix Tables ........................................................................................................... 40  
Chapter 3 Study 2: Prior-knowledge Effects on Associative Encoding ............................. 45  
  3.1 Introduction..................................................................................................................... 45  
  3.2 Method .......................................................................................................................... 47
3.2.1 Participants ............................................................................................................ 47
3.2.2 Procedure .............................................................................................................. 47
3.2.3 Structural and functional MRI scan ...................................................................... 53
3.2.4 fMRI data preprocessing ....................................................................................... 53
3.2.5 fMRI analysis ........................................................................................................ 54

3.3 Results ............................................................................................................................... 62
3.3.1 Behavioral results .................................................................................................. 62
3.3.2 fMRI results .......................................................................................................... 62

3.4 Discussion ......................................................................................................................... 74
3.4.1 The role of the hippocampus in prior-knowledge effects during associative encoding ................................................................................................................ 74
3.4.2 The role of the vmPFC in prior-knowledge effects during associative encoding. 77
3.4.3 The role of the aTPL in prior-knowledge effects during associative encoding .... 78
3.4.4 The role of posterior neocortical regions in prior-knowledge effects during associative encoding ............................................................................................. 79
3.4.5 Interactions between the hippocampus and neocortical structures in producing prior-knowledge effects on associative encoding ................................................. 79
3.4.6 Conclusions ........................................................................................................... 80

3.5 Supplementary Tables ....................................................................................................... 82

3.6 Supplementary Figures ..................................................................................................... 90

Chapter 4 Study 3: Prior-knowledge Effect on Post-encoding Brain Connectivity and Its Relation to Subsequent Memory .............................................................................................. 95

4.1 Introduction ....................................................................................................................... 95
4.2 Method .............................................................................................................................. 97
4.2.1 Participants ............................................................................................................ 97
4.2.2 Procedure .............................................................................................................. 97
4.2.3 Structural and functional MRI scan .................................................................... 102
4.2.4 Data analysis ....................................................................................................... 102

4.3 Results ............................................................................................................................. 106
4.3.1 Behavioral results ............................................................................................... 106
4.3.2 Prior-knowledge effects on post-encoding brain connectivity ........................... 106
4.3.3 Post-encoding brain connectivity that were not significantly modified by encoding tasks predicting associative memory ................................................................. 110
4.3.4 Prior-knowledge effects on post-encoding brain connectivity: Using whole-brain anatomical ROIs ................................................................. 112
4.4 Discussion ....................................................................................................................... 113
4.5 Supplementary figures .................................................................................................... 119

Chapter 5 General discussion ...................................................................................................... 121
  5.1 Summary of the findings from all 3 experiments ........................................................... 121
  5.2 Schemas .......................................................................................................................... 123
  5.3 Resting state brain activity .............................................................................................. 128
  5.4 Memory consolidation .................................................................................................... 131
  5.5 Limitations and future directions .................................................................................... 132
  5.6 Conclusions ..................................................................................................................... 134

References ................................................................................................................................... 136
List of Tables

Appendix Table 1. Single face recognition accuracy: Mean, standard deviation (SD), and statistics for condition (famous vs. nonfamous) difference (Chapter 2) .......................................................... 40

Appendix Table 2. Single house recognition accuracy: Mean, standard deviation (SD), and statistics for condition (famous vs. nonfamous) difference (Chapter 2) .................................................. 41

Appendix Table 3. Mean proportion, standard deviation (SD), and condition comparison (famous vs. nonfamous) statistics of "Intact" responses per pair type (at the third step of the retrieval task) and associative identification measures (Chapter 2) ......................................................... 42

Appendix Table 4. Mean proportion, standard deviation (SD), and condition comparison (famous vs. nonfamous) statistics of "Recombined" responses per pair type (at the third step of the retrieval task) and associative identification measures (Chapter 2) ......................................................... 43

Appendix Table 5. Mean proportion, standard deviation (SD), and condition comparison (famous vs. nonfamous) statistics of "both old" responses per pair type (at the second step of the retrieval task) and associative reinstatement measures (Chapter 2) ......................................................... 44

Table 1. ROI prior-knowledge modulation effects on encoding brain activity in the famous condition (Chapter 3) ............................................................................................................................ 68

Supplementary Table 1. Brain regions that showed positive (famous > nonfamous) and negative (nonfamous > famous) fame effects during encoding (Chapter 3) ................................. 82

Supplementary Table 2. ROI prior-knowledge modulation effects on encoding brain activity in the famous condition for the first and second encoding run separately (Chapter 3) ............... 84

Supplementary Table 3. Brain regions that showed both positive prior-knowledge modulation effects and positive fame effects (Chapter 3) ................................................................. 85

Supplementary Table 4. Brain regions that showed subsequent memory effects (Chapter 3) ... 86

Supplementary Table 5. Brain regions with which the hippocampus formed stronger connectivity in the famous vs. nonfamous condition (Chapter 3) ............................................................. 88
List of Figures

**Figure 1.** Encoding and retrieval trials (Chapter 2) ................................................................. 21

**Figure 2.** Face and house item recognition memory performance (Chapter 2) ..................... 25

**Figure 3.** Associative identification accuracy (Chapter 2) ......................................................... 27

**Figure 4.** Associative reinstatement accuracy (Chapter 2) ......................................................... 29

**Figure 5.** Correlations among different types of memory measures (Chapter 2) .................... 32

**Figure 1.** Schematic of experimental design (Chapter 3) ............................................................ 48

**Figure 2.** The surface and section views of the 5 regions of interest (ROIs) (Chapter 3) ......... 60

**Figure 3.** Prior-knowledge (i.e., fame) effects on memory performance. (Chapter 3) ............ 63

**Figure 4.** Associative encoding effects (face-house > scrambled) in each predefined ROI (Chapter 3) ............................................................................................................................................. 64

**Figure 5.** Fame effects (famous > nonfamous) in each predefined bilateral ROI (Chapter 3) .... 66

**Figure 6.** Prior-knowledge modulation (PKM) effects (Chapter 3) ........................................... 70

**Figure 7.** Subsequent memory effects (remembered > forgotten contrast) for the famous condition in each predefined ROI (Chapter 3) .................................................................................. 72

**Figure 8.** Relationship between the HPC-vmPFC connectivity and associative memory performance across participants in the two fame conditions (Chapter 3) ............................................. 75

**Supplementary Figure 1.** Associative encoding effects for each encoding run (Chapter 3) ..... 90

**Supplementary Figure 2.** Activation for each ROI in each encoding run and fame condition (Chapter 3) ............................................................................................................................................. 91

**Supplementary Figure 3.** Activation in remembered and forgotten trials for the famous condition (Chapter 3) .................................................................................................................. 92
Supplementary Figure 4. Subsequent memory effects for the famous and nonfamous condition (Chapter 3) .......................................................................................................................................................... 93

Supplementary Figure 5. Graphic illustrations of the HPC connectivity fame effects from whole the brain analysis (Chapter 3) ........................................................................................................................................ 94

Figure 1. Schematic overview of the encoding and resting scans (Chapter 4) ......................... 98

Figure 2: ROI masks (Chapter 4) ............................................................................................ 105

Figure 3: Prior-knowledge effects on post-encoding brain connectivity: Predefined ROI results (Chapter 4) ........................................................................................................................................ 108

Supplementary Figure 1. Brain connectivity during the post-famous-encoding rest that positively predicted associative memory of the famous condition did not predict the face/house item memories (Chapter 4) ................................................................................................................ 119

Supplementary Figure 2. Post-encoding brain connectivity in the famous condition that was associated with participants' age and the vividness ratings of famous faces (Chapter 4)......... 120
Chapter 1

General Introduction

In our daily life, we need to make associations frequently, if not constantly, among different pieces of information, such as between different people, places, objects, events, or thoughts. This type of associative processing is crucial for building a large body of relational knowledge, which may serve as the foundation of our higher cognition and help us to adapt to this complex world.

We also know that associative memories are rarely built in a vacuum: Our prior-knowledge can have profound influences on how we make new associations (Jacobs & Kruschke, 2011; Tenenbaum, Griffiths, & Kemp, 2006; Tenenbaum, Kemp, Griffiths, & Goodman, 2011). Understanding how prior-knowledge affects new associative memory processing not only has important practical implications, such as to improve learning in educational settings, but also helps us advance our theoretical understanding of how our memory works.

In the psychological literature, previous experimental work has investigated prior-knowledge effects on associative learning using word pairs (Clark, 1992; Clark & Shiffrin, 1992; Madan, Glaholt, & Caplan, 2010). These studies usually manipulated prior-knowledge by using words with different frequencies, assuming that word frequencies are correlated with our prior-knowledge or experience. Other studies have also examined how existing mental structures such as schema, concepts, or general/semantic knowledge can affect associative memory (Bayen & Kuhlmann, 2011; DeWitt, Knight, Hicks, & Ball, 2012; Geraci & Franklin, 2004; Sherman & Bessenoff, 1999).

However, the types of prior-knowledge on which these previous studies have focused are usually semantics. Although some studies also experimentally induced prior-knowledge by familiarizing participants with the experimental material before experiments (Kinsbourne & George, 1974; Tulving & Kroll, 1995), this type of prior-knowledge is usually too recent and strictly limited to the experimental material or context. Real life content-rich prior-knowledge, however, usually contains different informational components, such as semantics, social emotions, vivid episodes, or detailed perceptions. Importantly, these different knowledge components are likely supported
by different brain regions. Thus, examining their effects on new memory processing at the brain level can help us to understand the interactions between new and old memories.

Although recent neural imaging studies started to investigate prior-knowledge effects on new learning (van Kesteren, Beul, et al., 2013; van Kesteren, Fernández, Norris, & Hermans, 2010), very few studies have examined the effects of this type of multiple-component prior-knowledge on new learning using a well-controlled associative memory paradigm. Investigating this question can help us to understand how prior-knowledge effects can be supported by different brain systems, which is also crucial for better understanding of prior-knowledge effects at the behavioral level. Moreover, at the behavioral level, recent studies have found that associative memory processing can be achieved by different retrieval processes such as familiarity and recollection (Cohn & Moscovitch, 2007). However, how prior-knowledge can affect these different types of associative memory has not been studied. Answering this question can help us to further distinguish different types of associative memory and understand their underlying processes. This dissertation research project was designed to tackle some of these questions.

However, one difficulty in investigating the effects of multiple-component prior-knowledge is to experimentally manipulate it. Recent studies, however, found that famous or familiar faces can elicit different components of existing memories, such as perceptual, episodic, semantic, and social emotional memories that are related to these famous or familiar people (Douville et al., 2005; Elfgren et al., 2006; Gobbini & Haxby, 2007; Ishai, 2008). Moreover, these different components of prior-knowledge can be reflected by the activation of distinct brain regions. An effective way to study multiple-component prior-knowledge effects, especially in neural imaging studies, is to use faces as stimuli and manipulate prior-knowledge using famous or familiar faces. Although some previous studies have used famous or familiar faces to investigate prior-knowledge effects (Johnston & Edmonds, 2009; Kerr & Winograd, 1982; Klatzky & Forrest, 1984; Reder et al., 2013), no studies have investigated how the multiple-component prior-knowledge evoked by famous or familiar (i.e., known) faces can affect specific item-to-item associations at the brain level.

To investigate prior-knowledge effects using faces, I designed a face-house paired-associate memory task in which participants were asked to associate pictures of houses with those of faces. Prior-knowledge manipulation was realized by using famous and nonfamous faces. I then used
this associative task in three experiments to examine prior-knowledge effects on associative
memory processing at the behavioral and brain level using functional neural imaging (fMRI).

Before reporting these studies, I briefly review the relevant literature on prior-knowledge effects
on associative memory processing at both the behavioral and brain level.

1.1 Prior-knowledge effects on associative memory processing
at the behavioral level

Interactions between new and old memories may provide a unique window through which we
can examine how memory works (McKenzie & Eichenbaum, 2011; Preston & Eichenbaum,
2013; van Kesteren, Ruiter, Fernández, & Henson, 2012; Wang & Morris, 2010). In the early
part of the 20th century, psychological research had started to investigate how prior-knowledge
can affect new learning (Bartlett, 1932; Ebbinghaus, 1913; Piaget, 1929). In the current
psychological literature, effects of prior-knowledge have been studied in research areas related to
schema effects (Brewer & Treyens, 1981; Ghosh & Gilboa, 2014; Spaniol & Bayen, 2002),
priming effects (Schacter, Dobbins, & Schnyer, 2004), stereotype effects (Dijksterhuis & Van
Knippenberg, 1995; Rojahn & Pettigrew, 1992), expertise effects (Chase & Simon, 1973; Chassy
& Gobet, 2011; Ericsson & Kintsch, 1995), practice or repetition effects (Bentin & Moscovitch,
novelty vs. familiarity effects (Poppenk, Köhler, & Moscovitch, 2010; Tulving & Kroll, 1995),
and categorical effects (Duffy, Huttenlocher, Hedges, & Crawford, 2010; Hemmer & Steyvers,
2009; Huttenlocher, Hedges, Lourenco, Elizabeth, & Corrigan, 2007; Huttenlocher, Hedges, &
Vevea, 2000).

Because associative memory processing is crucial for building our interconnected knowledge
and experience systems, researchers have also investigated how prior-knowledge affects new
associative processing. For example, using word paired-associate tasks, researcher have
manipulated prior-knowledge by using words with different frequencies (Clark, 1992; Clark &
Burchett, 1994; Clark & Shiffrin, 1992; de Groot, 1989; Hockley, 1994). It has been found that
associations between high-frequency words were better recalled and recognized, compared to
those between low frequency words. Therefore, although high frequency words have been found
to be recognized more poorly than low frequency words in single-word memory tasks (Glanzer
& Adams, 1985; Glanzer & Bowles, 1976; Kinsbourne & George, 1974), prior-knowledge
associated with high frequency words can facilitate associative memory between words. Moreover, compared to low frequency words, high frequency words can also serve as better cues to enhance the retrieval of their paired associates (Clark & Shiffrin, 1992). Previous studies (Hockley, 1994; Madan et al., 2010; Paivio, 1965, 1969) also found that words with high concreteness or imagery can enhance associative memory. Taken together, these studies provided evidence that existing experience related to words with high word frequency, concreteness, or imagery can be used to strengthen word-to-word associations.

Prior-knowledge effects on associative memory have also been studied using source memory paradigms (Bayen & Kuhlmann, 2011; Besken & Gülgöz, 2008; DeWitt et al., 2012; Geraci & Franklin, 2004; Hicks & Cockman, 2003; Kleider, Pezdek, Goldinger, & Kirk, 2008; Kuhlmann, Vaterrodt, & Bayen, 2012; Sherman & Bessenoff, 1999; Spaniol & Bayen, 2002). In a source memory task, memories of detailed context information associated with encoding tasks are tested together with the encoding material (Johnson, Hashtroudi, & Lindsay, 1993; Johnson & Raye, 1981). Using this paradigm, for example, DeWitt and colleagues (DeWitt et al., 2012) investigated how participants' prior-knowledge on different categories of objects and animals would affect their memory of whether individual object or animal stimuli were presented on the left or right of the screen (i.e., the source memory). There results showed that stronger prior-knowledge led to both better target item memory and location source memory, suggesting that prior-knowledge can promote more efficient episodic source encoding. Regarding the underlying mechanisms for the facilitation effects, it has been proposed that prior-knowledge on specific categories of objects or animals can enhance the distinctiveness of the individual items in those categories and therefore promote the memory for those items (DeWitt et al., 2012). Moreover, items with prior-knowledge also demand less cognitive processing resources so that more resources can be used for source memory encoding (DeWitt et al., 2012; Reder et al., 2013).

It is clear from this line of research that general knowledge, concepts, or schemas can affect source memory. However, the direction of the effects may depend on many factors, such as how well participants have remembered the encoding context, whether prior-knowledge retrieval becomes distractive to the main encoding task, or whether participants have used guessing strategies (Bayen & Kuhlmann, 2011; Bayen, Nakamura, Dupuis, & Yang, 2000, p. 200; Kim et al., 2012; Kuhlmann et al., 2012).
Although prior-knowledge effects have been demonstrated in a number of associative memory studies, none has distinguished between the effects of prior-knowledge on associative recollection and familiarity. Using an associative identification task, Cohn and her colleagues (Cohn, Emrich, & Moscovitch, 2008; Cohn, McAndrews, & Moscovitch, 2009; Cohn & Moscovitch, 2007) had participants explicitly distinguish originally learned associated pairs from recombined pairs made by re-pairing learned items. Thus, in this task participants have to rely on the learned associations to discriminate the intact from the recombined pairs. The extent to which they could do that was taken as a measure of recollection of the learned association. Familiarity type of associative memory can be measured by associative reinstatement, which is the facilitation effect that intact associated pairs, compared to the recombined pairs, have on item recognition (Cohn & Moscovitch, 2007; Kan, Giovanello, Schnyer, Makris, & Verfaellie, 2007). In this task, participants do not need to explicitly retrieve the original associations because their task is to judge whether the items in the intact or recombined pairs were studied. Therefore, any facilitation effects on the recognition of the items from the intact pairs may result from a familiar sense of the original intact association. Other approaches that target the familiarity processes of associative memory have also been developed, such as using compound word or source memory paradigms (Bastin et al., 2013; Diana, Yonelinas, & Ranganath, 2008; Quamme, Yonelinas, & Norman, 2007).

In a series of studies, Cohn and colleagues (Cohn et al., 2008, 2009; Cohn & Moscovitch, 2007) provided evidence showing that although both types of associative memory can be affected by depth of processing, only associative recollection can be influenced by strategic retrieval such as short response deadline, speeded recognition, or fan effects. In follow-up studies, Cohn and colleagues (Cohn et al., 2008) found that while the recollection type of associative memory was impaired during aging, the familiarity type was intact, providing further evidence that the two types of associative memory may be different. Therefore, the familiarity and recollection dual-processing model, which was originally developed in item recognition memory (Gardiner, 1988; Gardiner, Ramponi, & Richardson-Klavehn, 2002; Tulving, 1985; Yonelinas, 1999), may also be applied to associative memory.

However, how prior-knowledge can affect these two types of associative memory remains unknown. Investigating this question can help us to understand how associative memory can be achieved by different cognitive processes. More details regarding the rationale and experimental
design of the current studies are presented in the last section of this introduction. In the next two sections, I briefly review some neural imaging studies that investigated prior-knowledge effects on new memory processing at the brain level.

1.2 Prior-knowledge effects on new memory encoding at the brain level

Since the classic studies on patient H.M. (Corkin, 1968; Milner, Corkin, & Teuber, 1968; Scoville & Milner, 1957), a huge body of memory literature has shown that the medial temporal lobe (MTL) plays an important role in episodic and associative memory processing (Davachi, 2006; Diana, Yonelinas, & Ranganath, 2007; Eichenbaum, Yonelinas, & Ranganath, 2007; Kim, 2011; Mayes, Montaldi, & Migo, 2007; Milner, Squire, & Kandel, 1998; Olsen, Riggs, & Ryan, 2012). Anatomically, the MTL consists of the perirhinal cortex, entorhinal cortex, hippocampus (HPC), and parahippocampal cortex. It has been proposed that the perirhinal and parahippocampal regions preferentially process information related to objects and space respectively. Then these different types of information can be bound in the hippocampus via the entorhinal cortex (Brown & Aggleton, 2001; Davachi, 2006; Eichenbaum et al., 2007).

Early experimental work on prior-knowledge effects at the brain level can also be traced to studies on amnesic patients. For example, studies have found that compared to unfamiliar information, memories for familiar information such as high frequency words, familiar images, or semantically related words are less impaired in amnesic patients (Cutting, 1978; Huppert & Piercy, 1976; Mayes, Meudell, & Som, 1981; Shimamura & Squire, 1984; Warrington & Weiskrantz, 1974; Winocur & Weiskrantz, 1976). Similar results were also found in older adults who may have impaired hippocampal function (Bastin et al., 2013; Bastin & Van der Linden, 2003; Naveh-Benjamin, Brav, & Levy, 2007; Naveh-Benjamin, Hussain, Guez, & Bar-On, 2003; Naveh-Benjamin, M, Guez, & Kreuger, 2005). Relatedly, the HPC has been found to be involved to a lesser extent in processing familiar vs. novel information (Kaplan, Horner, Bandettini, Doeller, & Burgess, 2014; Kumaran & Maguire, 2009; Nyberg, 2005; Ranganath & Rainer, 2003; Tulving, Markowitsch, Craik, Habib, & Houle, 1996; Tulving, Markowitsch, Kapur, Habib, & Houle, 1994). These findings indicate that prior-knowledge modulates new memory processing such that the originally hippocampus-dependent memory processing may become less hippocampus-dependent (Diana et al., 2008; Greve, van Rossum, & Donaldson, 2007).
If the HPC is less important for processing memory information related to prior-knowledge, it is likely that other brain regions take over some of its functions. In a recent influential animal study, Tse and colleagues (Tse et al., 2007) found that after rats learned several spatial locations associated with different food scents, newly added location-scent associations could be learned much more quickly and the newly formed associative memory became hippocampus independent more quickly, compared to the initial learning. It is inferred that the initially learned location-scent associations might be used as schemas to facilitate new learning. In a follow-up study (Tse et al., 2011), the authors also found that the ventral medial prefrontal cortex (vmPFC) was crucial for the schema facilitative effects. These findings are intriguing because they indicate that neocortical regions such as the vmPFC can take over some of the MTL memory function when prior-knowledge is involved.

Similarly, Van Kesteren and colleagues (van Kesteren, Beul, et al., 2013; van Kesteren, Fernández, et al., 2010; van Kesteren, Rijpkmeka, Ruiter, & Fernandez, 2010) have conducted a series of fMRI studies in humans to investigate how existing mental structures such as schemas can affect new memory encoding and retrieval. For example, in one study (van Kesteren, Fernández, et al., 2010), the authors manipulated schema congruency of their memory task by presenting two groups of participants intact or reshuffled video clips of the first half of a movie. One day later, the two groups were asked to watch the second half of the movie while their brain activity was measured using fMRI. The authors found that the connectivity between the HPC and vmPFC during encoding was stronger for the inconsistent-schema, compared to the consistent-schema, group. They also found that the HPC-vmPFC connectivity in the inconsistent-schema group was negatively correlated with participants' memory of the gist of the movie. In another study, van Kesteren and colleagues (van Kesteren, Beul, et al., 2013) designed a paired-associate incidental encoding task in which object and scene images were paired in either a schema congruent (e.g. classroom–chalk) or incongruent (e.g. tennis court–soup ladle) way. They found that in successful encoding trials, the medial PFC activation increased, but the HPC activation decreased, with the increase of the trial schema congruency. The medial PFC connectivity with a parahippocampal region also increased with trial schema congruency. The authors interpreted their data as being consistent with previous animal studies (Tse et al., 2007, 2011) in that the vmPFC played a key role in schema facilitation effects. Similarly, studies using associative or transitive inference tasks (e.g., from associations of A-B and A-C to infer B-C) also found that
the HPC-vmPFC interaction is important in supporting the emergence of new knowledge from previous experiences (Kumaran, Melo, & Duzel, 2012; Kumaran, Summerfield, Hassabis, & Maguire, 2009; Preston & Eichenbaum, 2013; Zeithamova, Dominick, & Preston, 2012; Zeithamova, Schlichting, & Preston, 2012). Based on some of these findings, it has been proposed that the vmPFC activation or vmPFC-HPC interactions likely plays an important role in assimilating new information into existing knowledge, whereas the HPC is more important for encoding novel or schema incongruent information (van Kesteren et al., 2012).

Although the studies reviewed above have discovered that the vmPFC plays an important role in schema-related memory processing, there are a couple of problems that may deserve more attention. For example, although it is an interesting proposal that the vmPFC, or vmPFC-HPC interactions, support the assimilation of new information into existing knowledge systems, alternative interpretations of the vmPFC's involvement exist. Considering that a huge body of literature has shown that the vmPFC can support a wide range of social, affective, or evaluative processing, such as self-related processing, decision making, moral judgment, empathy, processing abstract semantic information, or even perceiving preferred every-day objects (Barrett & Bar, 2009; Binder, Desai, Graves, & Conant, 2009; Etkin, Egner, & Kalisch, 2011; Grabenhorst & Rolls, 2011; Luo et al., 2010; O’Reilly, 2010; Roy, Shohamy, & Wager, 2012), it is also likely that the vmPFC may play a similar evaluative role in those schema-related processes (Burin et al., 2014). For example, in the animal schema studies (Tse et al., 2007, 2011), the animals' associative learning performance was always related to food rewards. Thus, the medial PFC's involvement in schema-related learning can reflect stronger evaluative processes. It is unclear whether similar evaluative processes can also account for the vmPFC's involvement in the studies by van Kesteren and colleagues (van Kesteren, Beul, et al., 2013; van Kesteren, Fernández, et al., 2010). New studies using tasks that can trigger evaluative or affective processing without schema congruency manipulations may help us to explore these alternative explanations of the vmPFC's involvement.

Moreover, these previous studies mainly focused on the effects of schema, which is only one type of prior-knowledge. The long history of psychological research on schema effects has shown that specific effects of schema depend on how schema modulates the underlying processes of specific memory tasks (Alba & Hasher, 1983). Simply manipulating schema consistency of task material may not always produce consistent results. For example, in one
study van Kesteren and colleagues found that the vmPFC-HPC connectivity was stronger in the schema-inconsistent than schema-consistent condition (van Kesteren, Fernández, et al., 2010). However, another study (van Kesteren, Beul, et al., 2013) did not find schema effects on the vmPFC-HPC connectivity. Instead this study found that the vmPFC connectivity with a parahippocampal region increased with schema congruency. A recent neural imaging study (van Buuren et al., 2014) designed a similar associative memory task as the one used in the animal studies (Tse et al., 2007, 2011). However, it did not find schema modulation effects on the vmPFC activation or vmPFC-HPC connectivity during memory retrieval. Instead, the vmPFC connectivity with some posterior medial regions, such as the posterior cingulate cortex and precuneus, was found to be stronger when a schema was involved. Although these observations may be consistent with the model proposed by van Kesteren and colleagues (van Kesteren et al., 2012), more studies with different types of prior-knowledge manipulation are needed to explore the possible roles of different brain regions in prior-knowledge effects.

Furthermore, in addition to the HPC and vmPFC, other brain regions can also play a role in prior-knowledge effects. For example, the anterior pole regions (aTPL) have been proposed to be hub regions that support semantic knowledge (Patterson, Nestor, & Rogers, 2007). Studies have found that damage to aTPL is related to impairments in semantic knowledge or semantic learning in dementia and brain lesion patients (Gainotti, Ferraccioli, & Marra, 2010; Hsieh, Hornberger, Piguet, & Hodges, 2011; Lambon Ralph, Cipolotti, Manes, & Patterson, 2010; Lambon Ralph, Sage, Jones, & Mayberry, 2010; Sharon, Moscovitch, & Gilboa, 2011; Snowden, Thompson, & Neary, 2004). Electrically stimulating these regions can also improve retrieval of semantic memories of previous knowledge or experiences such as the names of famous people or well-known places (Ross, Coslett, Olson, & Wolk, 2011; Ross, McCoy, Wolk, Coslett, & Olson, 2010). Lesions of these regions also reduced prior-knowledge facilitation effects on new learning (Kan, Alexander, & Verfaellie, 2009; Sharon et al., 2011). Therefore, to better understand prior-knowledge effects on new memory processing, we should broaden our focus to take more brain regions or systems into consideration.

However, methodologically, using schema-congruency manipulation to study prior-knowledge effects on different brain regions are not ideal. More often than not schemas are complex mental structures and it is difficult to pinpoint which brain regions represent this type of prior-knowledge. Insofar as the vmPFC is implicated, as mentioned earlier, it remains to be resolved to
what extent the vmPFC activity directly supports schemas or it mainly reflects evaluative processes triggered by schemas and indirectly contributes to memory processing. On the other hand, there are also limitations to using stimuli such as high and low frequency words to study prior-knowledge effects at the brain level. As mentioned earlier, the type of prior-knowledge evoked by high frequency words (over low frequency words) is mainly related to linguistic properties of words and can be too narrow in its content. Also, brain level investigations on word frequency effects usually do not directly focus on the effects of prior-knowledge associated with high-frequency words, but on the additional processes evoked by low frequency words (Chee, Westphal, Goh, Graham, & Song, 2003; de Zubicaray, McMahon, Eastburn, Finnigan, & Humphreys, 2005). Therefore, to understand better the effects of prior-knowledge on new learning, e.g., whether and how prior-knowledge facilitation effects are mediate by multiple brain systems, we need to design a different task to elicit multiple-component prior-knowledge that can be tractable using neural imaging methods such as fMRI.

Fortunately, in recent decades a large literature has accumulated in human face processing research (Atkinson & Adolphs, 2011; Bruce & Young, 1986; Haxby, Hoffman, & Gobbini, 2000; Johnston & Edmonds, 2009; Park, Newman, & Polk, 2009; Yovel & Belin, 2013), which can inform us about the processing of different components of information related to faces by a variety of brain regions. For example, perceptual aspects of faces may be preferably processed in the fusiform gyrus (Kanwisher, 2010). Episodic memories related to familiar or famous faces can be supported by the MTL or HPC (Denkova, Botzung, & Manning, 2006; Douville et al., 2005; Elfgren et al., 2006). The aTPL may also support semantic information related to the face, such as the person's name, vocation, or social relationship (Abel et al., 2015; Ross et al., 2010; Ross & Olson, 2012; Tsukiura et al., 2002). Moreover, affective or social evaluative information related to the faces can be supported by the vmPFC or amygdala (Ishai, 2008; Rolls, 2007). Therefore, in this research project, I propose to use face images as stimuli in a face-house paired-associate task and manipulate prior-knowledge by using both famous and nonfamous faces. This design allows us to evoke multiple-component prior-knowledge in participants and use fMRI to examine its effects in different brain regions. More details regarding the rationale and design of the current studies are presented in the last section of this introduction. In the next section, I briefly review the literature on whether prior-knowledge could also affect brain activity during post-encoding time periods.
1.3 Prior-knowledge effects on post-encoding brain activity

Newly encoded memories need to go through consolidation processes to become stabilized (Dudai, 1996, 2004, 2006, 2012; Dudai & Morris, 2000; Girardeau & Zugaro, 2011; McGaugh, 1966, 2000; Moscovitch et al., 2005; Moscovitch & Nadel, 1998; Nadel & Moscovitch, 1997; Nader & Hardt, 2009; Sutherland & McNaughton, 2000; Wang & Morris, 2010). These consolidation processes may last from several hours to a few days, or even longer (Dudai, 2012; Izquierdo et al., 2006; Squire & Alvarez, 1995; Sutherland & Lehmann, 2011). One important question is whether prior-knowledge can not only affect on-line memory processes such as encoding and retrieval, but also the off-line memory consolidation processes. To study this question experimentally, we first have to identify post-encoding time windows in which evidence can be found to show the possible occurrence of memory consolidation processes.

One time window that has specifically attracted researchers' attention is post-encoding sleep. In a seminal study, Wilson and McNaughton (1994) found that the hippocampal place cells that fired together when rats were performing a spatial task also tended to fire together during the post-task slow-wave sleep, but not during the pre-task sleep. This observation provided important evidence that neural activity during post-encoding sleep may reflect an early memory consolidation process. Similar findings have been obtained in many other studies (Ji & Wilson, 2007; Kudrimoti, Barnes, & McNaughton, 1999; Lee & Wilson, 2002; Louie & Wilson, 2001; Mizunuma et al., 2014; Nádasdy, Hirase, Czurkó, Csicsvari, & Buzsáki, 1999; O’Neill, Senior, Allen, Huxter, & Csicsvari, 2008; Singer & Frank, 2009; Skaggs & McNaughton, 1996; Wikenheiser & David Redish, 2013). Importantly, it has been shown that memory replay can occur not only during sleep but also during post-encoding rest (Davidson, Kloosterman, & Wilson, 2009; Diba & Buzsaki, 2007; Dupret, O’Neill, Pleydell-Bouverie, & Csicsvari, 2010; Foster & Wilson, 2006; Jadhav, Kemere, German, & Frank, 2012; Karlsson & Frank, 2009; Kudrimoti et al., 1999). Moreover, memory replay can be found in brain regions other than the HPC, such as the striatum, medial PFC, visual, and motor cortex (Eagleman & Dragoi, 2012; Euston, Tatsuno, & McNaughton, 2007; Han, Caporale, & Dan, 2008; Hoffman & McNaughton, 2002; Ji & Wilson, 2007; Johnson, Euston, Tatsuno, & McNaughton, 2010; Lansink et al., 2008; Pennartz et al., 2004; Ribeiro et al., 2004; Yao, Shi, Han, Gao, & Dan, 2007). These findings from animal research provided empirical evidence that memory consolidation processes can be investigated by examining the brain activity during post-encoding sleep or rest.
Recently, human neural imaging studies started to investigate how post-encoding brain activity measured by fMRI or EEG was related to memory replay or consolidation. For example, using fMRI, Tambini and colleagues (Tambini & Davachi, 2013; Tambini, Ketz, & Davachi, 2010) found that associative encoding pattern in the HPC can persist into post-encoding rests and that the connectivity between the HPC and the posterior perceptual regions can be strengthened after associative encoding and be predictive of later memory performance. It has also been found that the HPC connectivity with other brain regions, such as the ventral tegmental area, during associative memory encoding can persist into post-encoding non-memory tasks and predict later associative memory (Tompary, Duncan, & Davachi, 2015). Recent studies also found that encoding brain activity in the entorhinal and retrosplenial cortex was more frequently reactivated during post-encoding rests for successfully encoded associations, compared to unsuccessful ones (Staresina, Alink, Kriegeskorte, & Henson, 2013). Similarly, using fMRI multivariate pattern analysis, Deuker and colleagues found that stimulus-specific activity patterns during encoding were reactivated during post-encoding rests and sleep (Deuker et al., 2013). Interestingly, newly encoded memory cued during post-encoding sleep (e.g., by using paired sound stimuli) could be retrieved better after sleep than those not cued (Oudiette, Antony, Creery, & Paller, 2013; Rudoy, Voss, Westerberg, & Paller, 2009), and that when slow-wave oscillations during the post-encoding sleep were enhanced by phase-synchronized acoustic stimulation, associative memory performance was also enhanced (Ngo, Martinetz, Born, & Mölle, 2013). These observations provided strong evidence for a causal link between the post-encoding brain activity and memory consolidation (Abel, Havekes, Saletin, & Walker, 2013; Girardeau & Zugaro, 2011; Oudiette & Paller, 2013; Sutherland & McNaughton, 2000).

It is also worth mentioning that in resting-state fMRI research, studies have found that recent learning experiences can modulate resting-state brain connectivity (Albert, Robertson, & Miall, 2009; Deuker et al., 2013; Groen, Sokolov, Jonas, Roebling, & Spitzer, 2011; Hasson, Nusbaum, & Small, 2009; Lewis, Baldassarre, Committeri, Romani, & Corbetta, 2009; Stevens, Buckner, & Schacter, 2009; Urner, Schwarzkopf, Friston, & Rees, 2013; Vahdat, Darainy, Milner, & Ostry, 2011; Wang et al., 2012). Although these studies did not specifically focus on memory consolidation processes during the post-task rests, they provide additional evidence showing that task modulation effects on brain activity can extend beyond the task execution phase and persist into post-task time windows.
However, there has been very little research on how prior-knowledge can affect post-encoding brain activity. In animal research, post-encoding neuronal replay of previous experiences was observed both after novel and familiar experiences (Gupta, van der Meer, Touretzky, & Redish, 2010; Kudrimoti et al., 1999; O’Neill et al., 2008; Ribeiro et al., 2004). In human neural imaging studies, to the best of my knowledge, only van Kesteren and colleagues examined how schema-congruency of encoding tasks could modify the HPC-vmPFC connectivity during post-encoding rests (van Kesteren, Fernández, et al., 2010). As mentioned earlier, in (van Kesteren, Fernández, et al., 2010), two groups of participants first watched video clips of the first half of a movie with the temporal order intact or reshuffled, creating a schema-consistent and schema-inconsistent condition, respectively. Then, in the scanner, all participants were asked to watch and encode the last part of the movie. Post-encoding brain activity following each condition was also recorded. This study found that the connectivity between the HPC and vmPFC was stronger in the schema-inconsistent than the schema-consistent condition during the post-encoding rest, indicating that existing schema can also affect post-encoding brain activity that is likely related to memory processes (van Kesteren, Fernández, et al., 2010).

The study by van Kesteren and colleagues (van Kesteren, Fernández, et al., 2010) is important in showing that post-encoding brain activity, likely reflecting early memory replay or consolidation, can be affected by whether prior-knowledge is involved in the preceding encoding task. However, that study raises some unresolved issues. For example, the movie encoding task in that study was rather complex, making it difficult to infer the functional role of the vmPFC's involvement. Also, considering that many animal studies have found that familiar experiences can lead to strong neuronal replay (Kudrimoti et al., 1999; O’Neill et al., 2008), it is worth exploring whether prior-knowledge can also lead to stronger, instead of weaker (van Kesteren, Fernández, et al., 2010), memory reactivation during post-encoding rest. It is also unclear from the previous study how other brain regions such as the aTPL could play a role in prior-knowledge effects during post-encoding time windows. Finally, whether the post-encoding brain activity is associated with memory performance has not been directly examined in van Kesteren and colleagues' study (van Kesteren, Fernández, et al., 2010). Therefore, more studies with an improved experimental design and analysis strategy are needed to further investigate how prior-knowledge can affect post-encoding brain activity.
1.4 Overview of the current study

In this research project, I designed a face-house paired-associate task and used famous and nonfamous faces to manipulate prior-knowledge. I think this design can address some of the problems mentioned earlier in this introduction. First, different from source memory tasks, paired-associate tasks allow us to examine more specific one-to-one, rather than one-to-many, type of associations between paired stimuli. This can help us to investigate prior-knowledge effects on associative memory processing at a better information resolution. Moreover, using this paired-associate task we can measure both associative familiarity and recollection processes and investigate whether prior-knowledge can differentially affect the two different types of associative processing.

Second, comparing to previous studies using schema-congruency manipulation of prior-knowledge, using famous faces allows us to elicit in participants multiple-component prior-knowledge whose representation has been well studied at both the behavioral and brain level. Numerous studies in the face processing literature has shown that famous or familiar faces can evoke rich perceptual, social evaluative, episodic, and semantic information (Fairhall & Ishai, 2007; Gobbini, Leibenluft, Santiago, & Haxby, 2004; Ishai, 2008; Ross & Olson, 2012; Simmons, Reddish, Bellgowan, & Martin, 2010). Combining this prior-knowledge manipulation method with the use of a paired-associate task, we can now investigate how this type of multiple-component prior-knowledge affects new associative memory processing. Although at the behavioral level, previous studies have investigated face fame effects on face recognition (Johnston & Edmonds, 2009; Kerr & Winograd, 1982; Klatzky & Forrest, 1984; Reder et al., 2013), no studies have used this paradigm to examine how prior-knowledge related to famous faces can differentially affect the familiarity and recollection types of face-house associations. This investigation can also help us to further test the theoretical question of how familiarity and recollection, i.e., the dual-processing memory model (Yonelinas, 1999, 2002), can be applied to associative memory.

Third, at the brain level, the multiple-component prior-knowledge corresponding to famous faces is supported by different brain regions or systems and can be examined using fMRI. For example, studies have found that famous or familiar faces or names can elicit episodic memories supported by the MTL, including the HPC (Denkova et al., 2006; Douville et al., 2005; Elfgren
et al., 2006), social semantic knowledge supported by the aTPL (Ross et al., 2010; Ross & Olson, 2012; Tsukiura et al., 2002), and evaluative or affective information supported by the vmPFC and amygdala (Ishai, 2008; Rolls, 2007). At the perceptual level, it has been shown that face and house information can be preferably processed in the parahippocampal place area (PPA) and the fusiform face area (FFA), respectively (Kanwisher, 2010). Therefore, using this face-house paired-associate task allows me to trace, among these different brain regions, the effects of the multiple-component prior-knowledge evoked by the famous faces during new associative processing. This investigation is crucial for understanding how prior-knowledge effects can be supported by different brain systems. Using this task, I can also examine the post-encoding time window to see how the connectivity among these brain systems can be modulated by the involvement of prior-knowledge in preceding encoding tasks. This can help us to understand whether prior-knowledge can influence early memory consolidation processes, for example, by recruiting more neocortical regions such as vmPFC and aTPL during post-encoding memory reactivation.

To achieve these research goals, it was first necessary to establish in a behavioural study that famous faces can produce a prior-knowledge effect. To this end, in the first experiment, I paired famous and non-famous faces with houses to see whether famous, as compared to non-famous, faces could facilitate the formation and retrieval of new associations. In this experiment, participants were asked to associate pictures of houses with those of famous and nonfamous faces during encoding. Then, they performed a three-step retrieval task that not only measured item and associative memory, but also differentiated associative familiarity from recollection. Based on the literature (Reder et al., 2013), I hypothesized that prior-knowledge elicited by famous faces should facilitate face item memory and the recollection type of face-house associative memory. Prior-knowledge effects on the familiarity type of associative memory were also explored but without any \textit{a priori} predictions. This study is reported in Chapter 2.

I then used this face-house association task in an fMRI study to investigate how prior-knowledge could affect brain activity during encoding. I chose the PPA, FFA, HPC, aTPL, and vmPFC as regions of interest, because the activation of these regions may reflect different aspects of the associative processing. By comparing the famous and nonfamous condition, I examined how prior-knowledge could affect these different component processes. Within the famous condition, I also examined how participants' prior-knowledge ratings on famous faces could modulate brain
activation in these regions of interest. Prior-knowledge effects on the HPC connectivity with other regions of interest were also investigated. Because the vmPFC, aTPL, and HPC may support the social evaluative, semantic, and episodic aspect of prior-knowledge, respectively, I predicted that these regions should show stronger activation when prior-knowledge is involved, especially for the successful encoding trials. Within the famous condition, these regions should also show stronger activation for the trials where the famous faces could elicit stronger prior-knowledge. This study is reported in Chapter 3.

I also measured post-encoding brain activity among these regions of interest in the two fame conditions. In addition to investigating how prior-knowledge could affect post-encoding brain connectivity, I also examined how these connectivity measures were correlated with associative memory performance. I predicted that compared to the nonfamous condition, the vmPFC, aTPL, and HPC, which support different aspects of prior-knowledge, should connect more strongly with the PPA and FFA during the post famous encoding rest, possibly reflecting persistent facilitative effects during early memory consolidation. This study is reported in Chapter 4.

Chapter 5 constitutes a general discussion, in which I summarize the findings from the 3 experiments and discuss their implications to research areas concerned with schema effects, the brain's default mode network, and memory consolidation. In Chapter 5, I also briefly discuss some limitations of the current study and future research directions.
Chapter 2

Study 1: Prior-knowledge Enhances Recollection of Associative Memory

2.1 Introduction

The goal of this experiment was to investigate how multiple-component prior-knowledge can affect new associative memory processing at the behavioral level. As mentioned in Chapter 1, the type of prior-knowledge manipulated by word frequency, concreteness, or imagery in previous studies (Clark, 1992; Madan et al., 2010) can be determined, to a large extent, by linguistic properties of different words. Prior-knowledge such as existing schemas or concepts targeted by previous studies (DeWitt et al., 2012; van Kesteren, Rijpkema, Ruiter, & Fernández, 2013) also mainly belongs to abstract semantics or complex general knowledge. In this experiment, I designed a face-house paired-associate task in which famous faces were used to elicit multiple-component prior-knowledge, such as prior semantics, social emotions, vivid episodes, or visual perceptions. These different components of prior-knowledge evoked by familiar or famous faces has been found to be supported by distinct brain systems (Fairhall & Ishai, 2007; Gobbini et al., 2004; Gobbini & Haxby, 2007; Ishai, 2008; Ross & Olson, 2012; Simmons et al., 2010). Moreover, previous studies have also found that prior-knowledge related to famous faces can enhance face recognition memory (Johnston & Edmonds, 2009; Kerr & Winograd, 1982; Klatzky & Forrest, 1984; Reder et al., 2013). Thus, using different types of face stimuli, such as famous vs. nonfamous faces, in a face-house paired associate task allowed me to examine how multiple-component prior-knowledge can affect new associative memory processing.

Moreover, as reviewed in Chapter 1, recent studies have found that processes such as familiarity and recollection can also apply to associative memory (Cohn et al., 2008, 2009; Cohn & Moscovitch, 2007; Quamme et al., 2007). Recollection type of associative memory can be measured by an associative identification procedure in which participants need to explicitly distinguish originally learned associated pairs from recombined pairs made by re-pairing learned
items (Cohn & Moscovitch, 2007). In this task, participants have to rely on the learned associations to discriminate the intact from the recombined pairs. Familiarity type of associative memory can be measured by associative reinstatement, which is the facilitation effect that intact associated pairs, compared to the recombined pairs, have on item recognition (Cohn & Moscovitch, 2007; Kan et al., 2007). In this task, participants do not need to explicitly retrieve the original associations because their task is to judge whether the items in the intact or recombined pairs were studied. Therefore, any facilitation effects on the recognition of the items from the intact pairs may result from a familiar sense of the original intact association. However, previous studies have not investigated how prior-knowledge can differentially affect these two types of associative memory. Answering this question can not only advance our understanding of associative memory processing and its prior-knowledge effects, but also guide brain-level investigations by providing refined conceptualization or behavioral assays of associative processing.

To investigate these questions, in this behavioral experiment I first asked participants to associate pictures of novel houses with those of famous and nonfamous faces. Then, during retrieval, a three-step retrieval task was administered to the participants in which both recollection and familiarity of single face/house items and face-house associations can be measured within each participant. I reasoned that prior-knowledge related to the famous faces can be used to make richer associations with the houses (Anderson, 1981; Dragoi & Tonegawa, 2013a, 2014). Also, participants can use social evaluative information related to famous people to process the face-house associations in a more selective, organized, or deeper manner (Anderson, 1983; Hargreaves & Pexman, 2012; Levine & Edelstein, 2009; Talmi, Schimmack, Paterson, & Moscovitch, 2007). Therefore, I hypothesized that the recollection type of associative memory, i.e., associative identification (introduced in Chapter 1), should be enhanced in the famous, as compared to the nonfamous, condition, much as it is enhanced by deeper levels of processing (Cohn & Moscovitch, 2007; Epstein, Phillips, & Johnson, 1975; Gallo, Meadow, Johnson, & Foster, 2008; Sheridan & Reingold, 2012; Toth, 1996).

It is less clear, however, whether similar prior-knowledge facilitation effects would occur in associative reinstatement. If associative reinstatement between pictorial stimuli used in the current study is similar to that between verbal stimuli investigated by previous studies (Cohn & Moscovitch, 2007), potential deep processing associated with prior-knowledge can strengthen
this type of associative memory. However, there is also evidence that recollection and familiarity of single items are not equally affected by depth of processing (Gardiner, Java, & Richardson-Klavehn, 1996), and that different cognitive processes are involved in tasks with pictorial vs. verbal stimuli (Nelson, Reed, & Walling, 1976; Paivio & Csapo, 1973; Standing, 1973). Thus, it is possible that associative reinstatement and identification can be differentially affected by prior-knowledge. Therefore, in this study I explored this question, i.e., how prior-knowledge affects associative reinstatement, without *a priori* predictions.

2.2 Method

2.2.1 Participants

Thirty university students of the University of Toronto participated in this study (9 males, 21 females, age *mean* = 20.7 years, *SD* = 2.57 years). All the participants were native English speakers with normal or corrected-to-normal vision and hearing. They were also screened for absence of any psychological/psychiatric and neurological conditions. Two additional participants were excluded because of equipment malfunctions and one for not correctly following task instructions. Participants either received academic credit or financial compensation ($15 Canadian) for their participation. The experimental protocol was approved by the Ethics Review Board at the University of Toronto.

2.2.2 Stimulus materials

Color pictures of faces and houses were collected from the Internet using Google Image Search. Among the total 192 face pictures, 96 were faces of famous people (48 females and 48 males). These famous people are all Caucasian movie actors/actresses, whose names were obtained from a list of top actors/actresses (ranked by a website based on averaged domestic box office gross http://www.the-movie-times.com/thrsdir/actors.mv?actors+ByAG). Originally about 100 famous face pictures for each gender were collected and their famousness was ranked by 9 undergraduate students. The top 48 famous face pictures for each gender were chosen. Non-famous faces (48 males and 48 females) were obtained from the Internet by searching people of different occupations, e.g., biologist, lawyer, professor, graduate student, etc. All face pictures were of the same size (231 by 300 pixels) and the faces were depicted in a full frontal pose. I also collected 192 house pictures with the size of 391 by 300 pixels. The luminance and contrast
were balanced within each picture category using SHINE toolbox (Willenbockel et al., 2010) and custom Matlab (MathWorks, Natick, MA) scripts.

For the encoding task, I paired 60 faces (half are males) and 60 houses for each fame condition (i.e., *famous* vs. *nonfamous* condition). The pictures were randomly selected from the available pictures for each participant.

For the retrieval task, there were 4 types of face-house testing pairs: *intact*, *recombined*, *half-old/new*, and *new-new* pairs. Each type had 24 pairs in each fame condition. For each participant, the intact pairs were randomly selected from the encoding pairs with face gender balanced. The recombined pairs were made by re-pairing the faces and houses of another set of 24 pairs that were also randomly chosen from the rest of the encoding pairs. To make the 24 half-old/new pairs, the remaining 12 encoding pairs were split and then paired with new house and face pictures, respectively. This produced 12 *old face - new house* and 12 *new face - old house* pairs. The 24 new-new pairs were made by pairing the rest of the face and house pictures in the original picture set. In total, there were 192 face-house pairs in the retrieval task.

It is worth mentioning that our random assignment of face-house encoding pairs to the 4 types of testing pairs in each participant should eliminate potential confounding effects caused by stimulus properties. I did not counterbalance this assignment procedure across participants because only 12 encoding pairs were needed to construct 24 half-old/new pairs, but 24 pairs were needed to construct other types of retrieval pairs. These unequal numbers made it difficult to completely counterbalance the assignment of encoding pairs to retrieval pairs.

2.2.3 Procedure

E-Prime software (version 1, Psychology Software Tools, Inc.) was used to present the encoding and retrieval task.

In each encoding trial (Figure 1A), after a one second fixation cross "+", a face-house picture pair was presented on the computer screen for 6 seconds, with the face picture on the top of the screen, the house at the bottom, and the fixation cross in between.
Figure 1. Encoding and retrieval trials (Chapter 2)

Figure 1. Encoding (A) and retrieval (B) trials. (Images used here are only for illustration purposes. Image sources: Jennifer Aniston's face image was downloaded and resized from http://www.justjared.com/photogallery/1696871/jennifer-aniston-hes-just-not-that-into-you-premiere-04/fullsize/. The house image paired with Jennifer Aniston was downloaded and resized from http://www.dichan.com/case-show-96727.html. The face image shown in the nonfamous condition was used with the person's written consent. The house image shown in the nonfamous encoding trial was downloaded and resized from http://bbb123.biz/ja/node/6943. The house image shown in the nonfamous retrieval trial was downloaded and resized from http://abhomedesigns.com/3-bedroom-house/3-bedroom-house-with-contemporary-design-on-decor-design-ideas/.)
Participants were instructed to look at the face and house picture, then imagine and memorize as vividly as possible the person (of the face) standing in front of the house. At the end of the 6 seconds, while the pictures were still on the screen, the words “Difficult” and “Easy” appeared for 2 seconds. Participants were required to press one of two buttons to indicate whether it was easy or difficult for them to make the association (1: Easy; 2: Difficult). The 60 encoding trials in each fame condition were presented continuously in one block. This encoding task was repeated to ensure sufficient memory performance, resulting in 4 encoding blocks in total (2 famous and 2 non-famous blocks). All 6 possible orders of the 4 blocks were counter-balanced across participants. The total time needed for each encoding block was about 9 minutes. Before the start of the real encoding task, 8 practice trials were given using additional images.

Retrieval task. Immediately after the encoding task, participants performed a 3-step retrieval task (Figure 1B). In each retrieval trial, after a 1 second fixation cross, a single picture (face OR house) of a face-house retrieval pair was presented, with faces being presented first in one half of the trials for each testing pair type with gender balanced. Participants were required to indicate whether they could recognize the single picture by pressing one of 3 number keys on the keyboard using a remember/know procedure (1: Re-experience; 2: Familiarity; 3: New). This remember/know procedure closely followed that of previous studies (Gardiner & Java, 1990; Rajaram, 1993; Tulving, 1985). Briefly, participants were instructed to give "Re-experience" responses when they thought that they saw the picture in the previous learning session and can vividly remember it being presented before. If they thought that they saw the picture in the previous learning session because the picture was familiar in that context, but they could not vividly recall the presentation of the picture, they were instructed to give "Familiar" response. If they thought the picture was not presented before, they were instructed to give "New" response. The time limit for this question was 6 seconds. From this retrieval step, I can obtain item familiarity and recollection measures.

Then, at Step 2, the other picture of that retrieval pair was added to form a face-house picture pair. This time participants were required to answer, within 6 seconds, whether both pictures had been presented in the encoding phase, without regard to whether the two pictures had been paired together or not, by pressing one of two number keys on the keyboard (1: Both old; 2: Not both old). By comparing item recognition responses between the intact and recombined pairs, I can
obtain associative familiarity, i.e., associative reinstatement, measure from this step of retrieval (Cohn & Moscovitch, 2007).

If they answered "Both old" at this second step, at the next step they were given 6 seconds to respond whether the pair was intact or recombined, by pressing one of the 3 number keys (1: Intact; 2: Recombined; 3: Don't know). If participants indicated at the second step that the two pictures in the face-house pair were not "both old", they would be asked at the third step whether only one or both pictures in the pair were new, by pressing one of the 3 number keys (1: One new; 2: Both new; 3: Don't know). If the participants indicated the single picture as new at the first step, they would also be directly asked this third question. Because participants need explicitly identify different types of retrieval pairs at Step 3, by comparing "Intact" hit responses for intact and recombined testing pairs, I can obtain associative recollection, i.e., associative identification, measure (Cohn & Moscovitch, 2007).

Similar to the encoding task, face pictures were always presented on the top of the screen. The pairs from each pair type and fame condition were randomized and the participants were given a one-minute break every 24 trials. This task lasted about 30 minutes. Before the start of the real encoding task, 7 practice trials were given using images from the encoding practice trials. It should be noted that participants were instructed to focus on response accuracy, not speed. Because of the complicated nature of the 3-step retrieval task, I only focused on memory accuracy measures in this study, not reaction time measures.

All the analyses were conducted using Matlab (MathWorks, Natick, MA) built-in functions and custom scripts. For specific hypothesis testing, I chose significant level $\alpha = .05$. For exploratory correlation analyses between item and associative memory measures, I used false discovery rate ($FDR$) of .05 to correct multiple testing (Benjamini & Hochberg, 1995). Cohen's $d$ and partial $\eta^2$ were used to reflect effect size for $t$ test and ANOVA, respectively.

### 2.3 Results

#### 2.3.1 Easy/difficult ratings for encoding trials

Before I tested the main hypotheses, first I examined participants' subjective ratings of how easy they found the encoding task in each block and fame condition. On average, 53% the trials in the first encoding block were rated as easy in both the famous ($SD = .13$) and nonfamous ($SD = .19$)
condition. For the second encoding block, 56% of the trials in the famous condition ($SD = .16$) and 59% in the nonfamous condition ($SD = .18$) were rated as easy. A 2 x 2 (fame by block) ANOVA revealed only significant main effects of encoding block, $F(1,28) = 5.57, p = .026, \eta^2_p = .17$, indicating that a higher percentage of trials was rated as easy in the second than the first encoding block. No significant fame main effects ($F(1,28) = .14, p = .71$) or fame by block interaction effects ($F(1,28) = 1.48, p = .23$) were found.

2.3.2 Single face and house recognition

Next, to examine the main research questions, I first tested whether single famous faces were recognized better than nonfamous faces. Specifically, I calculated single face recognition accuracy using participants' responses at the first step of the retrieval task. The hit rate, false alarm, and recognition accuracy (i.e., hit rate - false alarm rate) for recollection and familiarity responses in the famous and nonfamous condition are presented in Figure 2A. Paired t test showed that the recollection accuracy was higher for the famous faces ($t(29) = 5.23, p = .0001, \text{Cohen's } d = .97$). Although the accuracy for familiarity response was higher for the nonfamous faces ($t(29) = 2.30, p = .029, \text{Cohen's } d = .43$), the total recognition performance, after combining the recollection and familiarity accuracy, was still better for the famous faces ($t(29) = 3.68, p = .001, \text{Cohen's } d = .68$. Figure 2A). Moreover, the hit rate of the reported familiarity can underestimate the true familiarity rate because some faces were recognized through both recollection and familiarity but only reported as recollection. I corrected this bias using the formula $F/(1-R)$ ($F$: familiarity rate; $R$: recollection rate) according to (Yonelinas & Jacoby, 1996) and then compared the recalculated familiarity rate for the famous and nonfamous faces. $R$ and $F$ hit rates were changed to .98 and .02 to avoid zero denominator if $R = 1$ and $F = 0$. Paired t test showed that the adjusted familiarity rate for the nonfamous faces was not higher than the famous faces, $t(29) = 1.38, p = .18$, Figure 2A. I also calculated $d'$ scores for the total face recognition memory. When hit rates and false alarm rates were 1 or 0, they were adjusted to .02 and .98, respectively. Similarly, I found that $d'$ scores were higher for famous face than nonfamous face recognition, $t(29) = 3.80, p < .001, \text{Cohen's } d = .71$. Detailed descriptive data and inferential statistics for fame effects are also presented in Appendix Table 1 at the end of this chapter.
**Figure 2.** Hit rates, false alarm rates (FA), and corrected accuracy (Hit - FA) for single face (A) and house (B) familiarity and recollection in the famous and nonfamous condition. Adjusted familiarity was calculated using \( F/(1-R) \), where F and R refer to familiarity and recollection hit rates, respectively. The hit rates, false alarm rates, and corrected accuracy for the two fame conditions after combining the familiarity and recollection responses are also depicted in the embedded bar graphs. In all figures, unless otherwise mentioned, error bars denote 1 standard error of the mean. * \( p < .05 \); ** \( p < .001 \); *** \( p < .0005 \).
I next examined whether the single houses that had been paired with famous faces during encoding were recognized better than those paired with nonfamous faces at the first step of the retrieval task when no face cues are presented. This allowed me to investigate whether the prior-knowledge effects could propagate from the face to the house stimuli. Paired t tests revealed no significant fame effects for recollection accuracy ($t(29) = 1.12, p = .27$), familiarity accuracy ($t(29) = -.48, p = .63$), adjusted familiarity accuracy using $F/(1-R)$ corrections ($t(29) = 1.11, p = .28$), and total accuracy after familiarity and recollection were combined, $t(29) = .51, p = .62$, (Figure 2B). House recognition $d'$ scores also showed no differences between the two fame conditions ($t(29) = .95, p = .35$). Detailed descriptive and condition difference statistics are also given in Appendix Table 2.

### 2.3.3 Associative identification

Next, I tested the main hypothesis of the study, i.e., whether prior-knowledge with famous faces would facilitate associative memory between the face and house. First, I obtained the associative identification measure using participants' *Intact/Recombined/Don't know* responses at the third step of the retrieval task. Specifically, I subtracted the percentage of the recombined face-house pairs that were mistaken as intact pairs from the percentage of the intact pairs that were correctly recognized as intact pairs (Figure 3A). Paired t test showed that associative identification was better for the famous than the nonfamous pairs, $t(29) = 3.24, p = .005$, Cohen's $d = .60$ (Bar graphs embedded in Figure 3A). I also calculated associative identification $d'$ scores using "Intact" responses to intact pairs as hit rates and "Intact" responses to recombined pairs as false alarm rates. Similarly, I found that associative identification $d'$ scores were higher in the famous than nonfamous condition, $t(29) = 3.31, p = .005$, Cohen's $d = .61$. Detailed descriptive data and inferential statistics for fame effects are given in Appendix Table 3.

I next tested whether the recombined pairs with famous faces could also be identified better than those with nonfamous faces. Similarly, I subtracted the percentage of the intact pairs that were mistaken as recombined pairs from the percentage of the recombined pairs that were correctly identified as recombined pairs (bar graphs embedded in Figure 3B). It should be noted that
Figure 3. Associative identification accuracy (Chapter 2)

Figure 3. Associative identification accuracy. A.
Proportion of "Intact" response to each type of retrieval pair. Associative identification accuracy were calculated using "Intact" responses to intact pairs (i.e., hit rate) minus "Intact" responses to recombined pairs (i.e., false alarm rate), is presented in the embedded bar graph. B.
Proportion of "Recombined" response to each type of retrieval pair. Associative identification accuracy was calculated using "Recombined" responses to recombined pairs (i.e., hit rate) minus "Recombined" responses to intact pairs (i.e., false alarm rate), is presented in the embedded bar graph. For A and B, **p < .005; ***p < .0001. C. Relationship (scatter plots and regression lines) between the associative identification scores calculated from the intact (in A) and recombined responses (in B) for the famous and nonfamous condition separately.
because participants were given a response option of "don't know" at the third step of the retrieval task when they were asked to identify a testing pair as "intact" or "recombined, associative identification scores calculated using "Intact" responses and "Recombined" responses were not identical. Indeed, Pearson correlation analyses showed that the two measures were strongly, but not perfectly, correlated, $r(28) = .84$ and $.69$, for the famous and nonfamous condition, respectively, $p = .0001$ (Figure 3C). Therefore, it can be informative to test whether recombined pairs with famous faces were also identified better than those with nonfamous faces. The results supported this prediction and showed that recombined pairs with a famous face were identified better ($t(29) = 4.51, p = .0001$, Cohen's $d = .84$, Figure 3B). Analysis using d' scores revealed the same results, $t(29) = 4.30, p = .0005$, Cohen's $d = .80$. Detailed descriptive data and inferential statistics for fame effects are presented in Appendix Table 4. Taken together, these results supported my hypothesis that prior-knowledge related to famous faces facilitated recollection of newly formed face-house associations.

### 2.3.4 Associative reinstatement

I then investigated whether prior-knowledge with famous faces also facilitated associative memory measured by associative reinstatement procedure. Specifically, I obtained this measure by using the "Both old/Not both old" responses from the second step of the retrieval task. Following (Cohn & Moscovitch, 2007), I subtracted the percentage of the recombined pairs that were correctly recognized as "Both old" from the percentage of the intact pairs that were correctly recognized as "Both old". This method produced a measure that could reflect how the intact pairs, compared to the recombined pairs, can facilitate item recognition (i.e., the face and house recognition), given that both items in the two situations had been learned. The percentage of the "Both old" response for each type of retrieval pairs is presented in Figure 4A. Paired t tests showed that a higher percentage of face and house pictures were recognized in the famous than the nonfamous condition, for both intact ($t(29) = 3.54, Cohen's d = .66, p = .005$) and recombined pairs ($t(29) = 4.57, Cohen's d = .85, p = .0001$). I also found that the associative
Figure 4. Associative reinstatement accuracy (Chapter 2)

Figure 4. A. Percentage of "Both old" responses for different type of retrieval pairs at the second step of the retrieval task. B. Accuracy for associative reinstatement, which was calculated by subtracting percentage of "Both old" responses to recombined pairs from that to intact pairs in A. Associative reinstatement accuracy was larger than zero for both conditions, $p < .005$. C. Face-cued house recognition for the intact and recombined retrieval pairs in the famous and nonfamous condition. No interaction effect was found in the 2x2 ANOVA (fame by pair type). ** $p < .005$; *** $p < .0001$
reinstatement scores, calculated as the difference between the "Both old" hit rates for the intact and recombined pairs, were larger than zero in both the famous and nonfamous condition, $t(29) = 3.18$ and $3.32$, Cohen's $d = .59$ and .62, respectively, $ps = .005$. However, associative reinstatement scores in the two fame conditions were not different, $t(29) = - .66, p = .51$ (Figure 4B). I also calculated $d'$ scores for associative reinstatement by subtracting recognition $d'$ scores for the recombined pairs from those for the intact pairs. Similar nonsignificant results were found, $t(29) = -.19, p = .85$. Detailed descriptive data and inferential statistics for fame effects are given in Appendix Table 5. These results suggested that the familiarity type of associative memory measured this way was not affected by prior-knowledge.

To further confirm this null finding, I reasoned that if there was no prior-knowledge effect on associative reinstatement, cueing effects on house recognition from faces in the intact over recombined pairs should not be different between the famous and nonfamous condition (Kan et al., 2007). To test this, I calculated the accuracy of the "both old" responses at the second step of the retrieval task given that faces had already been correctly recognized. This gave a measure of cued recognition of houses by faces, a process that may underlie the associative reinstatement processing (Kan et al., 2007). False alarm rates for cued recognition were also obtained by calculating the percentage of the new pictures from the half-new and new-new pairs that were mistaken as old at the second step of the retrieval task. The face-cued house recognition measure was calculated separately for the intact and recombined pairs in the famous and nonfamous condition. Then, I used a 2 x 2 repeated-measure ANOVA (fame by pair type) to test whether the house recognition differences between the intact and recombined face cues were larger for the famous than nonfamous condition, i.e., whether there was an interaction effect between fame and pair type. The result was consistent with the previous analysis showing no significant interaction ($F(1,29) = .73, p = .39$). There were only significant main pair type effects ($F(1,29) = 15.49, p = .0005, \eta^2_p = .35$) and fame effects ($F(1,29) = 5.85, p = .023, \eta^2_p = .17$), with higher house recognition accuracy for intact cue condition and famous cue condition (Figure 4C).

Therefore, in contrast to associative identification, results from both analyses showed that prior-knowledge related to famous faces did not enhance the face-house associative familiarity measured by associative reinstatement. The differential prior-knowledge effects on the two types of associative memory were also confirmed by a significant interaction effect in a 2 x 2
ANOVA, with *fame* (famous vs. nonfamous) and *associative memory* (reinstatement vs. identification) as repeated-measure factors, $F(1,29) = 14.69, p = .0006, \eta^2_p = .34$.

### 2.3.5 Correlations among different memory measures

To examine the relationship between the two types of associative memory, I calculated Pearson correlation between associative identification and reinstatement measures. First, I found that associative reinstatement scores were positively correlated with associative identification scores that were calculated using "Intact" responses ($r(28) = .42, p = .02$). However, associative reinstatement measure was not correlated with associative identification measure obtained from "Recombined" responses ($r(28) = -.06, p = .74$, Figure 5A). Analyzing separately the famous and nonfamous condition yielded the same results. Therefore, although the two associative identification measures obtained from "Intact" and "Recombined" responses were highly correlated (Figure 3C), they showed different relationship with associative reinstatement scores. Because only associative identification of intact, not recombined, pairs was correlated with associative reinstatement, these results suggest that identifying intact pairs may also involve associative reinstatement processes, but identifying recombined pairs only involves associative identification processes.

I then explored how familiarity and recollection of single faces and houses were correlated with the two types of associative memory in the two fame conditions. A total of 16 correlations were computed. As mentioned in the Method section, to control for overall type I error for these exploratory analyses, I used false discovery rate (*FDR*) of .05 to ensure that the total false positive findings were below 5% (Benjamini & Hochberg, 1995). The results showed that recollection of single houses was positively correlated with associative identification (Figure 5B) in both the famous ($r(28) = .64, p = .001, FDR = .005$) and nonfamous condition ($r(28) = .59, p = .001, FDR = .005$). Single face recollection was also positively correlated with associative identification in the nonfamous ($r(28) = .66, p = .001, FDR = .005$), but not the famous condition ($r(28) = 16, p = .39, FDR = .52$, Figure 5C). Moreover, single picture familiarity measures were not correlated with associative identification scores (*FDR > .05*), and neither familiarity nor recollection of single pictures was correlated with associative reinstatement (*FDR > .05*). These data indicate that item and associative recollection are closely related, but item and associative familiarity are not.
Figure 5. Correlations among different types of memory measures (Chapter 2)

**A.** Associative reinstatement scores were correlated with associative identification scores calculated using "Intact" responses (left), but not with those calculated using "Recombined" responses (right). Two fame conditions were averaged. **B.** House recollection scores were correlated with associative identification scores in both fame conditions. **C.** Face recollection scores were correlated with associative identification scores in the nonfamous condition (right), but not in the famous condition (left). For **B** and **C,** associative identification scores were calculated using "Intact" responses. Same pattern occurred when using "Recombined" responses. Correlation $p$ values are also presented.
2.4 Discussion

In this study, I tested how prior-knowledge can facilitate associative memory processing. I used a face-house paired-associate task and manipulated prior-knowledge on the face stimuli by using famous and nonfamous faces. Consistent with previous studies, I found that single famous faces were memorized better in this associative memory task. Moreover, I found that prior-knowledge with faces facilitated the recollection type of face-house associative memory, measured by associative identification procedure (Cohn & Moscovitch, 2007). However, associative reinstatement, which reflects associative familiarity processes (Cohn & Moscovitch, 2007), was not affected by prior-knowledge. These findings provide further evidence for the differentiation of the two types of associative memory. In addition, I also found that houses, when presented singly during retrieval, were not recognized better if they had been paired with famous faces during encoding than if they had been paired with nonfamous faces. Although single famous faces were found to be recognized better than nonfamous faces, single famous face recollection memory was not correlated with associative identification scores in the famous condition. Taken together, these data suggest that prior-knowledge facilitates associative recollection mainly by enhancing the face-house associations, not the individual face and house stimuli themselves.

2.4.1 Prior-knowledge effects on face/house item memory

Studies have found that like famous names, famous faces can also elicit rich semantic, social/emotional, and episodic memories related to those famous people (Fairhall & Ishai, 2007; Gobbini et al., 2004; Ishai, 2008; Ross & Olson, 2012; Simmons et al., 2010) which, it is believed, leads to better face memory (Carbon, 2008; Jackson & Raymond, 2008; Johnston & Edmonds, 2009; Kerr & Winograd, 1982; Klatzky & Forrest, 1984; Leveroni et al., 2000; Reder et al., 2013; Rose, Olsen, Craik, & Rosenbaum, 2012; Zion-Golumbic, Kutas, & Bentin, 2009). In this study I also found similar prior-knowledge facilitation effects on single faces in an associative memory task. Specifically, using a remember-know paradigm (Gardiner, 1988; Gardiner et al., 2002; Tulving, 1985; Yonelinas, 1999), I found that famous faces were better recognized through recollection. This result is consistent with the literature showing that prior-knowledge can have facilitative effects on item memory (Hargreaves & Pexman, 2012; Hunt &
Rawson, 2011; Klatzky & Forrest, 1984; Rawson & Van Overschelde, 2008; Rose et al., 2012; Schustack & Anderson, 1979). I also found that face recognition by reported familiarity, i.e., familiarity processes without recollection, was better for the nonfamous than famous faces. However, it is worth mentioning that reported familiarity rate can be underestimated in this type of remember/know paradigm (Yonelinas & Jacoby, 1996). After correcting the possible bias using K/(1-R) corrections, familiarity rate for the famous and nonfamous faces was not different, indicating that this type of prior-knowledge had no facilitation effects on total item familiarity.

I also explored whether prior-knowledge facilitation effects could propagate from face to house stimuli. To this end, I tested whether single houses, without the presence of the paired faces, could be recognized better if the houses had been paired with famous faces during encoding than if they had been paired with nonfamous faces. The results did not show significant fame effects on single house recognition. Therefore, house stimuli themselves may not be processed more deeply when they were paired with famous vs. nonfamous faces. It is likely that participants spent most of their cognitive resources processing face-house associations, not the individual stimuli. Therefore, potential savings on cognitive resources caused by familiar faces cannot benefit the encoding of the individual houses. Item memory tasks in which houses are listed, but not paired, with famous and nonfamous faces can be used to test whether potential cognitive resource saving from familiar faces can enhance item recognition of houses.

2.4.2 Prior-knowledge effects on associative identification

Similar to the dual-processing model of item memory (Yonelinas, 2002), recent studies found that associative memory can also be processed by familiarity and recollection (Cohn & Moscovitch, 2007; Cohn, Moscovitch, & Davidson, 2010; Quamme et al., 2007). However, very few studies have investigated whether multiple-component prior-knowledge can affect both types of associative memory. Therefore, in this study, I first examined prior-knowledge effects on associative recollection, measured by associative identification procedure (Cohn & Moscovitch, 2007). The results showed that prior-knowledge significantly strengthened this recollection type of associative memory. This observation is consistent with previous studies that used linguistic stimuli such as words or proverbs and found facilitation effects of familiar items on source or associative memory (Clark, 1992; Clark & Shiffrin, 1992; Madan et al., 2010; Poppenk, Köhler, et al., 2010).
A number of mechanisms have been proposed to account for prior-knowledge effects. One is that the ease with which familiar stimuli are processed frees processing resources for other operations, leading to better memory for face-house associations in the famous condition (Poppenk & Norman, 2012; Reder et al., 2013). Base on this possibility, I expected that more encoding trials in the famous, compared to the nonfamous, condition should be rated as easy trials, because the famous faces were already familiar to the participants and may require fewer processing resources. However, the results showed that the two encoding conditions were rated equally in terms of their ease of processing. Although these findings can be interpreted as arguing against this proposal, it is possible that participants may have made their ratings mainly based on the relative difficulty of each trial to its adjacent trials within the respective fame conditions, due to the block design used in this study.

Previous memory traces related to famous faces can also provide more potential connections for the face-house associative encoding (Anderson, 1980, 1981; Dragoi & Tonegawa, 2014; Kerr & Winograd, 1982). Moreover, previous episodic or social/emotional memories related to the famous people can lead to deeper evaluative or selective processing in the famous condition (Iidaka, Harada, & Sadato, 2011; Ishai, Schmidt, & Boesiger, 2005; Kim & Johnson, 2012; Singer, Kiebel, Winston, Dolan, & Frith, 2004; Sugiura, Mano, Sasaki, & Sadato, 2010). For example, participants can use their prior-knowledge about a specific famous person to evaluate whether a specific house "fits" that person or whether that person would like or dislike some features of the house. Consequently, the depth of processing can be enhanced by these evaluative processes, or semantic elaborations or mediations, which can lead to better associative binding between the face and house stimuli.

Although the current study was not designed to differentiate these underlying cognitive mechanisms, they can be examined better in vivo using neural imaging methods such as fMRI (Poppenk, McIntosh, Craik, & Moscovitch, 2010; Poppenk & Norman, 2012; van Kesteren, Fernández, et al., 2010). Therefore, it would be interesting to use this face-house paired-associate task in fMRI studies to investigate whether brain regions that support prior social, semantic, and episodic memories will be recruited to a larger extent in the famous encoding condition. These types of results can provide brain level evidence that additional engagement of these memory processing components related to prior-knowledge may support the enhancement of associative memory.
2.4.3 Prior-knowledge effects on associative reinstatement

I also investigated whether prior-knowledge affected associative reinstatement, which may reflect associative familiarity processes. First, using the associative reinstatement measure in (Cohn & Moscovitch, 2007), I found that intact pairs, compared to recombined pairs, facilitated face and house item recognition equally in the two fame conditions, indicating no prior-knowledge effects on associative reinstatement. I also measured associative reinstatement effects as the beneficial effects of face cueing on house recognition from intact over recombined pairs (Kan et al., 2007). Here, too, I found that the gain in house recognition from the intact-pair face cues over the recombined-pair face cues was comparable in the two fame conditions. Therefore, in contrast to associative identification, associative reinstatement was not affected by prior-knowledge. Thus, this study provides further evidence supporting the idea that associative memory can be achieved by different cognitive processes (Cohn et al., 2008, 2009, 2010; Cohn & Moscovitch, 2007; Jou, 2010), one akin to recollection and the other to familiarity. These results also call for future brain level investigations to delineate the neural substrates of the two types of associative processing.

As mentioned earlier, prior-knowledge related to famous faces can lead to deeper processing of face-house associations, compared to the nonfamous encoding condition. Because prior-knowledge only benefited associative identification, not associative reinstatement, and because deep processing has also been found to benefit both associative identification and reinstatement in verbal paired-associate task (Cohn & Moscovitch, 2007), a depth of processing explanation cannot fully account for our results. Associative reinstatement effects in the current study, in contrast to ones using verbal stimuli (Cohn & Moscovitch, 2007), may be predominately perceptual and rely mainly on retaining the perceptual form of the original associations at test. In support of this interpretation, it has been found that familiarity-based associative memory can be mediated by unitization processes in which two members of a pair form a unitized whole stimuli (Clark & Gronlund, 1996; Clark & Shiffrin, 1992; Diana et al., 2008; Ford, Verfaellie, & Giovanelli, 2010; Haskins, Yonelinas, Quamme, & Ranganath, 2008; Murnane, Phelps, & Malmberg, 1999; Quamme et al., 2007). Due to the heavy perceptual components of the current face-house associative memory task, associative reinstatement effects also likely rely more on the perceptual integrity of associative memory, compared to tasks using verbal stimuli (Cohn & Moscovitch, 2007). Thus, although in the famous condition, the face-house associations can be
strengthened by deep processing such as semantic elaborations or evaluative processes, these effects may not operate at the perceptual level and therefore could not strengthen enough the unitized face-house *perceptual* ensemble to affect associative reinstatement. This can be supported by the finding that item familiarity and recollection of house stimuli were not affected by prior-knowledge related to faces. Analyses on the relationship between different memory measures, as discussed below, also provided further support for this interpretation.

2.4.4 Relationship between different memory measures

First, I found that associative identification scores calculated using "Intact" responses were correlated with associative reinstatement scores, suggesting that associative recollection of intact pairs can be accompanied by associative familiarity, similar to item recollection and familiarity processes (Yonelinas, 1999). However, associative identification scores calculated using "Recombined" responses were not correlated with associative reinstatement scores. The two associative identification measures were highly correlated with each other, and both should be valid measures of associative recollection. Therefore, these results suggest that using recombined, instead of intact, testing pairs in an associative identification procedure may allow a better measure of associative recollection that is not contaminated by associative familiarity.

Moreover, I found that recollection of single houses and nonfamous faces was highly correlated with associative identification scores, but familiarity of single houses and faces was not. These observations help to confirm that associative identification, similar to item recollection, indeed reflects a recollection type of memory processes to which item familiarity does not contribute significantly. Interestingly, I found that recollection of famous faces was not correlated with associative identification in the famous condition. Considering that single house recollection was not enhanced by famous faces, these results suggest that prior-knowledge related to famous faces may facilitate associative recollection mainly through strengthening the associations between the faces and houses, not the memory of individual face and house stimuli.

Consistent with this interpretation, I also found that recollection and familiarity of single pictures were not correlated with associative reinstatement, suggesting that single item recollection and familiarity cannot contribute to this type of associative memory. This can also explain why perceptual familiarity related to famous faces did not enhance associative familiarity between the faces and houses.
It is worth mentioning that the 3-step retrieval task used in this study allowed me to explore prior-knowledge effects on different memory measures and the relationship among them. However, it can also create some degree of dependency among these memory measures. Although I cannot exclude the possibility, I think that the main findings of this study are unlikely to be biased by the retrieval procedure. First, correlation analyses showed that item recollection and familiarity at the first step of the retrieval task were not correlated with associative reinstatement scores measured at the second step. Also, if recollection processes of single pictures at the first step had biased the associative reinstatement measure at the second step, we would have observed prior-knowledge facilitation effects on associative reinstatement because more faces were recollected in the famous than nonfamous condition. Moreover, associative reinstatement measured at the second step of the retrieval task should not have serious carry-over effects on associative identification measured at the third step. First, I found that prior-knowledge did not affect associative reinstatement but affected associative identification, which suggests that prior-knowledge effects on associative identification could not be due to its effects on associative reinstatement. Second, the data also showed that when intact pairs were used, associative identification may automatically evoke associative reinstatement processes, resulting in a positive correlation between the two measures. However, when recomposed pairs were used, the effects of associative reinstatement on identification were minimized (i.e., no correlations between the two measures), and I confirmed the prior-knowledge facilitation effects on associative identification.

2.4.5 Conclusion

In this study I found that prior-knowledge related to famous faces enhanced the recollection of face-house associations, but did not have significant effects on associative familiarity. These results provide further evidence for the dissociation of the two types of associative memory. Moreover, I found some evidence showing that prior-knowledge related to famous faces acts mainly on associations between faces and houses to facilitate the face-house associative recollection. Analyzing the relationship between different types of memory measures also informed us that associative reinstatement memory mainly relies on retaining the form of the original associations at test. Using recomposed, rather than intact, responses as a measure of associative identification can avoid contaminations from associative reinstatement. These findings, as well as the paradigm used in this study, may stimulate future research to investigate
how different brain systems support these memory processes and how these different types of memory processes can be affected by different physiological or pathological factors such as aging and neurological diseases.
## 2.5 Appendix Tables

### Appendix Table 1. Single face recognition accuracy: Mean, standard deviation (SD), and statistics for condition (famous vs. nonfamous) difference (Chapter 2)

<table>
<thead>
<tr>
<th></th>
<th>Famous</th>
<th></th>
<th>nonfamous</th>
<th></th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>t</td>
<td>p</td>
<td></td>
</tr>
<tr>
<td>Recollection (R)</td>
<td>.82 (.14)</td>
<td>.59 (.26)</td>
<td>6.02</td>
<td>.0001 *</td>
<td></td>
</tr>
<tr>
<td>Hit</td>
<td>.07 (.10)</td>
<td>.05 (.10)</td>
<td>.99</td>
<td>.33</td>
<td></td>
</tr>
<tr>
<td>Hit - FA</td>
<td>.75 (.14)</td>
<td>.54 (.26)</td>
<td>5.23</td>
<td>.0001 *</td>
<td></td>
</tr>
<tr>
<td>Familiarity (F)</td>
<td>.10 (.11)</td>
<td>.23 (.19)</td>
<td>-4.34</td>
<td>.0002 *</td>
<td></td>
</tr>
<tr>
<td>Hit</td>
<td>.11 (.11)</td>
<td>.15 (.17)</td>
<td>-1.51</td>
<td>.14</td>
<td></td>
</tr>
<tr>
<td>Hit - FA</td>
<td>-.01 (.13)</td>
<td>.08 (.22)</td>
<td>-2.30</td>
<td>.029 *</td>
<td></td>
</tr>
<tr>
<td>Adjusted Familiarity</td>
<td>F/(1-R)</td>
<td>.45 (.35)</td>
<td>.48 (.32)</td>
<td>1.38</td>
<td>.18</td>
</tr>
<tr>
<td>Total recognition</td>
<td>.93 (.08)</td>
<td>.83 (.14)</td>
<td>5.13</td>
<td>.0001 *</td>
<td></td>
</tr>
<tr>
<td>Hit</td>
<td>.18 (.16)</td>
<td>.21 (.20)</td>
<td>-.96</td>
<td>.35</td>
<td></td>
</tr>
<tr>
<td>Hit - FA</td>
<td>.75 (.17)</td>
<td>.62 (.23)</td>
<td>3.68</td>
<td>.001 *</td>
<td></td>
</tr>
<tr>
<td>d'</td>
<td>2.62 (.71)</td>
<td>2.06 (.86)</td>
<td>3.80</td>
<td>.001 *</td>
<td></td>
</tr>
</tbody>
</table>
**Appendix Table 2.** Single house recognition accuracy: Mean, standard deviation (SD), and statistics for condition (famous vs. nonfamous) difference (Chapter 2)

<table>
<thead>
<tr>
<th></th>
<th>Famous Mean</th>
<th>famed Mean</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(SD)</td>
<td>(SD)</td>
<td>t</td>
</tr>
<tr>
<td>Recollection (R)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hit</td>
<td>.54 (.27)</td>
<td>.53 (.20)</td>
<td>.72</td>
</tr>
<tr>
<td>FA</td>
<td>.11 (.12)</td>
<td>.12 (.11)</td>
<td>-.68</td>
</tr>
<tr>
<td>Hit - FA</td>
<td>.43 (.19)</td>
<td>.40 (.17)</td>
<td>1.12</td>
</tr>
<tr>
<td>Familiarity (F)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hit</td>
<td>.28 (.20)</td>
<td>.27 (.19)</td>
<td>.41</td>
</tr>
<tr>
<td>FA</td>
<td>.25 (.19)</td>
<td>.23 (.17)</td>
<td>.84</td>
</tr>
<tr>
<td>Hit - FA</td>
<td>.03 (.16)</td>
<td>.04 (.15)</td>
<td>-.48</td>
</tr>
<tr>
<td>Adjusted Familiarity F/(1-R)</td>
<td>.59 (.30)</td>
<td>.55 (.26)</td>
<td>1.11</td>
</tr>
<tr>
<td>Total recognition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hit</td>
<td>.82 (.15)</td>
<td>.79 (.15)</td>
<td>1.35</td>
</tr>
<tr>
<td>FA</td>
<td>.36 (.22)</td>
<td>.35 (.19)</td>
<td>.30</td>
</tr>
<tr>
<td>Hit - FA</td>
<td>.46 (.20)</td>
<td>.44 (.15)</td>
<td>.51</td>
</tr>
<tr>
<td>d’</td>
<td>1.51 (.67)</td>
<td>1.40 (.47)</td>
<td>.95</td>
</tr>
</tbody>
</table>
**Appendix Table 3.** Mean proportion, standard deviation (SD), and condition comparison (famous vs. nonfamous) statistics of "Intact" responses per pair type (at the third step of the retrieval task) and associative identification measures (Chapter 2)

<table>
<thead>
<tr>
<th></th>
<th>Famous Mean (SD)</th>
<th>nonfamous Mean (SD)</th>
<th>Statistics t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Intact&quot; responses per</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pair type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intact</td>
<td>.56 (.23)</td>
<td>.44 (.23)</td>
<td>3.49</td>
<td>.0015 *</td>
</tr>
<tr>
<td>Recombined</td>
<td>.11 (.10)</td>
<td>.13 (.11)</td>
<td>-.77</td>
<td>.45</td>
</tr>
<tr>
<td>Half new</td>
<td>.02 (.04)</td>
<td>.04 (.05)</td>
<td>-1.80</td>
<td>.08</td>
</tr>
<tr>
<td>New</td>
<td>.00 (.01)</td>
<td>.02 (.04)</td>
<td>-1.76</td>
<td>.09</td>
</tr>
<tr>
<td>Associative Identification</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intact - recombinced</td>
<td>.45 (.26)</td>
<td>.31 (.22)</td>
<td>3.24</td>
<td>.005 *</td>
</tr>
<tr>
<td>d'</td>
<td>1.57 (.92)</td>
<td>1.08 (.70)</td>
<td>3.31</td>
<td>.005 *</td>
</tr>
</tbody>
</table>

*Notes: d' for associative identification was calculated using "Intact" responses to intact pairs as hit rate and "intact" responses to recombinced pairs as false alarm rate.*
Appendix Table 4. Mean proportion, standard deviation (SD), and condition comparison (famous vs. nonfamous) statistics of "Recombined" responses per pair type (at the third step of the retrieval task) and associative identification measures (Chapter 2)

<table>
<thead>
<tr>
<th></th>
<th>Famous</th>
<th>nonfamous</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>t</td>
</tr>
<tr>
<td>&quot;Recombined&quot; responses per pair type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intact</td>
<td>.17 (.11)</td>
<td>.20 (.11)</td>
<td>-1.67</td>
</tr>
<tr>
<td>Recombined</td>
<td>.56 (.18)</td>
<td>.39 (.15)</td>
<td>5.11</td>
</tr>
<tr>
<td>Half new</td>
<td>.13 (.09)</td>
<td>.13 (.10)</td>
<td>-.26</td>
</tr>
<tr>
<td>New</td>
<td>.03 (.04)</td>
<td>.03 (.04)</td>
<td>0.81</td>
</tr>
<tr>
<td>Associative Identification</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recombined - intact</td>
<td>.39 (.24)</td>
<td>.19 (.20)</td>
<td>4.51</td>
</tr>
<tr>
<td>d'</td>
<td>1.22 (.82)</td>
<td>.63 (.69)</td>
<td>4.30</td>
</tr>
</tbody>
</table>

Notes: d' for associative identification was calculated using "Recombined" responses to recombined pairs as hit rate and "Recombined" responses to intact pairs as false alarm rate.
Appendix Table 5. Mean proportion, standard deviation (SD), and condition comparison (famous vs. nonfamous) statistics of "both old" responses per pair type (at the second step of the retrieval task) and associative reinstatement measures (Chapter 2)

<table>
<thead>
<tr>
<th></th>
<th>Famous Mean (SD)</th>
<th>nonfamous Mean (SD)</th>
<th>Statistics t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;both old&quot; responses per pair type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intact</td>
<td>.76 (.17)</td>
<td>.66 (.20)</td>
<td>3.54</td>
<td>.0014 *</td>
</tr>
<tr>
<td>Recombined</td>
<td>.68 (.18)</td>
<td>.56 (.19)</td>
<td>4.57</td>
<td>.0001 *</td>
</tr>
<tr>
<td>Half new</td>
<td>.16 (.10)</td>
<td>.19 (.14)</td>
<td>-1.75</td>
<td>.09</td>
</tr>
<tr>
<td>New</td>
<td>.05 (.05)</td>
<td>.05 (.07)</td>
<td>0</td>
<td>1.00</td>
</tr>
<tr>
<td>Intact d'</td>
<td>2.53 (.85)</td>
<td>2.24 (.70)</td>
<td>2.40</td>
<td>.023 *</td>
</tr>
<tr>
<td>Recombined d'</td>
<td>2.23 (.71)</td>
<td>1.92 (.64)</td>
<td>3.18</td>
<td>.0035 *</td>
</tr>
<tr>
<td>Associative reinstatement</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intact - recombed d'</td>
<td>.08 (.13)</td>
<td>.10 (.17)</td>
<td>-6.66</td>
<td>.52</td>
</tr>
<tr>
<td>Intact - recombed</td>
<td>.30 (.45)</td>
<td>.32 (.52)</td>
<td>-1.9</td>
<td>.85</td>
</tr>
</tbody>
</table>
Chapter 3

Study 2: Prior-knowledge Effects on Associative Encoding

3.1 Introduction

In the behavioral study reported in Chapter 2 (i.e., Experiment 1) I found that prior-knowledge related to famous faces can enhance the recollection of face-house associations. By analyzing the pattern of prior-knowledge effects on, and the correlations among, face/house item memory and face-house associative memory, I also found evidence that prior-knowledge related to famous faces acted mainly on associations between the faces and houses, not on the individual face or house stimuli, to facilitate the face-house associative recollection. These observations confirmed that the face-house associative memory task designed in Experiment 1 succeeded in manipulating multiple component prior-knowledge and revealing the facilitation effects of this type of prior-knowledge on new associative learning. Thus, this behavioral paradigm can now be used in a neural imaging (fMRI) study to investigate how this type of multiple component prior-knowledge exerts its effects on new learning at the brain level.

As mentioned in Chapter 1, comparing to the previous studies using schema-congruency or word-frequency to manipulate prior-knowledge, using famous and nonfamous faces in a face-house associative memory task, allows me to elicit in participants multiple-component prior-knowledge whose representation has been well studied at the brain level. For example, face and house images may be preferably processed in the fusiform face area (FFA) and parahippocampal place area (PPA), respectively (Axelrod & Yovel, 2015; Kanwisher, 2010; Yovel & Freiwald, 2013). Episodic memories related to familiar or famous faces can be supported by the medial temporal lobe (MTL) including the hippocampus (HPC) (Denkova et al., 2006; Douville et al., 2005; Elfgren et al., 2006). The anterior temporal lobe (aTPL) can also support semantic information related to the face, such as the person's name, vocation, or social relationship (Abel et al., 2015; Ross et al., 2010; Ross & Olson, 2012; Tsukiura et al., 2002). Also, affective or social evaluative information related to the faces can be supported by the ventral medial prefrontal cortex (vmPFC) or amygdala (Gobbini & Haxby, 2007; Ishai, 2008; Rolls, 2007; Trinkler, King, Doeller, Rugg, & Burgess, 2009). Therefore, combining this prior-knowledge
manipulation method with the use of a paired-associate task, we can now trace, among these
different brain regions, the effects of the multiple component prior-knowledge during new
associative processing.

To achieve this research goal, in this study I asked participants to associate novel pictures of
houses with those of famous and nonfamous faces in a MRI scanner. I chose the bilateral FFA,
PPA, HPC, aTPL, and vmPFC as our main regions of interest (ROIs) and analyzed fMRI brain
activation data in these regions. As mentioned earlier, the reason that I also included the FFA and
PPA as ROIs is that the two regions differentially process the face and house information,
respectively (Axelrod & Yovel, 2015; Kanwisher, 2010; Yovel & Freiwald, 2013). Moreover,
studies have shown that familiar faces may be processed differently in the FFA, compare to
unfamiliar faces (Gobbini & Haxby, 2006; Liu et al., 2014) and contextual information
associated with familiar people, likely supported by the parahippocampal regions, can be evoked
automatically by familiar faces (Bar, Aminoff, & Ishai, 2008). Thus, examining brain activation
in the FFA and PPA can help us to understand how prior-knowledge could affect early levels of
encoding processes during this associative memory task. Because the activation of these five
regions may reflect different aspects of associative processing, by comparing the famous and
nonfamous condition, I can examine how prior-knowledge related to famous faces affected the
different components of associative processing. In general, I hypothesize that prior-knowledge
may trigger additional evaluative, semantic, or episodic-binding processes, mainly supported by
the vmPFC, aTPL, and HPC, to facilitate new memory encoding.

More specifically, I hypothesized that during face-house associative encoding, the vmPFC,
aTPL, and HPC should show stronger activation when famous faces were involved, reflecting
the facilitation effects from the components of prior-knowledge supported by these brain regions.
Within the famous condition, I also examined how participants' prior-knowledge with famous
faces, such as emotions, vivid memories, general familiarity, and attractiveness, could modulate
brain activation in these ROIs. I predicted that the HPC, aTPL, and vmPFC should show stronger
activation for the trials in which famous faces elicited stronger prior memories and emotions, and
for trials in which the face-house associations were later remembered, compared to the later
forgotten trials.
I also examined prior-knowledge effects on the HPC connectivity with other ROIs. Because the vmPFC, aTPL, and HPC may support social evaluative, semantic, and episodic aspect of prior-knowledge, respectively, I hypothesized that the HPC should show stronger connectivity with the aTPL and vmPFC when prior-knowledge is involved, especially for the successful encoding trials. The HPC connectivity with the posterior perceptual regions may be stronger in the nonfamous condition because, without prior-knowledge, face-house associative encoding would rely primarily on perceptual binding processes (Eichenbaum et al., 2007).

3.2 Method

3.2.1 Participants

Twenty healthy young adults (12 females), between 18-24 years of age (Mean = 21.3, SD = 1.9), all right-handed and native English speakers, were recruited from the University of Toronto’s St. George campus. All participants were free of current, and past, psychiatric/neurological conditions. The participants were paid $76 and gave their informed consent. The study was approved by the Research Ethic Board at Baycrest Centre for Geriatric Care (University of Toronto).

3.2.2 Procedure

Overview of fMRI tasks. The scanned session consisted of several components (Figure 1A): following a structural MRI scan, there was a 6-minute rest period in which participants were asked to relax with their eyes closed. Participants then performed the face-house associative encoding task, for one of the fame conditions, twice, in each of two consecutive runs. Following this encoding task, there was another 6-minute rest period. Participants then similarly performed the associative encoding task for the other fame condition twice in two consecutive runs, following which there was a third 6-minute rest period. The three 6-minute resting scans were designed for Experiment 3 (Chapter 4). After this, a face/house localizer task was administered. Total time for the scanned session was about 1.5 hours (which included two final resting tasks that were not part of this dissertation research project). After the MRI session, participants were asked to perform a multi-step retrieval task in another testing room. The average time delay between the encoding and the retrieval tasks was 54.4 mins (SD = 4.5 mins).
Figure 1. Schematic of experimental design (Chapter 3)

A. Task sequence

B. Encoding trials

C. Retrieval trials

Figure 1. Schematic of experimental design. A. The sequence and approximate time length of the tasks in Experiment 2 and 3. B. Representative face-house encoding trials for the famous and nonfamous condition (upper) and control trials, i.e., scrambled pictures trials (lower). For the face-house trials, participants needed to imagine and memorize the two pictures together and indicate whether it was easy or not to do so. For the scrambled picture trials in both famous and nonfamous condition, participants needed to distinguish the pattern of the two pictures and indicate whether it was easy or not to do so (details see Method section). C. Typical retrieval trials for the famous and nonfamous condition. (Image sources: same as Study 1)
Stimuli. Similar to Experiment 1, for the associative encoding task, 192 colour pictures of Caucasian faces (210 x 300 pixels) and 192 of houses (350 x 300 pixels) were obtained from the Internet using Google Image Search. Half of the face pictures were of famous actors, whose names were obtained from a list of top actors (ranked by a website based on averaged domestic box office gross http://www.the-movie-times.com/thrsdir/actors.mv?actors+ByAG), and the other half, of nonfamous people. Gender was balanced for both famous and nonfamous faces. Among the 96 famous face pictures, 60 (30 females) were used in the scanned encoding task and each was paired with a house picture randomly chosen from the house picture set. Similarly 60 nonfamous face-house picture pairs were created for the nonfamous condition. The remaining pictures were used as foils in the retrieval task. I also created 72 pairs of scrambled pictures for control trials, by scrambling (in 10 x 10 pixel tiles) randomly selected original face and house pictures. Therefore, each pair of scrambled pictures consisted of one scrambled picture that was the same size as the face picture (210 x 300 pixels) and the other the same size as the house picture (350 x 300 pixels). In 20 (out of the 72) scrambled-picture pairs, the scrambled pattern of one picture was obtained by re-scrambling the pattern of the other picture to make the patterns of the two scrambled pictures in these pairs similar and difficult to distinguish. This was to make some control trials difficult (see next section). The luminance and contrast of pictures of the same size (e.g., the face and face-size scrambled pictures) were set to be equal using SHINE toolbox (Willenbockel et al., 2010) and custom scripts in Matlab (MathWorks, Natick, MA).

For the retrieval task, similar to Experiment 1, there were 4 types of face-house pairs: intact, recombined, old/new, and new-new pairs. Each type had 24 pairs for each fame condition. The intact pairs were randomly selected from the encoding pairs in each fame condition, with gender balanced. The recombined pairs were made by cross-pairing the face and house (i.e., the face of pair A paired with the house of pair B, and vice versa) in another set of 24 pairs that were randomly selected from the rest of the encoding pairs. To make the 24 old/new pairs, the remaining 12 encoding pairs were split and then paired with new house and face pictures, respectively. This produced 12 old face - new house and 12 new face - old house pairs (all called old/new pairs). The first and last two encoding pairs (4 in total) in each fame condition were always chosen to make the old/new pairs in order to exclude these pairs from the final associative memory performance calculation. The 24 new-new pairs were made by pairing the rest of the face and house pictures in the original picture set (i.e., those not used during
encoding). In total, there were 192 face-house pairs in the retrieval task. All pictures were randomized across participants.

**fMRI face-house associative encoding task.** There were 4 encoding runs in total, with 2 consecutive repeated runs (with same picture pairs) for each fame condition. Each run had 60 face-house trials and 36 scrambled picture trials.

In each face-house trial of this intentional encoding task (Figure 1B), first, a face-house picture pair was presented for 3.5 seconds, with the face on the top of the screen, the house at the bottom, and a cross “+” in between. Participants were required to look at the face-house pictures, and imagine and memorize as vividly as possible that the person (of the face) was standing in front of the house. Then, while the pictures were still on the screen, the words “Easy” and “Not easy” appeared for 1.5 seconds. Participants needed to press one of two buttons to indicate whether it was easy (or not easy) for them to imagine the associated pair. Finally, before the onset of the next trial, a jitter time of 1 – 4 seconds (with an exponential distribution across trials and mean time of 1.5 seconds) elapsed with only the "+" on the screen.

In addition to the 60 face-house picture trials, there were 36 scrambled picture-pair control trials with the same picture sizes, locations, contrast, and luminance (as the face-house trials). The presentation duration of the scrambled picture pairs was reduced to 1.5 seconds, and participants responded whether it was easy (or not easy) for them to differentiate the patterns of the two scrambled pictures when the words "Easy" and "Not easy" appeared. Except for these differences, the scrambled picture pair trials were identical to the face-house pair trials.

To make an efficient event-related experimental design, the 36 scrambled-picture pairs were pseudo-randomly dispersed into the 60 face-house pairs using an optimization method (Birn, Cox, & Bandettini, 2002; Dale, 1999). Specifically, 50,000 sequences were randomly generated with the first and last two positions of the sequences always given to face-house pairs as fillers. Then the sequence that most efficiently detected the contrast effect between the face-house vs. scrambled trials was chosen.

Both fame conditions used the same event-related design with identical presentation sequence. The 2 repeated encoding runs within each fame condition also used the same sequence, but for each encoding run the face-house and scrambled picture pairs were randomly assigned to the
sequence so that the order of the picture pairs was different across the two repeated runs. The first and last 2 face-house pairs were used as fillers and were not changed across the repeated encoding runs. To keep approximately the same time interval during which a specific picture pair was re-encoded, the random assignment of the face-house picture pairs to the presentation sequence was conducted within small groups of pictures. Specifically, first, the 56 face-house picture pairs (60 - 4 fillers = 56) in each fame condition were divided into 6 groups, with pair 1-9 being assigned to group 1, pair 10-18 to group 2, ..., and pair 46-56 to group 6. Then, for each repeated encoding run, the 9 pairs in group 1 were randomly re-assigned to the first 9 face-house trials in the presentation sequence, the 9 pictures in group 2 were randomly assigned to the next 9 face-house trials, and so on, until the last 11 pictures in the last group, which were randomly assigned to the last 11 trials in the sequence. The same method was used for the scrambled-picture pairs with 6 pairs per group.

Half of the participants performed the famous condition first, in 2 consecutive fMRI runs, and then performed the nonfamous condition twice (AA-BB order). The order was reversed (BB-AA order) for the other half of the participants. This counter-balanced design can significantly reduce potential confounding effects caused by the sequence of the tasks in the whole fMRI session or eliminate them entirely. It should be noted that the use of repeated encoding was to boost memory performance because a behavioral pilot study showed that the encoding task was difficult. The total time needed for each run was about 10 minutes. There was a 1 minute interval between the repeated encoding runs in each fame condition and a 6 minute rest interval between the two fame conditions. Participants were given 10 practice trials in the scanner with additional pictures before the first scanned encoding run started.

**Localizer scan task.** A block design was used for the face/house localizer scan, with 6 blocks for each of three picture categories: faces, houses, and objects. To reduce potential interference effects from the localizer task on the later memory retrieval of the main encoding task, a different set of face and house pictures was used. Specifically, 72 computer-generated face pictures, 72 multi-floor building pictures, and 72 common objects (furniture, toys, utensils, etc) were used. All pictures were black-and-white with a gray background and the size of 400 x 350 pixels. The luminance and contrast were also balanced across all pictures. In each picture-category block, 14 pictures were presented sequentially, with onset duration of 650 ms followed by a 550 ms fixation time per picture. Among the 14 pictures, 2 pictures were repeated and the
participants were asked to perform a 1-back task in which they needed to press a button whenever they saw the repeated pictures. Each picture block was also followed by a fixation (baseline) block of the same duration (i.e., 16 seconds). The order of the face, house, and object blocks was pseudo-randomized with the condition that the same category block would not repeat consecutively. This task lasted about 10 minutes.

**Unscanned retrieval task.** After the fMRI scan, participants completed a retrieval task in another testing room. The retrieval task was identical to that in Experiment 1. For completeness, this 3-step retrieval trial (Figure 1C) is re-described here. First, a single picture (face or house) of a face-house retrieval pair was presented, with faces being presented first in half of the trials for each pair type. Participants were asked to indicate whether they could recognize the single picture by pressing one of 3 number keys on the keyboard using a Recollection/Familiarity paradigm (1: Re-experience, 2: Familiar, and 3: New). Then, the other picture of the retrieval pair was added to form a face-house pair. This time participants needed to respond whether both pictures had been presented in the encoding phase by pressing one of two number keys (1: Both old and 2: Not both old). If they answered "Both old", at the next step they would be asked whether the pair was intact or recombined, by pressing one of the 3 number keys (1: Intact, 2: Recombined, and 3: Don't know). If at the second step participants responded “Not both old”, they needed at the third step to answer whether one or both pictures in the pair were new, by pressing one of the 3 number keys (1: One new, 2: Both new, and 3: don't know). Similar to the encoding task, face pictures were always presented on the top of the screen. The pairs from the 4 retrieval pair types and 2 fame conditions were randomly presented. This retrieval task lasted about 30 mins.

It should be mentioned that this study mainly focused on the associative memory measures derived from the last step of the retrieval task (i.e., the associative identification measure). Other measures obtained from the first two steps of the task were used for other purposes and not analyzed in depth in this study.

**Face evaluation.** After the retrieval task, participants were asked to evaluate the famous face pictures that had been used in the associative encoding task on familiarity, attractiveness, emotion, and memory using 5-point scales. Specifically, I instructed the participants to give a number, from 1 to 5, to indicate how familiar they were with those faces (familiarity), how
attractive they thought the faces were *(attractiveness)*, how strongly the faces evoked emotions or emotional opinions *(emotion)*, and how vividly memory of previous experiences were triggered by the faces *(memory)*. For the first 3 evaluation tasks, nonfamous faces were also added as fillers. Face pictures were randomized across both the evaluation tasks and participants. The order of these tasks was also randomized across participants. The tasks were self-paced, with each about 5 mins long.

### 3.2.3 Structural and functional MRI scan

A 3T Siemens MRI scanner with a standard 12-channel head coil at the Baycrest Hospital (University of Toronto), was used to acquire MRI images. Head movements were minimized by inserting soft cushions into the head coil. In the structural MRI scan, T1-weighted high-resolution MRI volumes were obtained using a standard 3-dimentional MPRAGE (magnetization-prepared rapid-acquisition gradient echo) pulse sequence (160 slices; field of view (FOV) = 256 x 256 mm; 192 x 256 matrix; 1 mm isotropic resolution, TE/TR=2.63/2000 ms, flip angle = 9 degrees, and scan time = 386 s). For the functional MRI scan, blood oxygenation level-development (BOLD) signal was assessed using T2-weighted EPI acquisition procedure with TE = 24 ms, TR = 2000 ms, 3.5 mm slices (with 0.5 mm gap and a bottom-up interleaved order), and flip angle = 70° (FOV = 200 x 200 mm; 64 x 64 matrix, 3.5 x 3.5 mm in-plane resolution). To reduce fMRI signal drop in the ventral medial prefrontal regions, the images were acquired in an oblique orientation 30 degree clockwise to the anterior - posterior commissure axis. T1 images acquisition used the same slice orientation. Visual stimuli were presented by E-Prime software (version 2, Psychology Software Tools, Inc.), back-projected to a screen, and viewed with a mirror mounted on the head coil. Responses were collected with an MRI-compatible response box.

### 3.2.4 fMRI data preprocessing

SPM8 (Statistical Parametric Mapping, Welcome Trust Center for Neuroimaging, University College London, UK; www.fil.ion.ucl.ac.uk/spm/, version 4661) in the MATLAB environment (MathWorks, Natick, MA) was used to preprocess the T2-weighted functional images. First, for each participant, several raw images were randomly selected from each run for quality check and no obvious fMRI artifacts were found for any participants. Then, slice timing was corrected using sinc-interpolation with the midpoint slice as the reference and all functional images were
aligned using a 6-parameter linear transformation. Next, anatomical images were co-registered to the aligned functional images, and segmented into white matter (WM), gray matter (GM), and cerebrospinal fluid (CSF) using SPM8 default tissue probability maps. These segmented images were then used to calculate the transformation parameters mapping from the individuals' native space to the MNI template space. Next, the resulting transformation parameters were used to transform all functional images to the MNI template. The final functional images were resampled at 2 x 2 x 2 mm resolution and smoothed using a Gaussian kernel with the FWHM (full-width at half maximum) of 8 mm. The first 3 fMRI volumes from each run were discarded to reduce the effects of magnetic field inhomogeneity.

3.2.5 fMRI analysis

**Overview:** First, SPM8 voxel-wise general linear model (GLM) was used to estimate all the contrasts of interest at the first (i.e., individual) level analysis. Because I hypothesized that specific brain regions, i.e., the vmPFC, aTPL, HPC, PPA, and FFA, should be differentially affected by prior-knowledge, I then conducted ROI analyses (ROI details described in *ROI definition* section) at the group level to test our hypotheses. Specifically, using Marsbar toolbox for SPM8 (Brett, Anton, Valabregue, & Poline, 2002) (http://marsbar.sourceforge.net/), I calculated mean values of the contrast estimates across each ROI from the first level contrast images and subjected the mean values to the second level one sample *t* tests to test whether these mean contrasts were greater than zero. To provide more data for potential future data synthesis, I also presented the SPM whole-brain voxel-wise results in Supplementary Tables at the end of this chapter.

As mentioned earlier, repeated encoding was used in this study to boost memory performance. However, the literature has shown that repetition of stimuli may change neural responses (Grill-Spector, Henson, & Martin, 2006; Hargreaves, Mattfeld, Stark, & Suzuki, 2012; Henson, Shallice, & Dolan, 2000; Johnson, Muftuler, & Rugg, 2008; Kremers et al., 2014; Kumaran & Maguire, 2009; Manelis, Paynter, Wheeler, & Reder, 2013; Suzuki, Johnson, & Rugg, 2011; Vannini, Hedden, Sullivan, & Sperling, 2013; Yanike, Wirth, Smith, Brown, & Suzuki, 2009). Therefore, although repetition effects were not the aim of this study and I focused mainly on the results from the two encoding runs combined, I also presented results for individual encoding
runs and tested repetition effects when the results for two encoding runs were significantly different.

It is also worth mentioning that the face-house associative task used in this study was mainly a visual-spatial task, which may recruit the right hemispheric ROIs to a larger extent, compared to tasks using semantic or verbal stimuli (de Schotten et al., 2011; Hervé, Zago, Petit, Mazoyer, & Tzourio-Mazoyer, 2013; Kelley et al., 1998). However, prior-knowledge elicited by famous faces can contain rich social semantic information, which has been found to engage predominantly the left hemisphere (Gainotti, 2011; Hervé et al., 2013; Ross & Olson, 2012). In the face processing literature, there is also evidence showing that the left and right aTPL and FFA may support different types of face-related information (Gainotti, 2007; Heide, Skipper, & Olson, 2013; Meng, Cherian, Singal, & Sinha, 2010, 2012; Yovel, Tambini, & Brandman, 2008). Due to the potentially complex laterality effects involved in this task, I treated all the left and right side ROIs separately. However, laterality effect itself was not the aim of the current study.

**Encoding effects.** First, to test brain activation differences between different encoding conditions (i.e., house-face vs. scrambled pictures or famous vs. nonfamous pairs), at the individual-level GLM analysis, I concatenated all 4 encoding runs, i.e., the first and second encoding run in the famous and nonfamous conditions. In the event-related design matrix, I added trial onsets of the face-house picture and the scrambled picture trials, convolved with the SPM8 canonical hemodynamic response function (HRF) and its time derivative as separate regressors in each run. Therefore, there were 16 regressors of interest in total, with 4 regressors in each run. I also included 6 motion parameters obtained from the image alignment processing, as well as the linear drift and mean activation for each run, as regressors of no interest. Default high pass filter with cutoff of 128 seconds was applied. A first-order autoregressive model AR(1) was used to account for the serial correlation in fMRI time series in the restricted-maximum-likelihood estimation of the GLM. I constructed two contrasts using only HRF convolved regressors at the first level analysis: First, to identify brain regions that were commonly engaged by our associative encoding task (i.e., the main effect of picture type), I constructed a \( t \) contrast to compare the face-house encoding trials with the scrambled picture trials while collapsing the two fame conditions. Second, for the main hypothesis testing of prior-knowledge (i.e., the face fame) effects during the associative encoding, I constructed a fame by picture type interaction \( t \) contrast to compare the face-house encoding trials in the two fame conditions while controlling
for the scrambled picture trials in each condition. For these analyses, the two repeated runs were included and given the same weight. The contrast images obtained from the first level analyses were then used in group-level ROI and voxel-wise one sample t tests (with participants as a random factor).

**Prior-knowledge modulation effects within the famous condition.** Second, I conducted SPM8 parametric modulation analyses to examine whether the brain regions that showed stronger activation in the above-mentioned famous vs. nonfamous contrast analysis also showed stronger activation for the encoding trials in the famous condition where famous faces were reported to elicit more/stronger prior-knowledge. These analyses could help us to confirm whether the fame effects obtained from the famous vs. nonfamous contrast were indeed related to participants' prior-knowledge even within the famous condition. Specifically, I used ratings of familiarity, emotion, memory, and attractiveness to assess the strength of participants' prior-knowledge associated with the faces. The parametric modulation analysis was conducted separately for the 4 types of face ratings. In each individual-level parametric modulation analysis, I first concatenated the 4 encoding runs as I did in the previous analysis. Then I included 8 HRF-convolved regressors, with one regressor for the face-house encoding trials and one for the scrambled picture trials for each encoding run in each fame condition. For the famous condition, I then included a parametric modulation regressor for each run using trial-by-trial famous face evaluation scores. Because these ratings may not necessarily have linear modulation effects and the contrast effects between strong and weak prior-knowledge, rather than the linearity of the modulation effects, are more relevant for the purpose of this study, I re-coded the face evaluation scores into binary contrast scores with the original score of 1, 2, 3 being re-coded as -1 (i.e., weak prior-knowledge) and 4 and 5 as 1 (i.e., strong prior-knowledge). I categorized trials with rating of 3 into "weak prior-knowledge" trial group because whether the rating score of 3, which is at the middle point of the rating scale, can reflect strong rating responses was not certain. This re-coding also simultaneously resulted in acceptable trial counts for all 4 rating dimensions: Mean trial counts for weak and strong prior-knowledge ratings were 37.9 and 18.1 for emotion, 33.8 and 22.2 for memory, 19.5 and 36.5 for attractiveness, and 29.4 and 26.6 for familiarity (total trials number = 56. Four filler trials were not counted). Regressors of no interest were identical to those in the previous analysis. A t contrast that averaged the two parametric modulation regressor estimates (for the two repeated runs in the famous condition) was used to
investigate the prior-knowledge modulation effects. The parameter modulation contrast images at the first-level were then used in the second-level ROI and voxel-wise one sample $t$ tests.

**Subsequent memory effects.** Third, to examine whether the brain regions showing stronger activation in the famous encoding condition indeed played a role in the associative memory formation, I conducted another parametric modulation analysis to examine the subsequent memory effects in the famous condition. The design matrix was similar to the above-mentioned face evaluation parametric analysis except that the parametric modulators were constructed from memory performance data and two more parametric modulator regressors were added for the nonfamous condition. Specifically, the encoding trials that were used as intact pairs in the retrieval condition, and were indeed correctly identified as intact pairs by the participants, were coded as 1 (i.e., remembered). For the encoding trials that were used as recombined pairs in the retrieval, if both the cross-recombined pairs were correctly identified as recombined pairs, indicating a high likelihood that the participant remembered both of the two original pairs, these recombined pairs were also coded as 1 (i.e., remembered). All other pairs were coded as -1 (i.e., forgotten). This resulted in an average of 16.1 trials/run x 2 runs = 32.2 remembered trials, ranging from 6 to 66 trials, and 43.9 trials/run x 2 runs = 87.8 forgotten trials, ranging from 54 to 114 trials. Only one participant had less than 10 remembered trials. Then, $t$ contrast images from the first level analysis that averaged the two parametric modulation regressor estimates (for the two repeated runs in the famous condition) were used in the ROI and voxel-wise one-sample $t$ test at the second level analysis.

It should be noted that this parametric modulation analysis on subsequent memory effects should be equivalent to the analysis in which parameter estimates of beta values are obtained separately for the remembered and forgotten trials at the individual level, and then compared at the group level. Because I was interested in brain activation differences between the two types of trials, I chose to obtain directly their contrast values for simplicity of data presentation. However, parameter estimates for the remembered and forgotten trials separately were also given as supplementary material at the end of chapter (also see Results section).

**Fame effects on hippocampal connectivity.** Fifth, to investigate the brain connectivity differences between the famous vs. nonfamous encoding condition, I conducted a psychophysiological interaction (PPI) analysis using SPM and the generalized PPI toolbox
(Friston et al., 1997; McLaren, Ries, Xu, & Johnson, 2012), with the HPCs as seed regions. For the HPC seeds, only voxels within the structural HPC masks, defined by the Automated anatomical labeling (AAL) template (Tzourio-Mazoyer et al., 2002), that survived the threshold of \( p = .0001 \) (no correction) in the face-house vs. scrambled pictures contrast (mentioned in the first analysis) were included. In the PPI analysis procedure, time series data (i.e., the first eigenvalue) were extracted from the seed region and deconvolved with the HRF to reflect its corresponding neural events (Gitelman, Penny, Ashburner, & Friston, 2003). Then, interaction terms were formed between the deconvolved time series and all other condition regressors (McLaren et al., 2012). Finally, these interaction terms, as well as the seed region time series data, were added to the original univariate design matrix. Therefore, in each PPI GLM analysis design matrix, in addition to the 8 original HRF-convolved regressors, there were 8 corresponding PPI regressors (one for the face-house encoding trials and one for the scrambled picture trials for each encoding run in each fame condition) and one seed (i.e., the HPC) time-series regressor. Other regressors of no interest were identical to those in the univariate analysis.

A similar fame by picture type interaction \( t \) contrast was used to detect connectivity differences between the famous and nonfamous encoding conditions while controlling for the scrambled picture trials in each condition. The contrast images from the first level analysis were then used in the second level ROI and voxel-wise one-sample \( t \) test.

**Subsequent memory effects on hippocampal connectivity.** Next, to test the hypothesis that the stronger connectivity of the HPC with anterior brain regions (e.g., aTPL and vmPFC) in the famous condition would facilitate associative memory formation, I conducted another PPI analysis to examine the subsequent memory effects of the HPC's connectivity, i.e., to test whether the connectivity of the HPC with the aTPL and vmPFC would be stronger for the later remembered than forgotten face-house pairs during the famous encoding condition. In this analysis, I used the identical design matrix as I did in the previous PPI GLM analysis except that all the encoding trials (for both famous and nonfamous condition) were separated into later remembered and forgotten trials. Then a PPI regressor was formed for each of the 12 condition regressors (one for remembered face-house trials, one for forgotten face-house trials, and one for scrambled picture trials in each run and fame condition). In this analysis, I focused on the famous condition. Therefore, a contrast that compared the remembered and forgotten trials in the two runs of the famous condition was estimated in the first level GLM analysis. Similar to the
previous analysis, these contrast images were then used in the second level ROI one-sample *t* test.

**Hippocampal connectivity predicting memory performance across participants.** Finally, I explored *across participants* how the HPC connectivity was associated with associative memory performance. The motivation of this analysis was based on a previous study that found that the HPC connectivity with the vmPFC was associated with memory performance differently depending on whether prior-knowledge was involved (van Kesteren, Fernández, et al., 2010). In this second-level regression analysis, I used the first-level contrast images from the first PPI GLM analysis, i.e., the HPC connectivity contrast between the face-house encoding trials and the scrambled picture trials (for each fame condition separately) as the dependent variable. The associative memory performance, calculated by subtracting the false alarm rate, i.e., the percentage of the recombined retrieval pairs that were mistaken as intact pairs, from the hit rate of the intact pairs, was used as the independent variable of interest. Participants' age and the fame order during encoding (i.e., the block order of AABB or BBAA) were included as covariates. Potential fame order effects were also covaried out from the associative memory performance measure. The regression analysis was conducted separately for the famous and nonfamous condition.

**ROI definition.** Automated anatomical labeling (AAL) template (Tzourio-Mazoyer et al., 2002) and the WFU-Pickatlas toolbox (Maldjian, Laurienti, Kraft, & Burdette, 2003) were used to generate structural ROI masks for the vmPFC, aTPL, and HPC (Figure 2). The vmPFC mask consisted of the gyrus rectus and the medio-orbital section of the frontal gyrus. The aTPL mask consisted of the temporal pole region of the superior and middle temporal gyrus. For the PPA and FFA regions, I generated bilateral functional ROI masks using the analysis of the localizer task (see Figure 2). The preprocessing procedure was identical to the main encoding task. In the first level analysis, a block-design GLM was used. Specifically, a boxcar function (16 s) convolved with the canonical HRF was used for each of the 3 picture blocks (faces, houses, and objects) and all fixation blocks. I also included 6 motion parameters and the total
Figure 2. The surface and section views of the 5 regions of interest (ROIs) (Chapter 3).

*Note:* All surface views in this study were generated using BrainNetViewer http://www.nitrc.org/projects/bnv/.
mean as the regressors of no interest. Default high pass filter with cutoff of 128 seconds was applied and a default autoregressive model AR(1) was used. I then used the face vs. house contrast and house vs. face and object contrast to localize the FFAs and PPAs, respectively. These contrast images were then used in the second level one-sample t-tests. Both the FFAs and PPAs were easily identified in the fusiform and parahippocampal gyrus at the threshold of $p = .005$, with 10-voxel extension. To make the final functional ROI masks, I took a small volume correction using a spherical volume with 8 mm radius around the maximum activation voxel (left FFA: [-42 -50 -26], right FFA: [44 -52 -18], left PPA [-28, -40 -10], and right PPA [24, -40 -10]: see Figure 2).1

**Statistical thresholding.** As mentioned earlier in this section, group level one-sample $t$ tests were used to test all hypotheses regarding condition differences (i.e., famous - nonfamous condition). These one-tailed $t$ tests (with $df = 19$, unless otherwise mentioned), as specified by default in SPM group-level analysis, were appropriate for testing all a priori directional hypotheses of this study (specified at the end of the introduction section). Statistical significance level $\alpha$ was set at .05 for these ROI analyses.

However, in this study, most of the hypotheses that I made on the neural mechanism of prior-knowledge facilitation effects simultaneously involved 5 bilateral ROIs. Consequently, for each interested contrast, ten one-sample $t$ tests were conducted. Thus, a more stringent statistical threshold may be preferable, considering that prior-knowledge effects on all these ROIs have not been simultaneously tested by previous studies using the same paradigm as used in the current study. Therefore, when all 10 ROI $t$ tests were simultaneously conducted for a specific contrast effect, I used false detection rate (FDR) of .05 to ensure that the total false positive findings from these tests were below 5% (Benjamini & Hochberg, 1995). Effects with $p < .05$, but $FDR > .05$

1 It should be noted that using contrast of face vs. house and object can localize the same FFA cluster, but the threshold need to be lowered to $p = .05$. 
and < .1, were reported as marginally significant (i.e., trend level) effects and interpreted with caution.

Finally, I also added results from whole brain voxel-wise analyses into supplementary tables. These results are thresholded at \( p = .005 \) with 10 voxel extension to facilitate future meta-analysis (Lieberman & Cunningham, 2009). To find the anatomical labels for all activated regions in each analysis, I used the automated anatomical labeling (AAL) toolbox (Tzourio-Mazoyer et al., 2002). This statistical threshold was also used to produce brain section or surface plots only for illustration purposes.

### 3.3 Results

#### 3.3.1 Behavioral results

Associative memory accuracy was calculated by subtracting the false alarm rate, i.e., the percentage of the recombined trials that were mistaken as intact pairs, from the hit rate of the intact pairs. A paired \( t \) test showed that associative memory accuracy was higher in the famous than nonfamous condition \( (t(19) = 4.60, p = .0002. \) Figure 3). I also calculated memory performance for single face and house pictures. The hit rate was calculated as the percentage of the face or house pictures that were correctly recognized from all three steps of the retrieval task. The false alarm rate was the percentage of the new pictures that were mistaken as old pictures. The results showed that memory of both faces and houses was better in the famous than nonfamous condition \( (t(19) = 5.32, p < .0001 \) for face memory and \( t(19) = 2.52, p = .021 \) for house memory. Figure 3).

#### 3.3.2 fMRI results

**Encoding effects: House-face pairs vs. scrambled pictures.** First, to test whether the associative memory encoding task used in this study recruited our predefined ROIs, I contrasted the face-house pairs in the two fame conditions with the scrambled picture pairs. After combining the two encoding runs, I found that the left vmPFC, bilateral HPC, PPA, and FFA were more strongly activated in the face-house encoding condition than the scrambled picture condition, \( FDR = .0001 \sim .005 \) (see Figure 4 for detailed statistics). The right vmPFC and bilateral aTPL did not show significant encoding effects, \( p = .11 \sim .55, FDR > .05 \).
Figure 3. Prior-knowledge (i.e., fame) effects on memory performance. (Chapter 3)

Figure 3. Prior-knowledge (i.e., fame) effects on face-house associative memory and face and house item memory.

In all figures, unless otherwise mentioned, error bars denote 1 standard error of the mean.
Figure 4. Bar graphs showing associative encoding effects (face-house > scrambled) in each predefined ROI (Chapter 3)

Figure 4. Bar graphs showing associative encoding effects (face-house > scrambled) in each predefined ROI. ** indicates false detection rate (FDR) < .00001; * indicates FDR < .005. \( t \) statistics and \( p \) values from one sample \( t \) tests (for ROIs that survived FDR correction) are also indicated. For illustration purposes only, the embedded brain section views show the voxels or clusters in the bilateral PPA, FFA, HPC, and right vmPFC that survived \( p < .005 \), with 10 voxel extension, no correction. It should be noted that although the bilateral aTPL and right vmPFC did not show significant encoding effects when the two encoding runs were combined, the left aTPL and right vmPFC showed significant encoding effect during the first encoding run (FDR < .05, see Supplementary Figure 1).
I also checked the encoding effects in the two encoding runs separately to see whether similar patterns occurred. The results showed that during the first encoding run, all ROIs, except the right aTPL, showed significant encoding effects, $FDR = .0001 \sim .01$ (Supplementary Figure 1 at the end of the chapter). During the second encoding run, only the PPA, FFA, and HPC, bilaterally, showed significant encoding effects $FDR < .0001$. In general, these observations were consistent with the literature and indicated that our associative encoding task was effective in recruiting our predefined ROIs. Detailed statistics ($t$ and $p$ values) are presented in Supplementary Figure 1.

**Encoding fame effects: Famous vs. nonfamous face-house pairs.** Second, I tested our main hypothesis to examine which brain regions showed stronger activation when prior-knowledge was involved by comparing the famous with the nonfamous condition. ROI analysis showed that the left and right vmPFC were more strongly activated in the famous than nonfamous condition ($FDR = .0007$ and $.008$, respectively). Similar trend level effects were found in the bilateral HPC and FFA ($FDR = .052 \sim .069$). Detailed statistics ($t$ and $p$ values) are given in Figure 5A. Whole brain analysis results are listed in Supplementary Table 1 (at the end of this chapter). I did not find significant fame effects in the bilateral aTPL regions, although the anterior middle temporal and inferior frontal gyri (see Supplementary Table 1), which also belong to the semantic network (Binder et al., 2009), appeared to be activated more strongly in the famous than nonfamous encoding condition.

I also examined the fame effects separately for the two encoding runs and found that the fame effects mentioned above were mainly contributed by the first encoding run. As can seen in Figure 5B, during the first encoding, the bilateral FFA, HPC, vmPFC, and right PPA were activated more strongly in the famous than nonfamous condition ($FDR = .004 \sim .0006$. Detailed statistics see Figure 5B). No significant fame effects were found in the second encoding, $FDR = .16 \sim .98$ (Figure 5C). The fame effect differences between encoding runs were confirmed by significant encoding run by fame interaction effects in the bilateral FFA and HPC, and the right PPA and aTPL ($p = .016 \sim .0001$. No $FDR$ correction for these complementary analyses). Beta values for all ROIs in each fame condition and encoding run are also provided in Supplementary Figure 2, in which ANOVA main effect and interaction $p$ values are also provided.
Figure 5. Fame effects (famous > nonfamous) in each predefined bilateral ROI (Chapter 3)

**Figure 5. A.** Bar graphs showing the fame effects (famous > nonfamous) in each predefined bilateral ROI after the two encoding runs were combined. The embedded brain section views show the locations of the clusters in the left FFA, HPC, and vmPFC that exhibited fame effects at $p < .005$, with 10 voxel extension (no correction) only for illustration purposes. Similar bar graphs reflecting fame effects for the first and second encoding run separately are also presented in **B** and **C**. Significant *encoding run by fame* interaction effects were found for the bilateral FFA and HPC and the right PPA and aTPL. + indicates uncorrected $p < .05$ and FDR $< .10$; * indicates FDR $< .05$. 
In general, these observations, consistent with our hypotheses, indicate that brain regions that support perceptual processes (FFA and PPA), episodic or associative memory processes (HPC), and social evaluative processes (vmPFC), play a more important role in new associative learning when prior-knowledge is involved, compared to when it is not.

Prior-knowledge modulation effects within the famous condition. Third, I conducted parametric modulation analyses to investigate whether the brain regions that showed stronger activation in the famous, compared to the nonfamous, condition were indeed related to the strength of the participant's prior-knowledge. To test this, I only used the data from the famous condition and examined whether encoding trials in which famous faces elicited stronger prior-knowledge would recruit these ROIs to a larger extent. Specifically, I used participants' face evaluation data on memory, familiarity, emotion, and attractiveness scales, separately, to construct a binary contrast parametric modulator. As mentioned earlier, because the original 5-point ratings may not necessarily have linear modulation effects and the contrast effects between strong and weak prior-knowledge are more relevant for this study, the original rating score of 1, 2, 3 was re-coded as -1 (i.e., weak prior-knowledge) and 4 and 5 as 1 (i.e., strong prior-knowledge). The mean beta value for each ROI from the individual level analysis was then tested at the group level to reveal whether the ROI was activated more strongly for the encoding trials with higher, compared to lower, face rating scores. As can be seen in Table 1, after the two encoding runs were combined, our ROI analyses revealed that the bilateral vmPFC, HPC, aTPL, and right FFA showed stronger activation in the trials in which the famous faces evoked stronger emotions ($FDR = .006 \sim .05$). Moreover, the left HPC and aTPL ($FDR = .033$) significantly, as well as the left vmPFC, right aTPL, right HPC, and left PPA at a trend level ($FDR = .06 \sim .07$. See Table 1 for detailed statistics), showed stronger activation in the trials in which the famous faces elicited more vivid memories. Importantly, face attractiveness and familiarity did not modulate the activation of these regions, confirming that it was the vivid prior memories and emotions, not general familiarity or facial attractiveness, that affected new associative processing. Similar results were found when the two encoding runs
Table 1. ROI prior-knowledge modulation effects on encoding brain activity in the famous condition (Chapter 3)

<table>
<thead>
<tr>
<th>Face ratings</th>
<th>PPA</th>
<th>FFA</th>
<th>HPC</th>
<th>aTPL</th>
<th>vmPFC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Emotion</th>
<th>2.27*</th>
<th>3.37*</th>
<th>3.06*</th>
<th>2.12*</th>
<th>1.90*</th>
<th>3.97*</th>
<th>3.27*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(.019)</td>
<td>(.002)</td>
<td>(.004)</td>
<td>(.025)</td>
<td>(.038)</td>
<td>(.0001)</td>
<td>(.002)</td>
</tr>
<tr>
<td>Memory</td>
<td>1.83+</td>
<td>2.74*</td>
<td>2.14+</td>
<td>2.92*</td>
<td>1.87+</td>
<td>2.12+</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(.042)</td>
<td>(.007)</td>
<td>(.023)</td>
<td>(.004)</td>
<td>(.039)</td>
<td>(.024)</td>
<td></td>
</tr>
<tr>
<td>Familiarity</td>
<td>1.94</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(.034)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attractiveness</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Note: The numbers in the table are t statistics and the corresponding p values (in parentheses) from the second level one sample t test. Only effects survived uncorrected threshold of p < .05 are included. For the results of each ROI, * indicates effects survived false detection rate (FDR < .05); + indicates effects survived FDR < .10. Two encoding runs were combined. Sample size N = 20 for memory and familiarity analyses. N = 17 for emotion analysis and N = 19 for attractiveness analysis. Exclusion of participants was due to zero trial count in rating categories.
were analyzed separately (Supplementary Table 2), although modulation effects of memory ratings were significant \((FDR < .05)\) only in the second encoding run. To illustrate the modulation effects of different ratings, voxel-wise results for the four face ratings, using the left hemisphere as an example, are presented in Figure 6A. These results indicate that participants' prior-knowledge, such as more vivid memories and stronger emotions elicited by the famous faces, triggered stronger social evaluative, semantic, and memory binding processing, supported by the vmPFC, aTPL, or HPC, and facilitated new learning.

Next, to illustrate further the overlap, at single voxel level, between the prior-knowledge modulation effects (within the famous condition) and the fame effects (between the famous and nonfamous condition), I first combined, i.e., made a union of, the brain regions from the 4 face modulation analyses \((at \ p < .005, with 10\ voxel\ extension\ for\ this\ illustration\ purpose)\) to form a prior-knowledge modulation network ROI \((PKM+; \ The\ positive\ sign\ means\ that\ these\ brain\ regions\ showed\ stronger\ activation\ when\ participants\ encoded\ the\ faces\ with\ stronger\ prior-knowledge). Then, I overlaid the brain regions that showed significant fame effects, i.e., stronger activation in the famous than nonfamous condition \((at \ p < .005, with\ 10\ voxel\ extension\ for\ this\ illustration\ purpose)\) onto this PKM+ network. As can be seen from Figure 6B, many brain regions within this PKM+ network also showed stronger activation in the famous vs. nonfamous comparison. I then conducted an SPM small volume correction on the fame effects using the PKM+ network as an ROI and confirmed that the overlap between the PKM+ network and the brain network with fame effects was not due to chance, set-level \(p < 10^{-7}\) (Friston, Holmes, Poline, Price, & Frith, 1996). These regions included the bilateral vmPFC and the left HPC, as I hypothesized, and other regions such as the posterior cingulate, left superior frontal gyrus, and left middle temporal gyrus (Supplementary Table 3).

*Encoding subsequent memory effects.* Fourth, to investigate whether the brain regions that showed prior-knowledge effects were indeed important for associative memory formation, I tested subsequent memory effects for the famous encoding condition using parametric
Figure 6. Prior-knowledge modulation (PKM) effects (Chapter 3)

A. PKM effects for different face ratings

B. Overlap between positive PKM effects and fame (famous > nonfamous) effects

Figure 6. A. Surface views (left hemisphere only) of the Prior-knowledge modulation (PKM) effects (positive effects in warm color and negative effects in cold color) separately for each face evaluation rating. B. The overlap (in blue) between the positive PKM effects in the famous condition (in green, and all 4 ratings combined) and the positive fame (famous > nonfamous) effects (in red). Two encoding runs were combined. The enlarged sagittal view shows that the left hippocampus was among the overlapped regions. In A and B, for illustration purposes, $p < .005$, with 10 voxel extension, no correction.
modulation analysis. ROI analyses showed that both the left and right HPC ($t = 2.72$ and $2.56$, $p < .007$ and .01, $FDR = .014$ and .016, respectively) and vmPFC ($t = 2.97$ and $2.50$, $p = .004$ and .011, $FDR = .013$ and .016, respectively) exhibited stronger activation for the encoding of the face-house pairs whose associations were later correctly remembered during retrieval than those forgotten pairs. Posterior perceptual regions such as the left and right PPA ($t = 4.24$ and $2.80$, $p = .0002$ and .006, $FDR = .002$ and .014, respectively) and FFA ($t = 1.92$ and $4.01$, $p = .04$ and .0004, $FDR = .044$ and .002, respectively) also showed significant subsequent memory effects. Estimated beta values for the contrasts between remembered and forgotten trials in each ROI are presented in Figure 7A. Original beta values for the remembered and forgotten trials separately are also given in Supplementary Figure 3. I also noted that after excluding one participant who had fewer than 10 remembered trials, subsequent memory effects in all ROIs remained significant ($FDR < .05$) except for the left FFA ($p = .048$, $FDR = .059$). The whole brain analysis results are also shown in Supplementary Table 4.

I also compared subsequent memory effects between the two encoding runs and found no significant difference in the bilateral PPA, FFA, HPC, and vmPFC. Only for the aTPL, subsequent memory effects were stronger in the second than the first encoding ($ps < .03$ for between-run $t$ test. No $FDR$ correction for these complementary analyses). Further analysis revealed that only in the second encoding, subsequent memory effects of the left and right aTPL were significant ($t = 2.30$ and $1.99$, $p = .017$ and .03, respectively, $FDR = .038$). Embedded bar graph in Figure 7). These data together indicate that brain regions more strongly activated by the famous, compared to the nonfamous, encoding condition indeed played a role in face-house associative memory formation.

For the nonfamous condition, on average there were only 8.35 remembered trials per run and 7 participants had no more than 10 remembered trials. Due to the low number of trials, analyses on subsequent memory effects in the nonfamous condition may not be robust. Therefore, I did not include these results in the main text. However, I presented subsequent memory effects of the nonfamous condition and subsequent memory effect differences between the two fame conditions in Supplementary Figure 4 for readers who may be curious about the results.
**Figure 7.** Subsequent memory effects (remembered > forgotten contrast) for the famous condition in each predefined ROI (Chapter 3)

**Subsequent memory (remembered > forgotten) effects**

![Brain section views showing the locations of clusters in the PPA, FFA, left HPC, and left vmPFC that exhibited subsequent memory effects in the famous condition at $p < .005$, with 10 voxel extension (no correction) only for illustration purposes.](image)

![Bar graphs showing the subsequent memory effects (i.e., the beta estimates for the remembered > forgotten contrast) for the famous condition in each predefined ROI. Two encoding runs were combined. * indicates significant subsequent memory effects ($FDR < .05$) for those ROIs.](image)

**Figure 7.** Bar graphs showing the subsequent memory effects (i.e., the beta estimates for the remembered > forgotten contrast) for the famous condition in each predefined ROI. Two encoding runs were combined. * indicates significant subsequent memory effects ($FDR < .05$) for those ROIs. Brain section views show the locations of the clusters in the PPA, FFA, left HPC, and left vmPFC that exhibited subsequent memory effects in the famous condition at $p < .005$, with 10 voxel extension (no correction) only for illustration purposes. Subsequent memory effects were not statistically different between the first and seconding encoding for all ROIs except the aTPL, which showed significant effects only in the second encoding run (embedded bar graphs). The original fMRI activation beta values, separately for remembered and forgotten trials, are given in Supplementary Figure 3.
Fame effects on hippocampal connectivity. I then conducted a psychophysiological interaction (PPI) analysis to examine whether the functional connectivity of the HPC, a region that is crucial for associative binding, could be affected by prior-knowledge by comparing the famous vs. nonfamous encoding condition. Although the ROI analyses showed that the left HPC connectivity with the right aTPL and right vmPFC, and the right HPC connectivity with the right vmPFC, appeared to be stronger in the famous than nonfamous condition ($t = 1.78, 1.73, \text{ and } 2.06, p = .046, .05, \text{ and } .027, \text{ respectively}$), these effects did not survive the FDR correction ($FDR = .21$). Similarly, no significant results were found when the two encoding runs were analyzed separately. Supplementary Table 5 lists the whole-brain HPC connectivity analysis. The pattern of the results in Supplementary Table 5 is also presented graphically in Supplementary Figure 5.

Analyses on subsequent memory effects showed that although the left HPC connectivity with the left and right aTPL in the famous condition appeared to be stronger for the encoding of the later remembered than forgotten trials ($t = 1.76$ and $1.89, p = .047$ and .037, respectively. $FDR = .24$), the results did not survive the FDR correction and cannot be interpreted with appropriate confidence.

Hippocampal connectivity predicting memory performance across participants. Finally, because a previous study (van Kesteren, Fernández, et al., 2010) found that the HPC connectivity with the vmPFC was associated with memory performance across participants differently depending on whether prior-knowledge was involved, I also examined whether a similar brain-behavior association occurred in this study. To this end, I conducted across participants regression analyses to investigate whether the HPC connectivity with the vmPFC in each fame condition could be related to participants' associative memory performance. Using ROI regression analyses, I found that the right HPC connectivity with the right vmPFC was positively predicted by participants' associative memory performance in the famous condition (regression coefficient $\beta = .53$, explained variance $R^2 = .18$, $t(16) = 1.95$, and $p = .036$. No FDR correction for this planed ROI analysis). For the nonfamous condition, the ROI analyses revealed that the associative memory performance negatively predicted the left HPC connectivity with the left vmPFC (regression coefficient $\beta = -.41$, explained variance $R^2 = .16$, $t(16) = -1.84$, and $p = .042$. No FDR correction for this planned ROI analysis). For illustration purposes, the different
brain-behavioral patterns of the two fame conditions are presented in Figure 8 using HPC connectivity with selected clusters in the vmPFC ROI.

3.4 Discussion

In this study, I found that prior-knowledge about faces facilitated associative memory between these faces and houses. At the neural level, I found that the FFA, PPA, vmPFC and HPC showed stronger activation in the famous encoding condition. Activity in the HPC, aTPL, and vmPFC was positively related to the extent of emotion elicited by the faces, and the vividness of the memories they evoked, but not by their mere attractiveness or familiarity. The FFA, PPA, vmPFC, HPC, and aTPL also showed subsequent memory effects in the famous condition, indicating that these regions likely played a causal role in the prior-knowledge enhancement effects. Our connectivity results suggested that the HPC connectivity with anterior ROIs such as the vmPFC was important for the prior-knowledge facilitation effects on new learning. These results support our hypotheses that prior-knowledge may trigger enhanced evaluative, semantic, associative binding, or perceptual processing, each supported by different brain regions, such as the vmPFC, aTPL, HPC, FFA, and PPA, respectively, to facilitate new memory processing.

3.4.1 The role of the hippocampus in prior-knowledge effects during associative encoding

As predicted from our behavioural study that prior-knowledge, which influences associative recollection, but not familiarity (Liu & Moscovitch, under revision), should exert its effect via the hippocampus, I also found that the HPC was more strongly activated in the famous than nonfamous condition. This hippocampal activation may reflect a spontaneous reinstatement of previous memories elicited by the famous faces (Ishai, 2008; Ishai, Haxby, & Ungerleider, 2002; Trinkler et al., 2009) as such memories are elicited by names of famous people and mediated by the hippocampus (Renoult et al., 2014; Renoult, Davidson, Palombo, Moscovitch, & Levine, 2012; Westmacott, Black, Freedman, & Moscovitch, 2004; Westmacott & Moscovitch, 2003). It may also be indicative of a stronger binding process associated with the famous condition. The two possibilities are not mutually exclusive and likely occurred simultaneously (Zeithamova, Dominick, et al., 2012; Zeithamova & Preston, 2010). These possibilities can also be supported
**Figure 8.** Relationship between the HPC-vmPFC connectivity and associative memory performance across participants in the two fame conditions (Chapter 3)

Scatter plots that illustrate the opposite relationship between the HPC-vmPFC connectivity and associative memory performance across participants in the two fame conditions. The MNI coordinates for the selected clusters (6 mm sphere) in the vmPFC are indicated. Regression analysis $p$ value and explained variance are also indicated.

**Figure 8.** Scatter plots that illustrate the opposite relationship between the HPC-vmPFC connectivity and associative memory performance across participants in the two fame conditions. The MNI coordinates for the selected clusters (6 mm sphere) in the vmPFC are indicated. Regression analysis $p$ value and explained variance are also indicated.
by our findings that the HPC was recruited to a larger extent by the trials in which famous faces evoked stronger prior memory and the trials in which famous face-house pairs were later remembered, compared to those forgotten pairs. In either event, our results indicate that modulation of associative recollections by prior-knowledge, like the recollections themselves, is mediated in part by the hippocampus.

It has been proposed that the HPC may mainly support encoding of novel information (Kumaran & Maguire, 2009; Tulving & Kroll, 1995; Tulving et al., 1996; van Kesteren, Beul, et al., 2013). Consistently, in this study I also found that activation in the HPC was reduced during the second, compared to the first, encoding run (Supplementary Figure 2). However, I also found that the subsequent memory effects, as well as the prior memory modulation effects of famous faces, in the HPC remained the same during the repeated encoding. Considering that other brain regions such as the PPA, FFA, and vmPFC also showed repetition related activation reduction, future studies should investigate to what extent the activation reduction in the HPC in repeated encoding is specifically related to the intrinsic functional property of this brain region, or whether it is mainly caused by reduced involvement of other processing systems (such as very early sensory or perceptual systems). Moreover, I found that the HPC was activated more strongly in the famous encoding condition in which more familiar stimuli were involved, compared to the nonfamous condition, which suggests that novelty alone cannot explain all activity in the HPC. If familiar stimuli elicit strong previous episodic or associative memories, the HPC can be engaged to a larger extent, compared to novel stimuli, not only to support the elicited prior memories, but also facilitate new memory formation. Consistent with our results, recent neural imaging and animal studies also found that the HPC was involved in encoding of prior-experience related new associative processing (Poppenk, McIntosh, et al., 2010; Tse et al., 2007).

It is also worth mentioning that both the anterior and posterior HPC were activated during the face-house encoding task, compared to the processing of scrambled pictures (see brain section views in Figure 4). According to a recent proposal (Poppenk, Evensmoen, Moscovitch, & Nadel, 2013), this two-loci activation pattern may suggest that the associations between the face and house stimuli can be processed at both a detailed perceptual level, which mainly recruits the
posterior HPC, and gist-like semantic or social emotional level, which mainly recruits the anterior HPC. The former may be driven more strongly by the house stimuli and the latter by the face stimuli. However, when the two fame conditions were compared, only the anterior HPC showed stronger activation during the famous encoding (see brain section views in Figure 5), in accord with Poppenk et al.'s proposal. Consistent with previous studies (Chua, Schacter, Rand-Giovannetti, & Sperling, 2007; Sperling et al., 2003), the anterior HPC activation also showed subsequent memory effects (see brain section views in Figure 4). These results suggest that the types of prior-knowledge involved in the famous condition may make the face-house associations processed at a more semantic or social emotional level, compared to the no prior-knowledge situation (Poppenk et al., 2013). Our finding that stronger involvement of the vmPFC, HPC, amygdala, and aTPL occurred when famous faces elicited stronger prior emotions and memories (Figure 6) lends support to this interpretation.

3.4.2 The role of the vmPFC in prior-knowledge effects during associative encoding

In general, the current finding that the vmPFC played an important role in prior-knowledge effects is consistent with previous studies (Preston & Eichenbaum, 2013; Trinkler et al., 2009; Tse et al., 2007; van Kesteren, Beul, et al., 2013; van Kesteren, Rijpkema, et al., 2010, 2010; van Kesteren, Rijpkema, Ruiter, Morris, & Fernández, 2014; Zeithamova, Dominick, et al., 2012). It has been proposed that the vmPFC interacts with the medial temporal lobe in supporting the encoding of schema related information (van Kesteren et al., 2012). Due to its broad anatomical connections (Barbas, 2000; Carmichael & Price, 1996), the vmPFC can serve as a hub region that integrates memory information from different modalities (Nieuwenhuis & Takashima, 2011). It is still unclear, however, through what processing mechanisms the vmPFC can have the integrative function. Different from the previous studies which used complex schemas (van Kesteren, Rijpkema, et al., 2010), the current study used famous faces to elicit participants' prior-knowledge. This type of prior-knowledge, which involves the recruitment rich social emotional, semantic, or episodic information (Henson et al., 2003; Ishai, 2008; Ishai et al., 2002) can recruit the vmPFC and exerts its facilitatory effects. This result raise the possibility that merely using prior-knowledge associated with evaluative processing, is an important determinant for vmPFC involvement (Benoit, Szpunar, & Schacter, 2014). This interpretation can be supported by our findings that the more strongly the famous faces evoked emotion responses and vivid memories,
the more strongly the vmPFC was activated and the better the memory. From this processing-focused perspective, I suggest that similar evaluative processes evoked by schema congruency may contribute to the schema related vmPFC engagement found in previous studies (Kroes & Fernández, 2012).

These findings and interpretations are also consistent with the large body of literature showing that the vmPFC is a key structure to support social/evaluative/affective processing, including, but not limited to, self-related processing, decision making, moral judgment, empathy, processing abstract semantic information, or even perceiving preferred every-day objects (Barrett & Bar, 2009; Binder et al., 2009; Etkin et al., 2011; Grabenhorst & Rolls, 2011; O’Reilly, 2010; Roy et al., 2012). This evaluative processing could result in selective or predictive, and likely deeper, encoding of some aspects of the face-house associative information through a top-down process (Bar, 2007, 2009; Henson & Gagnepain, 2010; Preston & Eichenbaum, 2013; Summerfield, Lepsien, Gitelman, Mesulam, & Nobre, 2006). Such effects may have contributed to the better associative memory in the famous condition. Therefore, it is likely that this type of evaluative processing, enhanced by prior-knowledge and supported by the vmPFC, enables the vmPFC to act as a hub region to make available the structures that mediate prior-knowledge effects on the one hand, and support the assimilation of new information, on the other.

### 3.4.3 The role of the aTPL in prior-knowledge effects during associative encoding

Similarly, as a semantic hub region (Patterson et al., 2007), the aTPL has been found to mediate prior-knowledge effects (Kan et al., 2009) and support face processing (Axelrod & Yovel, 2013; Heide et al., 2013; Ross & Olson, 2012). Lesions of the aTPL can lead to impairments in semantic knowledge or learning (Gainotti et al., 2010; Hsieh et al., 2011; Lambon Ralph, Cipolotti, et al., 2010; Lambon Ralph, Sage, et al., 2010; Sharon et al., 2011; Snowden et al., 2004). Stronger activation in this region has also been found in neuroimaging studies when familiar versus unfamiliar faces, names, houses, and voices are processed (Gorno-Tempini & Price, 2001; Nakamura et al., 2000, 2001; Tsukiura et al., 2010; Tsukiura, Mochizuki-Kawai, & Fujii, 2006). Moreover, the aTPL is functionally and anatomically connected with the vmPFC (Kondo, Saleem, & Price, 2003), indicating that the semantic system can work closely with the evaluative or affective system (Binder & Desai, 2011; Olson, McCoy, Klobusicky, & Ross, 2013; Simmons et al., 2010; Skipper, Ross, & Olson, 2011; Zahn et al., 2007) in supporting
prior-knowledge effects, e.g., by providing semantic valence and structures. In this study, I found that the aTPL showed stronger activation during trials in which famous faces elicited stronger emotions and memories, suggesting that prior-knowledge related to famous faces may trigger stronger semantic processing which, in turn contributes to better memory performance.

### 3.4.4 The role of posterior neocortical regions in prior-knowledge effects during associative encoding

I also found that posterior perceptual regions such as the FFA and PPA were activated more strongly during the famous than nonfamous encoding (Figure 5B). These regions were also engaged to a larger extent for later remembered than forgotten famous trials (Figure 7). With regard to prior-knowledge effects on the FFA activation during face processing, inconsistent findings exist in the literature, with studies reporting no effects (Gorno-Tempini & Price, 2001), positive effects (Liu et al., 2014; Simon et al., 2011), or negative effects (Gobbini & Haxby, 2006; Rossion, Schiltz, Robaye, Pirenne, & Crommelinck, 2001). However, most of these previous studies employed perceptual, not memory, tasks. In the current study, because the FFA activation was also modulated by participants' prior emotions elicited by the famous faces (Table 1), it is likely that social evaluative processes were evoked in the famous condition and made some aspects of the famous faces processed more deeply at the perceptual level. This modulation also facilitated the face-house associative processing and consequently strengthened the activation of the PPA in the famous condition. In addition, it has been found that episodic context information related to famous faces, supported by the parahippocampal cortex, can be automatically evoked while processing familiar faces (Bar et al., 2008). Consistently, I also found marginally significant modulation effects of prior memory in the PPA (Table 1). Therefore, it is possible that retrieved context information related to famous faces was involved or utilized in the new face-house associative processing, which may also explain the stronger PPA activation in the famous condition.

### 3.4.5 Interactions between the hippocampus and neocortical structures in producing prior-knowledge effects on associative encoding

I also predicted that the HPC should show stronger connectivity with the vmPFC and aTPL in the famous condition to reflect stronger involvement of rich semantic or social emotional prior-knowledge in new associative binding. Although I observed that the HPC showed numerically
stronger connectivity with the aTPL and vmPFC in the famous than nonfamous condition, and that within the famous condition, the HPC-aTPL connectivity was stronger for the remembered than forgotten trials, these results did not survive multiple testing corrections, making it difficult to draw firm conclusions based on these findings. Similarly I did not find significant HPC-FFA or HPC-PPA connectivity differences between the two fame conditions. Future studies with higher statistical power are needed to examine this issue.

However, consistent with our hypothesis, the finding that the HPC connectivity with the vmPFC was positively associated with participants' memory performance in the famous condition suggests that communication among anterior ROIs is important for prior-knowledge facilitation effects. In the previous study by van Kesteren and colleagues (van Kesteren, Fernández, et al., 2010), there was a positive trend between the HPC-vmPFC connectivity and memory performance in the schema-congruent condition, although the relationship was not significant. Moreover, in the current study the HPC-vmPFC connectivity in the nonfamous condition was negatively related to memory performance, similar to the schema-incongruent condition in (van Kesteren, Fernández, et al., 2010). These data suggest that using prior-knowledge to solve new problems, which involves memory retrieval, decision making, or goal/reward relatedness monitoring processes, drives vmPFC-HPC connectivity.

3.4.6 Conclusions

In this study, I found that prior-knowledge facilitated new associative encoding by recruiting additional activation in posterior perceptual regions, such as the FFA and PPA, anterior brain regions, such as the vmPFC, and the key associative memory processing structure, the HPC. This strengthened brain-activation pattern likely reflects additional perceptual, evaluative, and associative binding processes engaged by prior-knowledge. I also found that these additional processes enhanced specifically later recollection of the encoded face-house associations, indicating that the familiar famous faces used in the current study indeed had profound influences on new associative processing. These observations may reflect a general mechanism by which multiple component prior-knowledge can affect new learning.

These findings are also consistent with the component processing model of memory (Cabeza & Moscovitch, 2013; Moscovitch, 1992), which posits that different processing components, supported by different brain regions, can be dynamically recruited in a memory task. From this
perspective, we can propose that the type of prior-knowledge that is invoked, and more importantly, how different aspects of that prior-knowledge influence component memory processes, are the key factors that determine prior-knowledge effects. Thus, future studies that employ similar paradigms as used in the current study to manipulate more specifically different components of prior-knowledge and examine their effects on memory component processing at a more causal and biological level (Tse et al., 2007, 2011; Wiltgen, Wood, & Levy, 2011) will significantly advance our understanding of how new and old memories interact in the brain.

Moreover, these brain-level findings, and the conclusions I drew from them regarding component processes, are also consistent with those drawn from a long history of psychological research on schema (e.g., Alba and Hasher, 1983). Therefore, this processing-focused perspective should also benefit the current neuroscientific research on schema (Richards et al., 2014; Tse et al., 2007; van Kesteren, Fernández, et al., 2010), in that directly targeting these processing components would prove to be an effective and efficient means of revealing the neural mechanism mediating schema effects.
### 3.5 Supplementary Tables

**Supplementary Table 1.** Brain regions that showed positive (famous > nonfamous) and negative (nonfamous > famous) fame effects during encoding (Chapter 3)

<table>
<thead>
<tr>
<th>Anatomical areas</th>
<th>Cluster size</th>
<th>t value</th>
<th>p value</th>
<th>MNI coordinates x</th>
<th>y</th>
<th>z</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Famous &gt; nonfamous</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebelum_9_R</td>
<td>355</td>
<td>6.87</td>
<td>0.000</td>
<td>16 -44 -42</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frontal_Sup_R</td>
<td>228</td>
<td>6.15</td>
<td>0.000</td>
<td>24 38 40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frontal_Inf_Tri_L</td>
<td>517</td>
<td>5.55</td>
<td>0.000</td>
<td>-36 22 14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rectus_L R *</td>
<td>840</td>
<td>5.49</td>
<td>0.000</td>
<td>-2 42 -22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fusiform_R</td>
<td>93</td>
<td>4.81</td>
<td>0.000</td>
<td>38 -42 -10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temporal_Mid_R</td>
<td>382</td>
<td>4.78</td>
<td>0.000</td>
<td>48 -64 22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frontal_Sup_L</td>
<td>133</td>
<td>4.71</td>
<td>0.000</td>
<td>-26 0 68</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebelum_10_L</td>
<td>113</td>
<td>4.66</td>
<td>0.000</td>
<td>-10 -28 -40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frontal_Sup_Medial_R</td>
<td>1057</td>
<td>4.66</td>
<td>0.000</td>
<td>6 54 34</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fusiform_R *</td>
<td>310</td>
<td>4.63</td>
<td>0.000</td>
<td>42 -28 -20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Precuneus_R</td>
<td>958</td>
<td>4.47</td>
<td>0.000</td>
<td>2 -52 20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frontal_Inf_Orb_R</td>
<td>78</td>
<td>4.31</td>
<td>0.000</td>
<td>34 36 -12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hippocampus_L *</td>
<td>229</td>
<td>4.26</td>
<td>0.000</td>
<td>-16 -16 -10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebelum_Crus2_R</td>
<td>32</td>
<td>4.24</td>
<td>0.000</td>
<td>10 -86 -42</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temporal_Inf/fusiform_</td>
<td>248</td>
<td>3.95</td>
<td>0.000</td>
<td>-44 -50 -16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caudate_L</td>
<td>26</td>
<td>3.94</td>
<td>0.000</td>
<td>-18 -28 20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frontal_Inf_Orb_L</td>
<td>18</td>
<td>3.90</td>
<td>0.000</td>
<td>-20 34 -6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Precentral_L</td>
<td>23</td>
<td>3.84</td>
<td>0.000</td>
<td>-32 2 46</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hippocampus_R *</td>
<td>102</td>
<td>3.80</td>
<td>0.000</td>
<td>18 -12 -8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frontal_Inf_Orb_L</td>
<td>100</td>
<td>3.56</td>
<td>0.001</td>
<td>-36 38 -14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temporal_Mid_R</td>
<td>25</td>
<td>3.51</td>
<td>0.001</td>
<td>38 -50 16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anatomical areas</td>
<td>Cluster size</td>
<td>t value</td>
<td>p value</td>
<td>MNI coordinates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------------------</td>
<td>--------------</td>
<td>---------</td>
<td>---------</td>
<td>----------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temporal_Mid_L</td>
<td>22</td>
<td>3.44</td>
<td>0.001</td>
<td>-56 -60 20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Putamen_L</td>
<td>10</td>
<td>3.40</td>
<td>0.001</td>
<td>-20 18 8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temporal_Mid_L</td>
<td>85</td>
<td>3.39</td>
<td>0.001</td>
<td>-50 -16 -12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temporal_Mid_L</td>
<td>16</td>
<td>3.38</td>
<td>0.001</td>
<td>-58 -44 -12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebelum_Crus2_R</td>
<td>21</td>
<td>3.38</td>
<td>0.001</td>
<td>22 -76 -42</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caudate_L</td>
<td>21</td>
<td>3.28</td>
<td>0.002</td>
<td>-10 14 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caudate_R</td>
<td>19</td>
<td>3.26</td>
<td>0.002</td>
<td>16 16 8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebelum_Crus1_R</td>
<td>11</td>
<td>3.14</td>
<td>0.002</td>
<td>32 -70 -32</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occipital_Mid_L</td>
<td>11</td>
<td>3.10</td>
<td>0.002</td>
<td>-26 -80 36</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Nonfamous > famous**

<table>
<thead>
<tr>
<th>Anatomical areas</th>
<th>Cluster size</th>
<th>t value</th>
<th>p value</th>
<th>MNI coordinates</th>
</tr>
</thead>
<tbody>
<tr>
<td>SupraMarginal_R</td>
<td>938</td>
<td>6.26</td>
<td>0.000</td>
<td>52 -26 24</td>
</tr>
<tr>
<td>Supp_Motor_Area_L</td>
<td>79</td>
<td>5.16</td>
<td>0.000</td>
<td>-6 -16 58</td>
</tr>
<tr>
<td>Insula_L</td>
<td>163</td>
<td>4.42</td>
<td>0.000</td>
<td>-40 4 -4</td>
</tr>
<tr>
<td>SupraMarginal_L</td>
<td>58</td>
<td>4.22</td>
<td>0.000</td>
<td>-64 -40 34</td>
</tr>
<tr>
<td>Insula_R</td>
<td>59</td>
<td>3.78</td>
<td>0.000</td>
<td>34 -10 12</td>
</tr>
<tr>
<td>Cingulum_Mid_L</td>
<td>65</td>
<td>3.67</td>
<td>0.000</td>
<td>-10 0 42</td>
</tr>
<tr>
<td>Rolandic_Oper_L</td>
<td>12</td>
<td>3.35</td>
<td>0.001</td>
<td>-58 2 2</td>
</tr>
</tbody>
</table>

Note: All clusters survived the threshold of $p < .005$, with 10 voxel extension, no correction. * indicates brain regions/clusters that contain or fall into predefined ROIs. The names of anatomical regions in all tables follow the automated anatomical labeling (AAL) template naming convention (Tzourio-Mazoyer et al., 2002). R/L - right/left hemisphere; Mid - middle; Sup - superior; Inf - inferior; Med - medial; Orb - orbital; Oper - opercular. Two encoding runs were combined.
**Supplementary Table 2.** ROI prior-knowledge modulation effects on encoding brain activity in the famous condition for the first and second encoding run separately (Chapter 3)

<table>
<thead>
<tr>
<th>Face ratings</th>
<th>PPA</th>
<th>FFA</th>
<th>HPC</th>
<th>aTPL</th>
<th>vmPFC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left</td>
<td>Right</td>
<td>Left</td>
<td>Right</td>
<td>Left</td>
</tr>
<tr>
<td>First encoding</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Memory</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Familiarity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Attractiveness</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Second encoding</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotion</td>
<td>1.80*</td>
<td>2.93*</td>
<td>2.47*</td>
<td>1.74*</td>
<td>3.05*</td>
</tr>
<tr>
<td>-</td>
<td>(0.045)</td>
<td>(0.05)</td>
<td>(0.12)</td>
<td>(0.05)</td>
<td>-</td>
</tr>
<tr>
<td>Memory</td>
<td>1.89*</td>
<td>2.82*</td>
<td>2.86*</td>
<td>2.62*</td>
<td>2.70*</td>
</tr>
<tr>
<td>-</td>
<td>(0.037)</td>
<td>(0.06)</td>
<td>(0.05)</td>
<td>(0.008)</td>
<td>(0.007)</td>
</tr>
<tr>
<td>Familiarity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Attractiveness</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**Note:** The numbers in the table are *t* statistics and the corresponding *p* values (in parentheses) from the second level one sample *t* test. Only effects survived uncorrected threshold of *p* < .05 are included. For the results of each ROI, * indicates effects survived false detection rate (*FDR* < .05); + indicates effects survived *FDR* < .10. Sample size *N* = 20 for memory and familiarity analyses. *N* = 17 for emotion analysis and *N* = 19 for attractiveness analysis. Exclusion of participants was due to zero trial count in rating categories.
**Supplementary Table 3.** Brain regions that showed both positive prior-knowledge modulation effects and positive fame effects (Chapter 3)

<table>
<thead>
<tr>
<th>Anatomical areas</th>
<th>Cluster size</th>
<th>Peak t value</th>
<th>Peak p value</th>
<th>MNI coordinates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectus_R L *</td>
<td>533</td>
<td>5.49</td>
<td>0.0000</td>
<td>-2 42 -22</td>
</tr>
<tr>
<td>Fusiform_R</td>
<td>11</td>
<td>4.81</td>
<td>0.0001</td>
<td>38 -42 -10</td>
</tr>
<tr>
<td>Frontal_Sup_L</td>
<td>323</td>
<td>4.47</td>
<td>0.0001</td>
<td>-16 56 10</td>
</tr>
<tr>
<td>Temporal_Mid_R</td>
<td>37</td>
<td>4.45</td>
<td>0.0001</td>
<td>52 -66 22</td>
</tr>
<tr>
<td>Hippocampus_L *</td>
<td>143</td>
<td>4.24</td>
<td>0.0002</td>
<td>-18 -16 -10</td>
</tr>
<tr>
<td>Temporal_Mid_R</td>
<td>94</td>
<td>4.19</td>
<td>0.0002</td>
<td>56 -10 -16</td>
</tr>
<tr>
<td>Frontal_Sup_L</td>
<td>91</td>
<td>4.15</td>
<td>0.0003</td>
<td>-18 38 36</td>
</tr>
<tr>
<td>Cingulum_Post_L</td>
<td>294</td>
<td>4.08</td>
<td>0.0003</td>
<td>-4 -50 20</td>
</tr>
<tr>
<td>Temporal_Mid_L</td>
<td>15</td>
<td>3.44</td>
<td>0.0014</td>
<td>-56 -60 20</td>
</tr>
<tr>
<td>ParaHippocampal_R</td>
<td>21</td>
<td>3.40</td>
<td>0.0015</td>
<td>22 -14 -20</td>
</tr>
<tr>
<td>Frontal_Inf_Orb_L</td>
<td>16</td>
<td>3.36</td>
<td>0.0016</td>
<td>-44 32 -6</td>
</tr>
<tr>
<td>Temporal_Mid_L</td>
<td>19</td>
<td>3.25</td>
<td>0.0021</td>
<td>-54 -12 -16</td>
</tr>
</tbody>
</table>

*Note: All clusters survived the threshold of $p < 0.005$, with 10 voxel extension, no correction. * indicates brain regions/clusters that contain or fall into predefined ROIs. Two encoding runs were combined.*
**Supplementary Table 4.** Brain regions that showed subsequent memory effects (Chapter 3)

<table>
<thead>
<tr>
<th>Anatomical areas</th>
<th>Cluster size</th>
<th>t value</th>
<th>p value</th>
<th>MNI coordinates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>x</td>
</tr>
<tr>
<td><strong>Famous condition</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fusiform_L *</td>
<td>1889</td>
<td>6.69</td>
<td>0.0000</td>
<td>-26</td>
</tr>
<tr>
<td>Lingual_R</td>
<td>2529</td>
<td>5.45</td>
<td>0.0000</td>
<td>26</td>
</tr>
<tr>
<td>Rectus_R *</td>
<td>410</td>
<td>4.85</td>
<td>0.0001</td>
<td>6</td>
</tr>
<tr>
<td>Hippocampus_L *</td>
<td>299</td>
<td>4.77</td>
<td>0.0001</td>
<td>-12</td>
</tr>
<tr>
<td>Occipital_Mid_R</td>
<td>1332</td>
<td>4.69</td>
<td>0.0001</td>
<td>44</td>
</tr>
<tr>
<td>Cerebelum_8_L</td>
<td>32</td>
<td>4.41</td>
<td>0.0001</td>
<td>-22</td>
</tr>
<tr>
<td>Temporal_Pole_Sup_L *</td>
<td>280</td>
<td>4.40</td>
<td>0.0002</td>
<td>-48</td>
</tr>
<tr>
<td>Rolandic_Oper_L</td>
<td>340</td>
<td>4.37</td>
<td>0.0002</td>
<td>-58</td>
</tr>
<tr>
<td>Insula_R</td>
<td>64</td>
<td>4.29</td>
<td>0.0002</td>
<td>40</td>
</tr>
<tr>
<td>Postcentral_R</td>
<td>101</td>
<td>4.15</td>
<td>0.0003</td>
<td>32</td>
</tr>
<tr>
<td>Precuneus_L</td>
<td>122</td>
<td>3.97</td>
<td>0.0004</td>
<td>-4</td>
</tr>
<tr>
<td>Cerebelum_8_R</td>
<td>122</td>
<td>3.82</td>
<td>0.0006</td>
<td>10</td>
</tr>
<tr>
<td>Fusiform_R</td>
<td>24</td>
<td>3.71</td>
<td>0.0007</td>
<td>40</td>
</tr>
<tr>
<td>Frontal_Sup_L</td>
<td>21</td>
<td>3.68</td>
<td>0.0008</td>
<td>-16</td>
</tr>
<tr>
<td>Cerebelum_8_R</td>
<td>67</td>
<td>3.59</td>
<td>0.0010</td>
<td>26</td>
</tr>
<tr>
<td>Thalamus_R</td>
<td>11</td>
<td>3.58</td>
<td>0.0010</td>
<td>6</td>
</tr>
<tr>
<td>Supp_Motor_Area_R</td>
<td>31</td>
<td>3.57</td>
<td>0.0010</td>
<td>6</td>
</tr>
<tr>
<td>Precentral_L</td>
<td>17</td>
<td>3.50</td>
<td>0.0012</td>
<td>-54</td>
</tr>
<tr>
<td>Frontal_Inf_Tri_R</td>
<td>17</td>
<td>3.20</td>
<td>0.0024</td>
<td>46</td>
</tr>
<tr>
<td>Parietal_Sup_R</td>
<td>14</td>
<td>3.18</td>
<td>0.0025</td>
<td>12</td>
</tr>
<tr>
<td>Precentral_L</td>
<td>10</td>
<td>3.12</td>
<td>0.0028</td>
<td>-50</td>
</tr>
<tr>
<td><strong>Nonfamous condition</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cingulum_Ant_R</td>
<td>15</td>
<td>4.33</td>
<td>0.0002</td>
<td>4</td>
</tr>
<tr>
<td>Anatomical areas</td>
<td>Cluster size</td>
<td>t value</td>
<td>p value</td>
<td>MNI coordinates</td>
</tr>
<tr>
<td>-----------------------</td>
<td>--------------</td>
<td>---------</td>
<td>-----------</td>
<td>-----------------</td>
</tr>
<tr>
<td>Frontal_Inf_Tri_L</td>
<td>25</td>
<td>3.97</td>
<td>0.0004</td>
<td>-34 28 12</td>
</tr>
<tr>
<td>Occipital_Inf_R</td>
<td>82</td>
<td>3.93</td>
<td>0.0005</td>
<td>38 -62 -8</td>
</tr>
<tr>
<td>Temporal_Inf_L</td>
<td>33</td>
<td>3.58</td>
<td>0.0010</td>
<td>-50 -40 -20</td>
</tr>
<tr>
<td>Putamen_L</td>
<td>39</td>
<td>3.50</td>
<td>0.0012</td>
<td>-18 14 6</td>
</tr>
<tr>
<td>Frontal_Inf_Tri_L</td>
<td>22</td>
<td>3.31</td>
<td>0.0018</td>
<td>-40 16 22</td>
</tr>
<tr>
<td>Frontal_Inf_Oper_R</td>
<td>13</td>
<td>3.27</td>
<td>0.0020</td>
<td>40 0 22</td>
</tr>
<tr>
<td>Frontal_Inf_Orb_L</td>
<td>10</td>
<td>3.22</td>
<td>0.0022</td>
<td>-30 30 -16</td>
</tr>
<tr>
<td>Temporal_Mid_R</td>
<td>17</td>
<td>3.12</td>
<td>0.0028</td>
<td>42 -70 20</td>
</tr>
</tbody>
</table>

Note: All clusters survived the threshold of $p < .005$, with 10 voxel extension, no correction. * indicates brain regions/clusters that contain or fall into predefined ROIs. Two encoding runs were combined.
Supplementary Table 5. Brain regions with which the hippocampus formed stronger connectivity in the famous vs. nonfamous condition (Chapter 3)

<table>
<thead>
<tr>
<th>Anatomical areas</th>
<th>Cluster size</th>
<th>t value</th>
<th>p value</th>
<th>MNI coordinates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L-HPC: famous &gt; nonfamous</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rectus_L *</td>
<td>27</td>
<td>3.80</td>
<td>0.0006</td>
<td>-4  40  -16</td>
</tr>
<tr>
<td>SupraMarginal_L</td>
<td>21</td>
<td>3.71</td>
<td>0.0007</td>
<td>-64 -24  36</td>
</tr>
<tr>
<td>Frontal_Mid_R</td>
<td>11</td>
<td>3.68</td>
<td>0.0008</td>
<td>42  36  20</td>
</tr>
<tr>
<td>Insula_R</td>
<td>16</td>
<td>3.63</td>
<td>0.0009</td>
<td>40  -14  4</td>
</tr>
<tr>
<td>Frontal_Inf Orb_L</td>
<td>15</td>
<td>3.49</td>
<td>0.0012</td>
<td>-28 20  -22</td>
</tr>
<tr>
<td>Temporal_Pole_Sup_R *</td>
<td>44</td>
<td>3.44</td>
<td>0.0014</td>
<td>40  22  -26</td>
</tr>
<tr>
<td>Temporal_Pole_Sup_L *</td>
<td>13</td>
<td>3.31</td>
<td>0.0018</td>
<td>-34 24  -28</td>
</tr>
<tr>
<td>L-HPC: nonfamous &gt; famous</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occipital_Sup_R</td>
<td>195</td>
<td>6.46</td>
<td>0.0000</td>
<td>22  -70  30</td>
</tr>
<tr>
<td>Caudate_L</td>
<td>271</td>
<td>5.07</td>
<td>0.0000</td>
<td>-16 12  28</td>
</tr>
<tr>
<td>Temporal_Mid_R</td>
<td>45</td>
<td>3.85</td>
<td>0.0005</td>
<td>38  -50  12</td>
</tr>
<tr>
<td>Occipital_Mid_L</td>
<td>39</td>
<td>3.65</td>
<td>0.0009</td>
<td>-32 -74  14</td>
</tr>
<tr>
<td>Putamen_R</td>
<td>19</td>
<td>3.57</td>
<td>0.0010</td>
<td>28  -14  10</td>
</tr>
<tr>
<td>Paracentral_Lobule_R</td>
<td>24</td>
<td>3.56</td>
<td>0.0010</td>
<td>8  -28  62</td>
</tr>
<tr>
<td>Occipital_Inf_R</td>
<td>59</td>
<td>3.55</td>
<td>0.0011</td>
<td>32  -86  -4</td>
</tr>
<tr>
<td>Cerebelum_8_R</td>
<td>17</td>
<td>3.50</td>
<td>0.0012</td>
<td>22  -46  -44</td>
</tr>
<tr>
<td>Cerebelum_4_5_L</td>
<td>43</td>
<td>3.46</td>
<td>0.0013</td>
<td>-14 -54 -24</td>
</tr>
<tr>
<td>Occipital_Mid_R</td>
<td>17</td>
<td>3.44</td>
<td>0.0014</td>
<td>34  -88  20</td>
</tr>
<tr>
<td>Frontal_Sup_R</td>
<td>13</td>
<td>3.44</td>
<td>0.0014</td>
<td>18  14  60</td>
</tr>
<tr>
<td>Cingulum_Mid_R</td>
<td>30</td>
<td>3.33</td>
<td>0.0018</td>
<td>4  -22  28</td>
</tr>
<tr>
<td>Putamen_R</td>
<td>20</td>
<td>3.33</td>
<td>0.0018</td>
<td>24  -2  14</td>
</tr>
<tr>
<td>Cerebelum_4_5_L</td>
<td>21</td>
<td>3.32</td>
<td>0.0018</td>
<td>-16 -34 -26</td>
</tr>
<tr>
<td>Cingulum_Mid_L</td>
<td>15</td>
<td>3.29</td>
<td>0.0019</td>
<td>-10 -22 42</td>
</tr>
<tr>
<td>R-HPC: famous &gt; nonfamous</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anatomical areas</td>
<td>Cluster size</td>
<td>t value</td>
<td>p value</td>
<td>MNI coordinates</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>--------------</td>
<td>---------</td>
<td>---------</td>
<td>-----------------</td>
</tr>
<tr>
<td>SupraMarginal_L</td>
<td>40</td>
<td>4.33</td>
<td>0.0002</td>
<td>-64 -24 36</td>
</tr>
<tr>
<td>Frontal_Inf_Orb_R</td>
<td>13</td>
<td>4.04</td>
<td>0.0004</td>
<td>24 28 -20</td>
</tr>
<tr>
<td>Postcentral_R</td>
<td>10</td>
<td>3.70</td>
<td>0.0008</td>
<td>16 -30 76</td>
</tr>
<tr>
<td>Frontal_Med_Orb_R *</td>
<td>42</td>
<td>3.64</td>
<td>0.0009</td>
<td>8 50 -8</td>
</tr>
<tr>
<td>Temporal_Pole_Sup_R *</td>
<td>21</td>
<td>3.46</td>
<td>0.0013</td>
<td>44 16 -28</td>
</tr>
<tr>
<td>Frontal_Inf_Tri_R</td>
<td>40</td>
<td>3.46</td>
<td>0.0013</td>
<td>40 34 24</td>
</tr>
<tr>
<td>Temporal_Pole_Sup_L *</td>
<td>19</td>
<td>3.34</td>
<td>0.0017</td>
<td>-36 26 -26</td>
</tr>
<tr>
<td>R-HPC: nonfamous &gt; famous</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frontal_Mid_L</td>
<td>336</td>
<td>5.16</td>
<td>0.0000</td>
<td>-22 6 38</td>
</tr>
<tr>
<td>Occipital_Mid_L</td>
<td>131</td>
<td>4.68</td>
<td>0.0001</td>
<td>-30 -74 16</td>
</tr>
<tr>
<td>Fusiform_L</td>
<td>47</td>
<td>4.51</td>
<td>0.0001</td>
<td>-30 -68 -4</td>
</tr>
<tr>
<td>Cerebelum_4_5_L</td>
<td>183</td>
<td>4.44</td>
<td>0.0001</td>
<td>-30 -42 -24</td>
</tr>
<tr>
<td>Cerebelum_Crus2_L</td>
<td>18</td>
<td>4.32</td>
<td>0.0002</td>
<td>-2 -80 -40</td>
</tr>
<tr>
<td>Thalamus_L</td>
<td>19</td>
<td>4.16</td>
<td>0.0003</td>
<td>-20 -20 0</td>
</tr>
<tr>
<td>Frontal_Inf_Orb_R</td>
<td>13</td>
<td>3.99</td>
<td>0.0004</td>
<td>26 40 -8</td>
</tr>
<tr>
<td>Occipital_Mid_L</td>
<td>15</td>
<td>3.81</td>
<td>0.0006</td>
<td>-40 -90 -4</td>
</tr>
<tr>
<td>Temporal_Inf_L</td>
<td>32</td>
<td>3.75</td>
<td>0.0007</td>
<td>-38 -12 -22</td>
</tr>
<tr>
<td>Paracentral_Lobule_R</td>
<td>19</td>
<td>3.74</td>
<td>0.0007</td>
<td>8 -28 64</td>
</tr>
<tr>
<td>Putamen_R</td>
<td>35</td>
<td>3.71</td>
<td>0.0007</td>
<td>26 0 16</td>
</tr>
<tr>
<td>Cerebelum_4_5_L</td>
<td>12</td>
<td>3.47</td>
<td>0.0013</td>
<td>-18 -30 -28</td>
</tr>
<tr>
<td>Precentral_R</td>
<td>14</td>
<td>3.44</td>
<td>0.0014</td>
<td>46 -2 32</td>
</tr>
<tr>
<td>Caudate_R</td>
<td>16</td>
<td>3.38</td>
<td>0.0016</td>
<td>8 20 0</td>
</tr>
<tr>
<td>Caudate_L</td>
<td>12</td>
<td>3.29</td>
<td>0.0019</td>
<td>-16 -24 22</td>
</tr>
</tbody>
</table>

*Note: All clusters survived the threshold of \( p < .005 \), with 10 voxel extension, no correction. * indicates brain regions/clusters that contain or fall into predefined ROIs. Two encoding runs were combined.*
3.6 Supplementary Figures

Supplementary Figure 1. Associative encoding effects for each encoding run (Chapter 3)

**Supplementary Figure 1.** Bar graphs showing associative encoding effects (face-house > scrambled) in each predefined ROI separately for the first (A) and second (B) encoding run. t statistics and p values from one sample t tests (which tested whether beta values for the face-house vs. scrambled contrast were larger than zero) are also indicated. Encoding effects that survived FDR < .05 are indicated by ** under each ROI bar. Notes: Paired t test statistics for left and right hemispherical ROI comparisons are also presented above the ROI bars. Significant laterality effects (p < .05) is indicated by *. It is worth mentioning that the right side of the posterior ROIs such as the right FFA and PPA were more strongly activated than their left counterparts, whereas the left side of the anterior ROIs such as the left aTPL and vmPFC were more strongly engaged than the corresponding right ROIs, especially for the first encoding. Although this study was not to examine laterality effects, this result, as we expected, indicated that the left and right ROIs may be engaged differently by the encoding task and are better to be separated in the analyses.
Supplementary Figure 2. Activation for each ROI in each encoding run and fame condition (Chapter 3)

Supplementary Figure 2. Bar graphs showing fMRI activation beta estimates for each ROI in each encoding run and fame condition. Two by two (encoding run by fame) ANOVA main effects and interaction $p$ values are also presented.
**Supplementary Figure 3.** Activation in remembered and forgotten trials for the famous condition (Chapter 3)

**Supplementary Figure 3.** Bar graphs showing beta estimates for the remembered and forgotten trials in the famous condition in each predefined ROI. Two encoding runs were combined. * indicates significant difference between the two types of trials (i.e., significant subsequent memory effects) at $FDR < .05$. Beta values for the direct contrast of remembered and forgotten trials (i.e., remembered - forgotten) are given in Figure 7 in the main text.
Supplementary Figure 4. Subsequent memory effects for the famous and nonfamous condition (Chapter 3)

Supplementary Figure 4. Bar graphs showing subsequent memory effects (i.e., the beta estimates for the remembered - forgotten contrast) for the famous and nonfamous condition in the left (A) and right (B) hemispheric ROIs. Two encoding runs were combined. Data for the famous condition is duplicated from Figure 7 of the main text. No significant subsequent memory effects were found for the nonfamous condition (all FDR > .05). Significant differences of subsequent memory effects between the two fame conditions were found in the bilateral HPC, aTPL, and vmPC, indicated by * above lines that connect the two fame conditions (FDR < .05). * above single bars indicates significant subsequent memory effects in the famous condition. Note: These data seem to suggest that activation in the anterior, not the posterior perceptual, ROIs contributed to a larger extent to the face-house associative memory during the famous, compared to the nonfamous, condition. However, cautions should be excised because the trial count of the remembered pairs in the nonfamous condition was very low, which may lead to less robust results.
Supplementary Figure 5. Graphic illustrations of the HPC connectivity fame effects from whole the brain analysis (Chapter 3)

Supplementary Figure 5. Graphic illustrations of the HPC connectivity fame effects using all clusters that survived the uncorrected voxel-wise threshold of $p < .005$, with 10 voxel extension. Precise anatomical information and size of the clusters are listed in Supplementary Table 5. The size of the sphere in the graph is proportional to the size of the cluster that survived the uncorrected threshold and the thickness of the connection line is proportional to the strength of the connectivity. Two encoding runs were combined.
Chapter 4

Study 3: Prior-knowledge Effect on Post-encoding Brain Connectivity and Its Relation to Subsequent Memory

4.1 Introduction

In the fMRI study reported in Chapter 3 (i.e., Experiment 2), I found that during face-house associative encoding, prior-knowledge related to famous faces facilitated new learning by recruiting additional perceptual, evaluative, or associative binding processes, supported by different brain regions such as the FFA, PPA, HPC, and vmPFC. However, we know that memory processing does not stop after the encoding phase (Nadel & Moscovitch, 1997; Squire & Alvarez, 1995; Wang & Morris, 2010). As mentioned in Chapter 1, a large body of animal literature has shown that post-encoding neural activity in different brain regions, including the HPC, medial PFC, and early sensory perception areas, may reflect memory replay and contribute to memory stabilization (Eagleman & Dragoi, 2012; Euston et al., 2007; Knauer, Jochems, Valero-Aracama, & Yoshida, 2013; O’Neill, Pleydell-Bouverie, Dupret, & Csicsvari, 2010; Singer & Frank, 2009; Wilson & McNaughton, 1994). Human neural imaging studies have also found that learning experience can modulate resting-state brain connectivity (Albert et al., 2009; Deuker et al., 2013; Groen et al., 2011; Hasson et al., 2009; Urner et al., 2013; Wang et al., 2012; Zou et al., 2013), and that the HPC activity during post-encoding rests or unrelated tasks can be correlated with memory performance (Staresina, Alink, et al., 2013; Tambini & Davachi, 2013; Tambini et al., 2010). These observations support the idea that post-encoding neural activity reflects early memory consolidation processes by which newly-encoded memory becomes more stable. As mentioned in Chapter 1, recent evidence has shown that prior-knowledge can hasten the memory consolidation process (Tse et al., 2007). Then, the question of whether prior-knowledge can also affect post-encoding brain activity and contribute to memory formation needs to be investigated.

To the best of my knowledge, only one human neural imaging study (van Kesteren, Fernández, et al., 2010) has examined prior-knowledge effects on post-encoding brain activity. In that study,
van Kesteren and colleagues found that the connectivity between the HPC and vmPFC became *weaker* during encoding and post-encoding rest when prior-knowledge was involved. However, as mentioned earlier, prior-knowledge manipulated in that study (i.e., using movie clips) is very complex, making it difficult to predict which brain regions support this type of complex prior-knowledge. Moreover, the memory task, i.e., movie encoding, was also complex, likely involving many different types of stimuli and processes. These complexities can lead to difficulties in examining in more detail how different components of prior-knowledge affect new memory processing. In addition, van Kestern et al. (2010a) mainly focused on the connectivity between the HPC and vmPFC, based on the assumption that the vmPFC plays an important role in supporting existing structured mental representations such as schemas (van Kesteren et al., 2012). While this assumption is reasonable, other regions such as the anterior temporal pole (aTPL) have also been shown to support prior-knowledge (Kan et al., 2009; Sharon et al., 2011; Staresina, Gray, & Davachi, 2009) and, therefore, should be considered in studying the effects of prior-knowledge on new learning.

Because the face-house associative encoding task used in Experiment 1 and 2 was designed to remediate these problems, it can also be used to investigate whether prior-knowledge related to famous faces can affect post-encoding brain connectivity. As mentioned in Experiment 2, after participants were asked to associate pictures of novel houses with pictures of either famous or nonfamous faces, they were also instructed to have a rest in the scanner after each fame encoding block. This block design, with counterbalanced fame order, allowed post-encoding brain activity to be recorded following each encoding condition in each participant. Thus, these data can be used to investigate whether prior-knowledge could also affect post-encoding brain connectivity by comparing the two fame conditions. Similar to Experiment 2, which focused on the encoding phase, in this post-encoding brain activity analysis, the HPC, aTPL, vmPFC, PPA, and FFA were also included as regions of interest (ROIs). All these 5 ROIs, which support different components of memory processing, were found to be involved in the face-house associative encoding in Experiment 2, indicating that it is possible that they also played a role in post-encoding memory processes. I also included a pre-encoding rest in this study to serve as a baseline condition for the post-encoding analyses.

The literature on memory consolidation has shown that neocortical regions become more important for supporting consolidated memory, whereas the medial temporal lobe, especially the
HPC, is more crucial for supporting new memory processing (Frankland & Bontempi, 2005; Moscovitch et al., 2005; Nadel & Moscovitch, 1997; Squire & Alvarez, 1995). This switch in neural substrates may also underlie changes in the nature of these memories during consolidation processes (Nadel & Moscovitch, 1997; Wiltgen & Silva, 2007; Winocur & Moscovitch, 2011). Because it has been found that prior-knowledge can facilitate memory consolidation (Tse et al., 2007, 2011), I hypothesized that the anterior cortical regions, namely, the vmPFC and aTPL, should form stronger connectivity with the HPC, PPA, and FFA during post-famous-encoding rest than the post-nonfamous-encoding rest, reflecting stronger cortical involvement from anterior brain regions during early memory consolidation when prior-knowledge was involved. These connectivity measures should also better predict the associative memory performance in the famous than the nonfamous condition. Moreover, if the episodic binding processing was also strengthened by existing prior-knowledge, which had been supported by the finding that the HPC and FFA/PPA activations were stronger in the famous than nonfamous encoding condition (Experiment 2), we would expect that the connectivity between the HPC and PPA/FFA should also be stronger during the post-famous-encoding than post-nonfamous-encoding rest.

4.2 Method

4.2.1 Participants

The same group of participants (N = 20, 12 females. Mean age = 21.3, SD = 1.9) participated in Experiment 2 and 3. As mentioned in Experiment 2 (Chapter 3), all participants gave their informed consent and were paid $76 for their participation of both experiments. The study was approved by the Research Ethic Board at Baycrest Centre for Geriatric Care (University of Toronto).

4.2.2 Procedure

Overview. Here I only describe the task procedure that was relevant to the current study. As mentioned in Experiment 2, there were 3 resting scans in Experiment 3 (see Figure 1 for these tasks). After the structural MRI scan, participants underwent the first, i.e., pre-encoding, resting
**Figure 1.** Schematic overview of the encoding and resting scans (Chapter 4)

A. Schematic overview of the encoding and resting scans. The order of the famous and non-famous condition was counter-balanced across the participants. B. An example of encoding trials from the famous condition. Identical trial structure was used for the non-famous condition. C. An example of retrieval trials in the famous condition. Identical trial structure was used for the non-famous condition. (More detailed information can be obtained from Figure 1 of Experiment 2 in Chapter 3.) (Image sources: same as Study 1)
scan which provided a baseline measure of resting brain activity. Participants then performed the face-house associative encoding task (Experiment 2) for one fame condition in two repeated runs (10 minutes/run), which was followed by a second resting scan. Participants then performed the associative encoding task for the other fame condition twice in two consecutive runs, which was again followed by a third resting scan. Each resting scan lasted 6 minutes during which participants were required to keep their eyes closed, remain still, and relax. Under these conditions, they were allowed to think freely. The participants were also informed that the same instructions should be applied to all 3 rests and they were reminded of the instructions before each resting scan started. After the third resting scan, participants also performed a face/house localizer fMRI task.

As mentioned in Experiment 2 in Chapter 3, the order of the two fame conditions was counterbalanced across the participants. After the MRI session, participants were asked to perform a multiple-step retrieval task in another testing room.

After the retrieval task, participants were asked to rate the famous faces on different dimensions (see face evaluation section). At the end of the experiment, participants were also asked to estimate how much time they spent during each rest in thinking about their past and planning for their future (see Post-experiment interview section).

**Face-house associative encoding task.** The details of the encoding task were reported in Experiment 2. For completeness, briefly, in each face-house encoding trial (Figure 1B), participants were asked to associate the face and house picture for 3.5 seconds and then indicate whether it was easy (or not) for them to make the association by pressing one of two buttons in a 1.5 seconds response window. The structure of scrambled picture-pair trials was almost identical to that of the face-house trials, except that the presentation duration was reduced to 1.5 seconds, and that participants were asked to answer whether it was easy (or not) for them to differentiate the pattern of the two scrambled pictures. A jitter time of 1 – 4 seconds (with an exponential distribution across trials and mean time of 1.5 seconds) was given between trials. The size, location, contrast, and luminance of face, house, and scrambled pictures were balanced across trials. Ten encoding practice trials were given before the encoding scan started.
**Pre-/post-encoding resting state scans.** During each of the three 6-minute resting scans, participants were required to relax, keep eyes closed, and remain still. Although participants were allowed to think freely, I stressed that they should relax. To avoid potential contamination on the first resting state scan from the encoding task, the practice block of the encoding task was always given after the first resting scan. Because the order of the two encoding fame conditions was counter-balanced, the order of the post-famous-encoding rest and post-nonfamous-encoding rest was also counter-balanced across the participants.

**Face/house localizer scan.** The same localize scan as described in Experiment 2 was used to localize the FFAs and PPAs.

**Unscanned retrieval task.** The details of the retrieval task were reported in Experiment 2. Briefly, 4 types of face-house retrieval pairs, i.e., *intact*, *recombined*, *old/new*, and *new-new* pairs, were constructed for this 3-step retrieval task (Figure 1C). Both the face and house pictures in the *intact* and *recombined* pairs were old, i.e., being encoded by the participants in the encoding phase, but for the *recombined* pairs, the face and house pictures were re-paired. For each retrieval trial, first, a single picture (face or house) from a face-house retrieval pair was presented and participants were asked to recognize this single picture using a Recollection/Familiarity paradigm. Then, the other picture of that retrieval pair was added to form a face-house pair and participants needed to respond whether both pictures had been encoded in the encoding phase regardless whether the two pictures had been paired together. At the third step, participants were asked to identify whether the pair was intact or recombined (if they had indicated that both pictures had been encoded in the encoding phase), or whether the pair contained one or two new pictures (if they had indicated that at least one picture had not been encoded). Face-house pairs from the 4 retrieval pair types and 2 fame conditions were randomly presented. This retrieval task lasted about 30 minutes.

In the current study, I mainly focused on the associative memory performance derived from the third step of the retrieval task. As mentioned in Experiment 1 and 2, the associative memory, i.e., associative identification (Cohn & Moscovitch, 2007), was measured by subtracting the percentage of the recombined trials that were mistaken as intact pairs (i.e., false alarm rate) from the percentage of the intact pairs that were correctly identified as intact pairs (i.e., hit rate).
**Face evaluation.** As mentioned in Experiment 2 in Chapter 3, to confirm that participants indeed had prior-knowledge about these famous people whose faces were used in this experiment, after the retrieval task, participants were asked to rate the famous face pictures on *familiarity*, *attractiveness*, *emotion*, and *memory* using 5-point scales. Specifically, I instructed the participants to give a number, from 1 ("none or extremely low") to 5 ("extremely high"), to indicate how familiar they were with those famous people (*familiarity*), how attractive they thought the faces were (*attractiveness*), how strongly the faces evoked emotions or emotional opinions (*emotion*), and how vividly memories of previous experiences were triggered by the faces (*memory*). For the first three evaluation tasks, nonfamous faces were also added as fillers. The order of the face pictures were randomized across both the evaluation tasks and participants. The order of these rating tasks was also randomized across participants. The tasks were self-paced, with each about 5 mins long. The mean rating score was 3.84 (SD = .91) for *familiarity*, 3.01 (SD =.64) for *memory*, 2.65 (SD =.84) for *emotion*, and 3.24 (SD =.34) for *attractiveness*. These data indicated that the participants did have prior-knowledge about these famous people.

**Post-experiment interview.** After the experiment, I asked the participants whether they had explicitly thought about the encoding task during each resting scan. Only two participants reported that they had thought very briefly (less than 10% of the total resting time) about something (e.g., objects, people, or events) that was related to the encoding stimuli at the very beginning of the post-encoding rest. Among the two participants, one reported that he/she did this similarly at the beginning of the post-famous-encoding rest and post-nonfamous-encoding rest, and the other reported that she/he only did this at the beginning of the post-famous-encoding rest. The other 18 participants reported that they had not thought about anything that was related to the encoding task. Importantly, none of the 20 participants reported explicit rehearsal of the face-house association task during the post-encoding rests. Therefore, the current analysis included the data from all 20 participants. However, the main findings of this study remained the same after excluding the two participants who claimed to have thought briefly about something related to the task material.

To further confirm that participants performed similar mental activity during the 3 rests, I also asked the participants to estimate how much time (in percentage) they spent during each rest on thinking about the future, remembering the past, or just mind-wandering. There was no difference on any of the 3 measures among the 3 rests (pre-encoding rest: *Mean* = 38%, 22%,
and 40%, $SD = 31\%$, 23%, and 32% for future thinking, past thinking, and mind-wandering, respectively; post-famous-encoding rest: $\textit{Mean} = 35\%, 23\%, \text{and } 42\%, SD = 30\%, 25\%, \text{and } 32\%$; post-nonfamous-encoding rest: $\textit{Mean} = 38\%, 22\%, \text{and } 40\%, SD = 30\%, 22\%, \text{and } 33\%; \text{all } p > .16)$. There were no correlations between the length of the time that participants spent in active thinking during the rests and the later associative memory performance in the two fame conditions (all $p > .45$), providing further confirmation that the participants did not actively rehearse the task material during the rests.

4.2.3 Structural and functional MRI scan

Identical imaging procedure was used for Experiment 2 and 3. For completeness, all MRI images were required in a 3T Siemens MRI scanner with a standard 12 channels head coil at the Baycrest Hospital (University of Toronto). T1-weighted images were obtained using a standard 3-dimentional MPRAGE (magnetization-prepared rapid-acquisition gradient echo) pulse sequence (160 slices; field of view (FOV) = 256 x 256 mm; 192 x 256 matrix; 1 mm isotropic resolution, TE/TR=2.63/2000 ms, flip angle = 9 degrees, and scan time = 386 s). Functional T2-weighted images were obtained using an EPI procedure with TE = 24 ms, TR = 2000 ms, 3.5 mm slices (with 0.5 mm gap and a bottom-up interleaved order), and flip angle = 70° (FOV = 200 x 200 mm; 64 x 64 matrix, 3.5 x 3.5 mm in-plane resolution). All images were acquired in an oblique orientation (30 degree clockwise to the anterior-posterior commissssure axis) to reduce the fMRI signal drop in the ventral medial prefrontal regions. Visual stimuli and instructions, presented by E-Prime software (version 2, Psychology Software Tools, Inc.), were back-projected to a screen and viewed with a mirror mounted on the head coil. Head movements were minimized by inserting soft cushion into the head coil.

4.2.4 Data analysis

fMRI resting data spatial preprocessing. Identical to Experiment 2, SPM8 (Statistical Parametric Mapping, Welcome Trust Center for Neuroimaging, University College London, UK; www.fil.ion.ucl.ac.uk/spm/, version 4661) in MATLAB environment (MathWorks, Natick, MA) was used to preprocess the T2-weighted functional images. In brief, first, slice timing was corrected using sinc-interpolation with the midpoint slice as the reference. Then, all functional images were aligned using a 6-parameter linear transformation. Next, anatomical images were co-registered to the aligned functional images, and segmented into white matter (WM), gray
matter (GM), and cerebrospinal fluid (CSF) using SPM8 default tissue probability maps. These segmented images were then used to calculate the transformation parameters mapping from the individuals' native space to the MNI template space. The resulting transformation parameters were used to transform all functional images to the MNI template. The functional images were then re-sampled at 2 x 2 x 2 mm resolution and smoothed using a Gaussian kernel with the FWHF (full-width at half maximum) of 8 mm. The first 3 fMRI volumes from each run were discarded.

**fMRI resting data temporal preprocessing.** Several sources of potential confounding variances were deleted from the spatially preprocessed functional time-series using functional connectivity toolbox conn (Whitfield-Gabrieli & Nieto-Castanon, 2012): First, signals from the white matter (WM) and cerebrospinal fluid (CSF) were used to regress out nonspecific variances from the functional time-series using a principal component based noise correction method (Behzadi, Restom, Liau, & Liu, 2007). The 6 motion parameters obtained from the re-alignment procedure and their first derivatives were used as regressors to further clean the potential confounding effects from the head motion. Five principal components were used for the WM/CSF regressors and six for the motion parameter regressors. Then, the resulting time-series were band-filtered (0.008 - 0.1 Hz) to further reduce potential confounding effects from low frequency drifts and high frequency physiological noises. Finally, a hypobolic tangent function was used to suppress (i.e., despike) extreme values in the fMRI time series to reduce effects of potential outliers (Whitfield-Gabrieli & Nieto-Castanon, 2012).

**ROI definition.** As mentioned earlier, five bilateral, pre-defined ROIs, i.e., the vmPFC, aTPL, HPC, PPA, and FFA were included. First, to make sure that the ROIs used in the current post-encoding connectivity analysis were the regions that played a functional role during encoding, I defined the vmPFC, aTPL, and HPC ROIs using the face-house associative encoding task analysis in Experiment 2. Specifically, I first conducted a first-level SPM general linear model (GLM) analysis, in which the face-house encoding trials were contrasted with the scrambled picture trials. Then, at the second level analysis, I used anatomical masks of the vmPFC, aTPL, and HPC ROIs using the face-house associative encoding task analysis in Experiment 2. Specifically, I first conducted a first-level SPM general linear model (GLM) analysis, in which the face-house encoding trials were contrasted with the scrambled picture trials. Then, at the second level analysis, I used anatomical masks of the vmPFC, aTPL, and HPC and SPM small volume corrections to obtain these functional ROIs. As mentioned in Experiment 2, the anatomical masks were generated using the automated anatomical labeling (AAL) template (Tzourio-Mazoyer et al., 2002) and the WFU-Pickaltas toolbox (Maldjian et al., 2003). The vmPFC mask consisted of the gyrus rectus and the orbital and medio-orbital section
of the superior frontal gyrus. The aTPL mask consisted of the temporal pole region of the superior and middle temporal gyrus. The HPC mask was directly obtained from the AAL atlas. For the small volume correction, a threshold of \( p = .0001 \) (no corrections) was used to obtain the aTPL and HPC ROIs. Because the vmPFC anatomical masks were relatively large and contained more heterogeneous functional areas, a slightly lenient threshold of \( p = .005 \) with 10 voxel extension (no corrections) was used to include more voxels for this ROI (Figure 2).

The PPA and FFA functional ROIs were identical to those in Experiment 2. In brief, I first conducted a block-design first-level GLM analysis and used the contrast of \textit{face} - \textit{house} and \textit{house} - 0.5\textit{face} - 0.5\textit{object} to localize the FFAs and PPAs, respectively. These contrast images were then used in the second level one-sample t test, in which both the FFAs and PPAs were easily identified in the fusiform and parahippocampal gyrus using the threshold of \( p = .005 \), with 10-voxel extension. To make the final functional ROI masks, I made a small volume correction using a sphere with 8 mm radius around the maximum activation voxels (left FFA: [-42 -50 -26], right FFA: [44 -52 -18], left PPA: [-28, -40 -10], and right PPA: [24, -40 -10]; see Figure 2). It should be noted that all these ROIs, including the PPA and FFA, were activated by the face-house encoding task (see Supplementary Figure 1 of Experiment 2).

\textbf{fMRI connectivity analysis.} Functional connectivity analyses were conducted using the conn toolbox (Whitfield-Gabrieli & Nieto-Castanon, 2012) and custom Matlab scripts. First, mean fMRI signals were extracted from all voxels in each of the five bilateral ROIs. Then, for each participant, Pearson correlations (\( r \)) among these ROI signals were calculated and transformed to Fisher's Z scores \( \frac{\ln(r+1)}{\ln(r-1)} \). To test the prior-knowledge effects on post-encoding brain connectivity, I directly compared the correlation Z scores among these predefined ROIs between the post-famous-encoding and post-nonfamous-encoding rests using paired \( t \) tests. To investigate the relationship between the post-encoding brain connectivity and associative memory performance, I conducted regression analyses in which the connectivity measures among these pre-defined functional ROIs were used to predict associative memory performance. These regression analyses were conducted separately for the two fame conditions.
Figure 2: ROI masks (Chapter 4)

Figure 2. The 5 bilateral ROIs used in this study, including the left and right ventral medial prefrontal cortex (i.e., L-vmPFC and R-vmPFC), the left and right anterior temporal pole (i.e., L-aTPL and R-aTPL), the left and right hippocampus (i.e., L-HPC and R-HPC), the left and right parahippocampal place area (i.e., L-PPA and R-PPA), and the left and right fusiform face area (i.e., L-FFA and R-FFA). The vmPFC, aTPL, and HPC ROIs were obtained from the encoding task using the face-house trial vs. scrambled trial contrast (Experiment 2). The PPA and FFA ROIs were obtained from the face-house localizer task (Experiment 2). The MNI coordinates of the FFAs and PPAs (at the peak activation locations) are also indicated. The surface-rendered brain images were generated using BrainNetView toolbox http://www.nitrc.org/projects/bnv/. The section view images were generated using MRICron http://www.mccauslandcenter.sc.edu/mricron/.
**Statistical thresholding.** Two-tailed $t$ tests ($\alpha = .05$) were used to test connectivity differences between conditions. Similar to Experiment 2, I used a false detection rate ($FDR$) of 0.05 to control for multiple testing in each seed-based connectivity analysis, including $t$ test and connectivity-behavior regression. This was to ensure that the total false positive findings from these analyses were below 5% (Benjamini & Hochberg, 1995). Effects with original $p < .05$, but $FDR > .05$ and < .1, were reported as marginally significant (i.e., trend level) effects. When $FDR$ correction was not necessary, e.g., for planned or selected ROI analyses, effects with original $p > .05$ but < .1 were considered as marginally significant effects.

### 4.3 Results

#### 4.3.1 Behavioral results.

As reported previously (Experiment 2), associative memory performance (hit rate - false alarm rate) was better for the famous ($M = .36, SD = .21$) than the nonfamous ($M = .19, SD = .14$) condition ($t(19) = 4.60, p < .0002$). The correlation between associative memory performance in the two conditions was significant ($r(18) = .47, p = .035$). Interestingly, participants' age predicted associative memory performance only in the famous ($r(18) = .60, p = .005$), but not the nonfamous condition ($r(18) = .11, p = .63$). A robust regression analysis also showed that age still predicted the associative memory performance of the famous condition after controlling for memory in the nonfamous condition ($p = .01$). Because there was no age-memory relationship for the nonfamous condition, the age effects on the associative memory of the famous condition should not be a general developmental effect. Instead, it may reflect a between-participant prior-knowledge facilitation effect, i.e., older participants likely had gained more knowledge about the famous people and, thereby, benefited more from their prior-knowledge when forming associations between novel houses with famous faces.

#### 4.3.2 Prior-knowledge effects on post-encoding brain connectivity

Before I tested the main hypotheses of this study, I checked whether face-house associative encoding task significantly modified resting state brain connectivity. To this end, I contrasted
functional connectivity among the 5 bilateral ROIs during post-encoding rest with pre-encoding rest. The analysis was conducted separately for the two fame conditions. For the famous condition, I found that the connectivity between the right aTPL and left FFA increased during post-encoding, compared to pre-encoding, rest \((t(19) = 3.43, p = .0028, FDR = .025)\). For the nonfamous condition, only the connectivity between the right HPC and right FFA was found to decrease after the nonfamous encoding task \((t(19) = -3.71, p = .0015, FDR = .014)\). No other significant results were found from these analyses.

Next, to test whether prior-knowledge differentially affected post-encoding brain activity, I directly compared brain connectivity among the 5 pre-defined bilateral ROIs between the two post-encoding rests. The results showed that only the connectivity between the left FFA and right HPC was different between the two post-encoding rests, being stronger in the post-famous-encoding rest than the post-nonfamous-encoding rest \((t(19) = 3.67, p = .0017, FDR = .015)\). As can be seen in the bar graphs in Figure 3A, this post-encoding connectivity difference was likely driven by the reduced connectivity in the post-nonfamous-encoding rest. Next, using regression analyses, I tested whether the connectivity between the left FFA and right HPC could predict associative memory performance in the two fame conditions. As can be seen in scatter plots in Figure 3A, the FFA-HPC connectivity during the post-famous-encoding rest positively predicted the associative memory of the famous condition at a trend level \((t(18) = 2.04, p = .056)\), but the connectivity between the same regions during the post-nonfamous-encoding rest negatively predicted the associative memory in the non-famous condition \((t(18) = -2.30, p = .03)\). Regression slopes for the two post-encoding conditions differed significantly \((t(38) = 3.03, p = .002)\), which confirmed the difference in brain-behavior relations between the two fame conditions. Critically, the connectivity between the left FFA and right HPC during the pre-encoding rest did not predict the associative memory performance in either of the two fame conditions \((ps > .34; \text{Figure 3A})\).
Figure 3: Prior-knowledge effects on post-encoding brain connectivity: Predefined ROI results (Chapter 4)

**Figure 3.** A. Brain connectivity differences between the post-famous-encoding rest and the post-non-famous-encoding rest. On the left brain surface plot, the connectivity that showed significant effects after $FDR = .05$ correction is indicated in red lines. Middle: The bar graph with individual data points showing that the L-FFA and R-HPC connectivity was stronger in the post-famous-encoding rest than the post-non-famous-encoding rest after $FDR$ correction. Pre-encoding connectivity data are also added for comparison. The connectivity in all 3 rests were...
significant larger than zero (*** \( p < .0005 \), **** \( p < .00005 \)). The t-test p values for the comparisons between the 3 rests are also indicated above the bars. Right: The scatter plots depict the relationship between connectivity measures and associative memory performance in the two fame conditions (upper: famous condition; bottom: nonfamous condition; gray: pre-encoding; red: post-famous-encoding rest; blue: post-nonfamous-encoding rest). B. Brain connectivity during post-famous-encoding rest positively predicted associative memory of the famous condition. On the brain surface plot, the connectivity that showed significant effects after \( FDR = .05 \) correction is indicated in thicker red lines. The connectivity whose effects did not survive the FDR correction but reached the uncorrected threshold of \( p =.05 \) is also indicated in thinner red lines (similar notations are used for the brain surface plots in C and D). Scatter plots (with regression lines) shows that the post-famous-encoding rest connectivity only predicted the associative memory performance of the famous (in red, \( FDR < .05 \)), not the nonfamous (in blue), condition. C. Brain connectivity between the R-FFA and L-HPC during the post-famous-encoding rest positively predicted associative memory of the famous condition at \( FDR < .05 \), after controlling for the pre-encoding brain connectivity. The connectivity between the left FFA and left HPC (in thinner red line) showed similar effects at \( p < .05 \) without \( FDR \) correction. D. The R-PPA and R-aTPL connectivity difference between the post-famous-encoding and post-non-famous-encoding rest positively predicted associative memory differences between the two fame conditions at \( FDR < .05 \). The connectivity between the right PPA and left aTPL/right HPC (in thinner red lines) showed similar effects at \( p < .05 \) without \( FDR \) correction.
4.3.3 Post-encoding brain connectivity that were not significantly modified by encoding tasks predicting associative memory

As can be seen from Figure 3, although post-encoding connectivity between the left FFA and the right HPC was not different from that in the pre-encoding rest at the group mean level ($t(19) = .70$ and -1.80, $p = .49$ and .087, $FDR = .64$ and .39 for the famous and nonfamous condition, respectively), individual participants’ connectivity strength during the post-encoding, but not during the pre-encoding, rest still predicted later associative memory. These results indicated that post-encoding brain connectivity can still be important for memory processing even it did not differ at the group level from the pre-encoding rest. Thus, it is also possible that brain connectivity that did not differ between the two post-encoding rests could still differentially predict associative memory of the two fame conditions.

To test this possibility, I conducted regression analyses using post-encoding brain connectivity that did not show fame effects to predict associative memory performance in the two fame conditions. For the famous condition, I found that the connectivity between the left PPA and the bilateral aTPL, between the right PPA and left aTPL, between the left aTPL and left FFA, and between the left HPC and right FFA during the post-famous-encoding rest positively predicted associative memory performance in the famous condition ($t(18) = 3.14, 2.97, 2.72, 2.80, \text{ and } 3.49, p = .006, .009, .014, .012, \text{ and } .003, \text{ respectively. } FDR = .023 \sim .043$. Figure 3B). Using a multiple linear regression analysis with age as a covariate, these 5 connectivity measures together explained 45.7% variance of associative memory performance in the famous condition ($F(5, 13) = 6.40, p = .003$). The connectivity of the left aTPL with right PPA and left FFA explained unique variance of associative memory ($t = 2.59 \text{ and } 2.48, p = .022 \text{ and } .028$, respectively) above and beyond the common contribution of these 5 predictors. The unique contribution of the connectivity between the left HPC and right FFA on memory performance was at a trend level ($t = 1.92, p = .078$). These data showed that post-encoding connectivity of the aTPL and HPC with posterior perceptual regions such as the FFA and PPA played an important role in associative memory processes when prior-knowledge was involved.
In addition, I also found that the connectivity between the left HPC and left FFA, between the right aTPL and PPA, and between the left and right FFA appeared to positively predicted associative memory in the famous condition \( t(18) = 2.64, 2.21, \) and \( 2.22, \ p = .017, .041 \) and \( .04), \) but the effects did not survive the \( FDR \) correction \( (FDR = .07 \sim .18; \) Figure 3B). It should be mentioned that all these connectivities in the post-famous-encoding rest that predicted the associative memory performance of the famous condition did not predict the associative memory of the non-famous condition (Figure 3B). Also, the pre-encoding connectivity among these regions did not predict the associative memory performance of the famous condition either. Following Tambini et al. (2010), when the connectivity in the pre-encoding rest was subtracted from the connectivity in the post-encoding rest, the left HPC and right FFA connectivity changes due to the encoding task still positively predicted the associative memory in the famous condition \( t(18) = 3.56, p = .0022, FDR = .02; \) Figure 3C). Moreover, I calculated the face and house item memory performance using the hit rate minus false alarm obtained from all 3 steps of the retrieval procedure and found that these post-encoding connectivities did not predict the house and face item memory of the famous condition (except that the connectivity between the left PPA and left aTPL positively predicted the famous face memory at \( FDR = .07; \) Supplementary Figure 1). Thus, the connectivity among these regions during the post-famous-encoding rest was specifically related to associative memory formation in the famous condition.

Because age positively predicted associative memory performance only in the famous condition, which may reflect a between-subject prior-knowledge facilitation effect, I also tested whether age could predict the connectivities that showed specific relationship with the associative memory of the famous condition. Our regression analyses showed that age positively predicted the connectivity between the right FFA and left HPC, between the left PPA and left aTPL, and between the left PPA and right aTPL during the post-famous-encoding rest at trend levels \( (p = .061, .087, \) and \( .066, \) respectively, no correction; Supplementary Figure 2). Interestingly, these three (out of five) connectivity measures also showed strongest prediction effects on the associative memory of the famous condition. It should be mentioned that age did not predict the connectivity among these regions in the pre-encoding and post-nonfamous-encoding rest. I also found that the connectivity between the right FFA and left HPC and the connectivity between the left PPA and left aTPL during the post-famous-encoding rest were stronger for the participants
who reported more vivid memories elicited by the famous faces \((p = .06\) and \(p = .01\), respectively, no correction; Supplementary Figure 2). Although most of the effects were weak (i.e., at trend levels) and should be interpreted with caution, they collectively seemed to form a clear pattern showing that the strength of the post-famous-encoding connectivity that predicted later memory was also positively related to the strength of individuals' prior-knowledge.

Next, I conducted similar analyses for the nonfamous condition and did not find significant relations between the post-encoding connectivity among these pre-defined ROIs and the associative memory of the nonfamous condition, except that, as mentioned earlier, the connectivity between the left FFA and right HPC negatively predicted associative memory performance in the non-famous condition.

I also tested whether the brain connectivity differences between the two post-encoding rests (using post-famous-encoding minus post-nonfamous-encoding) could also predict differences between the two fame conditions in associative memory performance. This analysis was to test whether prior-knowledge effects at the brain level can be directly related to those at the behavioral level. Regression analysis showed that the right PPA-aTPL connectivity differences positively predicted differences in associative memory performance \((t(18) = 3.23, p = .005, FDR = .042; \text{Figure 3D})\). The right PPA's connectivity with the left aTPL and right HPC also showed similar predictions at a trend level after the FDR correction \((t(18) = 2.71\) and 2.59, \(p = .015\) and .019, \(FDR = .056\)).

### 4.3.4 Prior-knowledge effects on post-encoding brain connectivity: Using whole-brain anatomical ROIs

For completeness, I explored the prior-knowledge effects on post-encoding brain connectivity beyond our pre-defined functional ROIs. Specifically, I used 90 cerebral brain regions, defined by the Automated Anatomical Labeling (AAL) template (Tzourio-Mazoyer et al., 2002), as anatomical ROIs and directly contrasted the post-famous-encoding rest with the post-nonfamous-encoding rest. Using \(FDR = .05\) as the statistical threshold, I found that only the left HPC connectivity with the orbital part of the right superior frontal regions (i.e., part of the vmPFC) and the left aTPL (in the superior temporal gyrus) connectivity with the right precuneus were stronger during the post-famous-encoding than post-nonfamous rest, \(t(19) = 4.41\) and 4.60, \(p =\)
.0003 and .0002, $FDR = .027$ and .018, respectively. No post-encoding connectivity was found to be stronger in the nonfamous than famous condition.

### 4.4 Discussion

Using an explicit encoding task in which participants associated novel houses with either famous or nonfamous faces, I investigated how associative encoding with or without prior-knowledge involvement differentially affected post-encoding brain connectivity. I hypothesized stronger post-encoding connectivity in the famous than non-famous condition among regions whose activation at encoding were found to play a role in associative memory performance. For the most part, our results were consistent with this hypothesis, thereby providing the first demonstration of post-encoding prior-knowledge effects on associative memory. Specifically, I examined prior-knowledge effects on post-encoding functional connectivity among pre-defined functional ROIs, i.e., the vmPFC, aTPL, HPC, PPA, and FFA, all of which had been found to play a role in the face-house associative encoding process (Experiment 2). The results showed that the right HPC connectivity with the left FFA was stronger during the post-famous-encoding than post-nonfamous-encoding rest. Using whole-brain anatomical ROIs, I also found that the left HPC connectivity with the vmPFC (i.e., the orbital part of the right superior frontal region) was stronger in the famous, compared to the nonfamous condition. Moreover, I found that the aTPL connectivity with the PPA and FFA, as well as the HPC connectivity with the FFA, specifically predicted the associative memory performance of the famous condition. The connectivity between the left aTPL and PPA and between the left HPC and right FFA during the post-famous-encoding rest appeared to be stronger for the participants who were older and reported more vivid memories about the famous people whose faces were used in this study. Although these results were only marginally significant and should be interpreted with caution, collectively they may indicate that at least some of the post-encoding connectivity measures that predicted later memory performance in the famous condition were indeed related to the strength or amount of participants' prior-knowledge. These observations are consistent with my hypotheses in that associative encoding tasks can differentially modulate post-encoding brain connectivity depending on whether prior-knowledge was involved. Moreover, these results indicate that, during the post-famous-encoding rest, the aTPL, a region that supports semantic prior-knowledge (Patterson et al., 2007), and the HPC, a medial temporal lobe region that supports episodic and associative memory processing (Davachi & Wagner, 2002; Winocur,
Moscovitch, & Bontempi, 2010), continue to interact with posterior perceptual regions such as the PPA and FFA to facilitate off-line associative memory processing.

Our finding that cognitive tasks can modulate post-learning brain connectivity or affect subsequent memory is consistent with a large body of animal literature (Eagleman & Dragoi, 2012; Euston et al., 2007; Girardeau, Benchenane, Wiener, Buzsaki, & Zugaro, 2009; Han et al., 2008; Hoffman & McNaughton, 2002; Jadhav et al., 2012; Johnson et al., 2010; Knauer et al., 2013; Lansink et al., 2008; O’Neill et al., 2010, 2008; Pennartz et al., 2004; Ribeiro et al., 2004; Wilson & McNaughton, 1994; Yao et al., 2007). This finding is also consistent with recent human neural imaging studies that focused on brain activity during post-encoding time windows (Albert et al., 2009; Groen et al., 2011; Hasson et al., 2009; Lewis et al., 2009; Staresina, Alink, et al., 2013; Tambini & Davachi, 2013; Tambini et al., 2010; Tompary et al., 2015; Wang et al., 2012) or immediately following offset of different encoding events (Ben-Yakov & Dudai, 2011; Ben-Yakov, Eshel, & Dudai, 2013). For example, in a human neural imaging study using a similar associative encoding task, Tambini and colleagues (Tambini et al., 2010) found that the HPC connectivity with the lateral occipital face area was enhanced after a face-object encoding task, compared to pre-encoding rest. The connectivity enhancement was also found to be positively correlated with later memory performance. Extending this line of research, I found in the current study that post-encoding connectivity between the right HPC and left FFA was differentially modulated by the same type of associative memory tasks (i.e., face-house associations) with vs. without prior-knowledge involvement. This finding suggests that brain activity during rests can be extraordinarily sensitive to preceding tasks, which may have implications for the current intensive research on resting state brain activity. It is worth mentioning that in Tambini et al. (2010), the enhanced HPC connectivity was observed only after associative encoding of face-object pairs, not face-scene pairs. In the current study, I used face-house pairs as stimuli, which were similar to the face-scene pairs used in Tambini et al. (2010), and similarly I did not find HPC connectivity enhancement from pre- to post-encoding in both fame conditions. However, I found that the connectivity between the right aTPL and left FFA was enhanced by the associative encoding task in the famous condition. This effect may reflect stronger semantic processes related to famous faces in the famous condition.

When directly comparing the two fame conditions, I found that the connectivity between the right HPC and left FFA was stronger during the post-famous-encoding than post-nonfamous-
encoding rest. Interestingly, however, this difference was driven by a connectivity decrease in the post-nonfamous-encoding rest. As mentioned above, Tambini and colleagues (Tambini et al., 2010) did not find significant changes in HPC-FFA connectivity after face-scene associative encoding. Although low memory performance of the face-scene condition can explain the null finding in that study, this explanation may not apply to the current study because the connectivity reduction in the nonfamous condition found in the current study appeared to be beneficial for memory processing. Specifically, lower HPC-FFA connectivity during the post-nonfamous-encoding rest was associated with better memory performance of the nonfamous condition. However, for the famous condition, although the post-encoding connectivity between the HPC and the contralateral FFA at the group level was the same as that in the pre-encoding rest, at the individual level the connectivity changed considerably and only became positively predictive of later memory performance during the post-encoding rest. A similar pattern of results was found in the HPC connectivity with the lateral occipital region in Tambini et al. (2010). Although it is still unclear why there was an opposite brain-behavior relationship for the two conditions, these results, taken together, suggest that prior-knowledge during the preceding encoding task can affect the strength of the post-encoding HPC connectivity in facilitating subsequent associative memory.

It should be noted that different from Tambini et al. (2010), which used different types of stimulus pairs (i.e., face-object and face-scene) in the two conditions of their within-subject design, the current study employed a similar within-subject design but used the same type of stimulus pairs (i.e., face-house) in the two experimental conditions. Thus, both types of face-house associative information can be processed among the same brain regions. Consequently, competition and interference among those associative memory traces can occur. If this is the case, the above-mentioned opposite brain-behavior relationship in the two fame conditions may reflect a mechanism by which the brain can reduce potential interferences or optimize neural resources among these similar, but not identical, memories. It is worth mentioning that the HPC and FFA also showed stronger activation during the encoding of the famous than nonfamous condition (Experiment 2), indicating that these two regions indeed played a more important role in processing associative memory in the famous condition. This may explain why the post-encoding HPC-FFA connectivity only positively predicted associative memory in the famous
condition. However, I acknowledge that this is only speculation and should be examined by future investigations.

Using these pre-defined functional ROIs, I also found that the left aTPL connectivity with the PPAs and left FFA, and the right aTPL connectivity with the left PPA during the post-famous-encoding rest, can positively predict later associative memory performance of the famous condition. Importantly, this brain-behavior relationship was specific for the associative memory, not the face/house item memory, and specific for the famous condition, not the nonfamous condition. Additionally, I also found that some of the memory-predictive post-encoding connectivity (e.g., the aTPL connectivity with the left PPA) appeared to be stronger (at a trend level) for older participants and the participants who reported more vivid memories about the famous people, indicating that these post-encoding connectivity measures can be directly related to the strength or extent of the participants' prior-knowledge. Therefore, these results provide evidence showing that when prior-knowledge is involved in the preceding encoding tasks, the semantic hub region aTPL also maintains its communication with posterior perceptual brain regions (e.g., the PPA and FFA) to facilitate the formation of new associative memory. These findings are also consistent with previous studies that have shown the importance of the aTPL and related semantic processing regions in prior-knowledge facilitation effects on new learning (Kan et al., 2009; Sharon et al., 2011; Staresina et al., 2009).

The vmPFC has been proposed to support social/evaluative processing (Etkin et al., 2011; Roy et al., 2012; Rushworth, Kolling, Sallet, & Mars, 2012), remote memory (Frankland & Bontempi, 2005; Nieuwenhuis & Takashima, 2011), or prior-knowledge (Kroes & Fernández, 2012; van Kesteren et al., 2012). During the encoding phase, I found that the vmPFC showed stronger activation in the famous than nonfamous condition (Experiment 2). Within the famous condition, the vmPFC also showed stronger activation for the encoding trials in which more vivid memories and emotions were evoked by the famous faces, and the trials in which the face-house pairs were subsequently remembered than forgotten (Experiment 2). In the current study, I hypothesized that the post-encoding vmPFC connectivity with the HPC and the posterior perceptual regions (FFA and PPA) should play a more important role in the off-line processing of the associative memory of the famous, compared to the nonfamous, condition (van Dongen, Takashima, Barth, & Fernández, 2011). However, predefined ROI analyses did not find evidence to support this
hypothesis: I found that the vmPFC connectivity did not differ between the two post-encoding rests and did not predict the associative memory of either condition.

However, the functional vmPFC ROI used in this study does not cover all the vmPFC anatomical regions, which leaves the possibility that prior-knowledge may still affect the HPC connectivity with other vmPFC regions. This possibility was supported by the whole-brain connectivity analysis using 90 anatomically defined ROIs, which revealed that the connectivity of the orbital part of the right superior frontal gyrus with the left HPC was stronger during the post-famous-encoding rest than the post-nonfamous-encoding rest. The orbital part of the superior frontal gyrus has been included as part of the vmPFC in the previous investigation (van Kesteren, Fernández, et al., 2010) that also focused on prior-knowledge (e.g., schema) effects on the vmPFC-HPC connectivity. It should be noted that the current finding appears to be different from that of van Kesteren, Fernández, et al. (2010) who found that the post-encoding vmPFC-HPC connectivity was stronger when prior-knowledge (i.e., schema) was not involved in the preceding encoding task. However, it is likely that in terms of the underlying cognitive processing, the encoding condition without prior schema in (van Kesteren, Fernández, et al., 2010), as described in the introduction, resembled more closely the famous encoding condition of the current study: In the former, participants needed to understand the later part of a movie using the information they had obtained from watching the temporally shuffled early part of the movie. In our study, participants were likely to use their prior-knowledge about those famous people to help them form face-house associations. Both conditions required cognitive or evaluative processing by which new information can be incorporated into an existing knowledge system. That this type of cognitive processing may require the vmPFC-HPC interaction was also supported by studies using associative inference paradigm (Preston & Eichenbaum, 2013; Zeithamova, Dominick, et al., 2012).

Finally, it is worth mentioning that different from animal studies that directly measure neuronal firing rates, the blood-oxygenation-level-dependent (BOLD) signal examined in this study is an indirect measure of neural activity. Therefore, it is unclear whether the post-encoding brain activity in the current study reflected the similar types of memory replay, or some underlying neurophysiological processes. Because our participants did not report conscious rehearsal of the encoding task, and the validity of subjective reports has been supported by different studies (Groen et al., 2011; Staresina, Alink, et al., 2013; Tambini et al., 2010), the memory-predictive
brain connectivity during the post-encoding rest probably did not reflect conscious voluntary memory replays. More likely, it may reflect continuous coordinated metabolic processes during post-encoding rest from brain regions where the neural/synaptic assemblies were recruited and tagged by the preceding encoding task. These metabolic demands can be related to the neurophysiological cascade events that are needed to stabilize the newly acquired memory traces (Lesburguères et al., 2011; Redondo & Morris, 2011; Wang, Redondo, & Morris, 2010). Future studies combining fMRI and cellular measures of the neural activity in animal models (Lee et al., 2010) are crucial to reveal the underlying neurophysiology of the post-encoding brain activity measured by BOLD signals.

In summary, consistent with my hypotheses, I found that when prior-knowledge is involved, the HPC, vmPFC, and aTPL, which support prior episodic, social-evaluative, and semantic memories, respectively, continue to interact with each other and the posterior perceptual brain regions (e.g., the PPA and FFA) during the post-encoding rest to facilitate off-line processing of the newly formed memory and lead to better memory for it.
4.5 Supplementary figures

**Supplementary Figure 1.** Brain connectivity during the post-famous-encoding rest that positively predicted associative memory of the famous condition did not predict the face/house item memories (Chapter 4)

**Supplementary Figure 1.** Brain connectivity during the post-famous-encoding rest that positively predicted associative memory of the famous condition did not predict the face/house item memories. Thicker red lines on the brain surface plot indicate the connectivity that positively predicted associative memory of the famous condition at $FDR = .05$. Thinner red lines indicate the connectivity prediction effects survived $p = .05$ threshold without $FDR$ correction. All regression line slopes for the item memory vs. connectivity were not significant except that the connectivity between the left PPA and left aTPL positively predicted famous face memory at $FDR = .07$. 
Supplementary Figure 2. Post-encoding brain connectivity in the famous condition that was associated with participants' age and vividness ratings of famous faces (Chapter 4)

Supplementary Figure 2. Some brain connectivity during the post-famous-encoding rest that most strongly predicted associative memory of the famous condition also increased, significantly or at trend levels, with participants' age and vividness ratings on memory that was elicited by the famous faces. Note: The connectivity between the left PPA and right aTPL did not show a significant or trend level relationship with memory ratings. It is presented here only for the purpose of completeness.
Chapter 5

General discussion

In this section, I first summarize the findings from the three experiments. Then, I discuss some implications of the current studies for related research areas such as those on schema effects, on the brain default mode network, and on memory consolidation. I end with a brief discussion of limitations of the current study and future research directions.

5.1 Summary of the findings from all 3 experiments

In this research project, I conducted three experiments to investigate how prior-knowledge affected new associative processing at both the behavioral and brain level. In experiment 1, I developed a behavioral paired-associate memory task to remediate some methodological issues of previous studies on prior-knowledge effects. Specifically, instead of using words with different frequency (Clark, 1992; Madan et al., 2010) or schema-congruency manipulation (Bayen et al., 2000; van Kesteren, Rijpkema, et al., 2013), I used famous, compared to nonfamous, faces to elicit multiple-component prior-knowledge that can be better defined both at the cognitive and brain level. Then, I investigated how this type of prior-knowledge affected face-house associative memory, achieved by either associative familiarity or recollection processes. The results showed that famous faces enhanced associative recollection, namely, how well participants recognized the intact face house pairs as compared to recombined pairs. However, I did not find prior-knowledge facilitation effects on associative familiarity measured by gains in item recognition from intact to recombined testing pairs (Cohn & Moscovitch, 2007; Kan et al., 2007). These findings provide further support for the idea that the two types of associative memory processes have different underlying neural and cognitive mechanisms (Cohn et al., 2009, 2009, 2010). Moreover, additional analyses on the relationship between associative and item memories suggested that prior-knowledge related to famous faces mainly acted on associations between faces and houses, not on the individual face and house stimuli themselves, to facilitate the face-house associative recollection.
Using the behavioral task developed in Experiment 1, I investigated, in Experiment 2, how this type of multiple-component prior-knowledge affected brain activity during associative encoding. In addition to activating face areas, such as the FFA, famous faces can elicit rich sources of social emotional, semantic, or episodic information in a network of brain regions including the vmPFC, aTPL, and HPC (Fairhall & Ishai, 2007; Gobbini et al., 2004; Ishai, 2008; Quian Quiroga, Kraskov, Koch, & Fried, 2009; Ross & Olson, 2012; Simmons et al., 2010; Viskontas, Quiroga, & Fried, 2009). This allowed me to investigate whether prior-knowledge related to these famous people could strengthen brain level processes among these different brain processing components to facilitate new memory formation. Consistent with my hypotheses, results showed that the vmPFC and HPC, as well as the PPA and FFA, were more strongly activated in the famous than nonfamous encoding condition. The vmPFC, HPC, and aTPL also showed stronger activation for trials in which the faces elicited stronger prior emotions and memories, indicating that the involvement of these brain systems was indeed related to participants' prior-knowledge of the famous people. These regions also showed stronger activation for the famous encoding trials in which the face-house associations were later remembered than forgotten, confirming that the participation of these brain regions was directly related to new associative memory formation.

Because the HPC, in addition to being activated by famous faces, also played an important role in associative encoding, I analyzed HPC functional connectivity during encoding. Although I found that the HPC appeared to form stronger connectivity with anterior brain regions, such as the aTPL and vmPFC, it did not survive corrections for multiple testing. However, I did find that the HPC connectivity with vmPFC positively predicted participants' subsequent associative memory performance in the famous condition. Moreover, the HPC-vmPFC connectivity showed a negative relationship with associative memory in the nonfamous condition. Taken together, these observations, consistent with my hypotheses, indicate that prior-knowledge can trigger additional social evaluative, semantic, or episodic encoding processes and contribute to the prior-knowledge facilitation effects on new associative memory processing.

The literature has shown that post-encoding brain activity can be related to early memory consolidation processes (Staresina, Alink, et al., 2013; Tambini & Davachi, 2013; Tambini et al., 2010; Tompary et al., 2015; Wilson & McNaughton, 1994). Thus, in Experiment 3, I examined whether prior-knowledge effects can persist into post-encoding rests and affect brain
connectivity among these different brain systems (i.e., the vmPFC, aTPL, HPC, PPA, and FFA). The results showed that the connectivity between the right HPC and left FFA was stronger at rest following the famous-encoding, than nonfamous-encoding, condition. This connectivity measure was positively related to later associative memory in the famous condition. Post-encoding connectivity between the left HPC and right vmPFC was also stronger in the famous than nonfamous condition. I also found that the aTPL and HPC connectivity with posterior brain regions such as the PPA and FFA predicted specifically the associative memory (not the item memory) in the famous (not the nonfamous) condition. Some of these memory-predictive connectivity measures were found, at a trend level, to be stronger for older participants who likely had more prior-knowledge and participants who reported more vivid memories elicited by the famous faces. These results collectively suggest that strength of the connectivity that predicted later memory performance may be directly related to the extent of the participants' prior-knowledge. These results together provide evidence showing that post-encoding brain activity can be affected by prior-knowledge. Importantly, these results also imply that when prior-knowledge is involved, the HPC, vmPFC, and aTPL, which support prior episodic, social evaluative, and semantic memories, respectively, continue to interact with each other and with the posterior perceptual brain regions (e.g., the PPA and FFA) during the post-encoding rest to facilitate off-line processing of the newly formed associative memory.

5.2 Schemas

This research project was partly motivated by the recent brain-level investigations on schema effects. Several human neuroimaging and animal studies have found that existing schemas can significantly facilitate new memory formation, modify brain activation patterns during encoding, post-learning rests, and retrieval, and hasten memory systems consolidation (Tse et al., 2007, 2011; van Kesteren, Fernández, et al., 2010; van Kesteren, Rijpkema, et al., 2010; van Kesteren et al., 2012). Based on this research (van Kesteren et al., 2012) proposed that while the HPC is important for encoding novel information, the vmPFC and vmPFC-HPC interactions support schema related assimilation of new information into existing schemas. Research on transitive inference added to the support for this proposal (Kumaran et al., 2009; Preston & Eichenbaum, 2013; Zeithamova, Dominick, et al., 2012). As a consequence, the focus of this line of memory research has expanded to include the vmPFC as another important player in addition to the medial temporal lobe (MTL).
The vmPFC has reciprocal connections with many other brain regions, including the MTL, aTPL, and amygdala (Barbas, 2000; Carmichael & Price, 1994, 1995, 1996; Öngür & Price, 2000), which makes the vmPFC a possible hub in integrating information from these different regions (Benoit et al., 2014). It has been proposed that the vmPFC can extract contextual information, abstract rules, information regularities, or schemas from repeated experience and use these types of information to control memory retrieval or encoding that is supported by the MTL (Kroes & Fernández, 2012; Preston & Eichenbaum, 2013). However, it is still unclear from these proposals through what mechanisms the vmPFC can have these powerful binding or controlling functions in memory processing. Because schemas can be multifaceted, likely including perceptual, procedural, emotional, semantic, episodic knowledge or experiences, or different combinations of them, they are more likely to be supported by different brain systems, rather than the vmPFC alone. Then, what is the unique role of the vmPFC in supporting the integration of new information with prior-knowledge?

Outside the memory research literature, there is a wealth of empirical data showing that the vmPFC is a key structure which supports social, evaluative, or affective processing, including, but not limited to, self-related processing, decision making, moral judgment, goal-directed behavior, empathy processing, understanding abstract semantic, or even perceiving preferred every-day objects (Barrett & Bar, 2009; Binder et al., 2009; Etkin et al., 2011; Grabenhorst & Rolls, 2011; Luo et al., 2010; O’Reilly, 2010; Roy et al., 2012). Because the vmPFC can mediate a variety of evaluative processes, we should then consider the possibility that the vmPFC may play a similar evaluative role in memory tasks (Rudy, Biedenkapp, & O’Reilly, 2005; Wang, Cohen, & Voss, 2015). That is, while schemas, or prior-knowledge in general, are mediated by many brain systems, evaluating memory processes or contents according to prior-knowledge or task-specific goals or demands, is likely to be mediated by the vmPFC. These evaluative processes referred to here are defined in a more general sense, not just assigning values to stimuli. These evaluations can be quick and automatic such as determining whether retrieved

---

2 The role of evaluative processes in associative learning has been discussed extensively in the conditioning literature (De Houwer, 2009; Hofmann, De Houwer, Perugini, Baeyens, & Crombez, 2010; Mitchell, De Houwer, & Lovibond, 2009). Although it is still in debate whether basic Pavlovian conditioning involves evaluative processes, it is widely accepted that complex associative learning in humans should involve, or maybe even rely on, evaluative processes (Mitchell et al., 2009).
memories are appropriate for current context (Gilboa et al., 2006), or they can be slow and elaborative, such as complex decision making processes involved in some memory tasks (Dahmani & Bohbot, 2015; Schacter, Benoit, De Brigard, & Szpunar, 2015). It is likely that different vmPFC sub-regions mediate different types of evaluation processes (Grabenhorst & Rolls, 2011) and contribute to memory processes in non-identical ways. However, in general, we can propose that it is these evaluative processes that serve as the "glue" for the vmPFC to bind the new information with existing memories (Kroes & Fernández, 2012; van Kesteren et al., 2012). Moreover, in some situations evaluative processes supported by the vmPFC may also function as a "commander" that actively controls memory encoding and retrieval mediated by posterior brain regions such as the MTL (Preston & Eichenbaum, 2013). For example, the vmPFC can directly suppress context-inappropriate, or select context-appropriate, memories that are retrieved through the MTL (Gilboa et al., 2006; Sotres-Bayon & Quirk, 2010). It can also facilitate strategic encoding or retrieval through decision making processes, as found in complex navigation or episodic future thinking tasks (Dahmani & Bohbot, 2015; Schacter et al., 2015).

From this perspective, we can conceptualize the role of the vmPFC in memory binding as evaluative binding to contrast with perceptual binding supported by the MTL. (This can also be applied to retrieval processes.) Although the two types of binding processes are not mutually exclusive, they differ in important ways. For example, first, evaluative binding supported by the vmPFC is likely more selective than the MTL's perceptual binding because only information relevant to evaluative processes can be processed in depth, which likely leads to sparser or less detailed memory traces, compared to the situation of perceptual binding. Second, evaluative binding in the vmPFC likely involves more prior-knowledge, such as semantics, schemas, concepts, or affects than pure perceptual binding because very often evaluative processes rely on these previous experiences or knowledge. Moreover, evaluative binding can also add evaluative tags to the bound information, such as personal preference, goal or reward relatedness, emotional valences, social appropriateness, utility functions, that can be used to facilitate future evaluative binding and retrieval.

Experiment 2 can be used to illustrate the idea of evaluative binding supported by the vmPFC. During a post-experiment interview, many participants reported use of evaluative encoding strategies when they associated houses with famous faces. For example, based on their knowledge of the famous people whose faces were paired with houses, some participants tried to
guess what part of the houses those famous people would like and dislike, whether a specific famous person would, or would not, buy the paired house, or whether some features of a house simply "matched" a famous person. Some of these evaluative processes are more elaborative, while others are more general and holistic. However, clearly these evaluative processes simultaneously involve, and therefore likely bind, the information of the house (especially the part that was used in those evaluative processes), the famous face, and existing knowledge related to the famous person that was used or activated during the evaluative process. Also, this type of evaluative binding process is likely more selective and involves more semantic and social emotional information than pure perceptual binding. Information bound in this way can also be used to facilitate retrieval of the face-house associations: During retrieval, when the features of the house used in previous evaluative binding matched the famous person, participants can quickly recognize the face-house associations and retrieve related evaluative information (e.g., "like/dislike", "buy/not buy", or "match/not match"). Moreover, the vmPFC is likely to support this type of evaluative processes, because, as found in Experiment 2, the vmPFC showed stronger activation in the famous than the nonfamous encoding condition, and in the trials in which famous faces evoked stronger prior emotion and memories. However, it is unlikely that all activated prior-knowledge related to famous people was solely supported by the vmPFC, because other regions such as the HPC, FFA, PPA, also showed stronger activation in the famous than nonfamous condition (Experiment 2).

It is possible that when memory tasks involve schema (or prior-knowledge in general), some of these evaluative processes supported by the vmPFC are recruited to a larger extent, compared to the situation where no schema is involved. However, whether schema congruence or incongruence requires more involvement from the vmPFC is likely situation dependent, rather than being governed by a fixed rule. For example, in (van Kesteren, Fernández, et al., 2010), when participants tried to understand the second part of a movie without watching the intact first part of the movie, stronger evaluative or decision-making processing were required to achieve a good understanding of the movie, compared to the situation where the first part of the movie was already known. This can explain the stronger HPC-vmPFC connectivity found in the schema-incongruent, rather than the schema-congruent, condition in (van Kesteren, Fernández, et al., 2010). In the current study, however, prior-knowledge, especially its social emotional aspects, triggered evaluative processing during the face-house associations and led to a positive
correlation between the HPC-vmPFC connectivity and associative memory performance, as found in Experiment 2.

Moreover, as mentioned earlier, the evaluative processing supported by the vmPFC is only one of the many processing components that can be triggered by prior-knowledge. When strong semantic processing is evoked, the aTPL can be involved in prior-knowledge facilitation effects even without the involvement of the vmPFC. Semantic processing can help to label experimental stimuli, build semantic associations for new stimuli, make information items more distinctive, or form gist semantic memory for new experiences (Binder & Desai, 2011; Gordon & Tanaka, 2011a, 2011b; Huttenlocher, Hedges, & Duncan, 1991; Konkle, 2010; Tulving & Markowitsch, 1998). The semantic and evaluative processing components can also work together in evaluating, selecting, extracting, or semanticizing relevant information to efficiently form new memories. Indeed, in Experiment 2 I found that both the aTPL and vmPFC showed stronger activation in the encoding trials in which famous faces evoked stronger prior emotion and memories, likely reflecting stronger involvement of semantic and social emotional knowledge in evaluative encoding processes. Similarly, early sensory perceptual processing components can play a role in prior-knowledge, or schema, effects. For example, evaluative or semantic processes evoked by prior-knowledge can modify early sensory perceptual processing through top-down control mechanisms (Barense, Rogers, Bussey, Saksida, & Graham, 2010; Ciaramelli, Grady, & Moscovitch, 2008; Ciaramelli & Spaniol, 2009; Cohen & Tong, 2015; Gazzaley & Nobre, 2012; Summerfield & Egner, 2009). Consistently, in Experiment 2 I found that the PPA and FFA showed stronger activation in the famous than nonfamous condition.

Therefore, together with the findings of the current studies, we can now understand that the vmPFC involvement in schema effects found by previous studies may reflect evaluative binding or retrieval processes. From this perspective, the somehow mysterious role of the vmPFC in assimilating new knowledge into existing knowledge system (van Kesteren et al., 2012) can be specified at a processing level and better corroborated by the current literature on the vmPFC functions. Moreover, the current studies showed that the focus of the current research on schema effects should be broadened to include more brain regions, which can eventually benefit more basic research, such as the neurobiology, of prior-knowledge effects (Tayler et al., 2011; Tse et al., 2011; Wiltgen et al., 2011). I think this perspective change is important, because research has already shown that it is the underlying cognitive processes triggered by schema, not schema-
congruency itself, that determines schema effects to be beneficial or detrimental (Alba & Hasher, 1983).

5.3 Resting state brain activity

In Chapter 4 (i.e., Experiment 3), I examined how prior-knowledge involved in a preceding associative encoding task could affect post-encoding brain activity measured by resting-state brain connectivity. I found that the HPC, vmPFC, and aTPL, which support prior episodic, social evaluative, and semantic memories, respectively, continued to interact with each other and with posterior perceptual brain regions such as the PPA and FFA during the post-encoding rest to facilitate off-line processing of the newly formed memory. However, as mentioned in Chapter 4, our participants did not consciously rehearse the memory task during post-encoding rests, which has also been shown by previous studies (Tambini et al., 2010). Thus, future studies are needed to investigate the cognitive or neurophysiological mechanisms whereby connectivity between these anterior and posterior regions facilitated new associative memory.

Different explanations have been proposed to account for functions of resting brain activity. For example, it has been shown that the resting brain activity, especially the functional connectivity within the default mode network which includes the medial PFC, lateral and anterior temporal cortex, hippocampus, posterior cingulate cortex, and inferior parietal lobule (Buckner, Andrews-Hanna, & Schacter, 2008; Gusnard & Raichle, 2001; Raichle et al., 2001), reflects mind wandering (Mason et al., 2007) or "internal mentation" of future- or past-related events (Andrews-Hanna, 2012; Andrews-Hanna, Smallwood, & Spreng, 2014). The default network has also been found to overlap considerably with semantic (Binder et al., 1999, 2009; Binder & Desai, 2011) and associative processing network (Bar, Aminoff, Mason, & Fenske, 2007). Therefore, the involvement of different brain systems in the default network can reflect different components of cognitive processing. However, it has also been found that resting-state brain activity such as connectivity among different brain networks remains similar in different animal species and in different states of consciousness (Larson-Prior et al., 2009; Raichle et al., 2001; Vincent et al., 2007), indicating that resting brain activity also reflects intrinsic brain functions that are important for all types of cognitive processes. Therefore, these different resting networks have been called intrinsic brain networks (Fox & Raichle, 2007). The two proposals, however, are not mutually exclusive: It is likely that component processing is built on or relies on the
intrinsic brain networks (Hermundstad et al., 2013; Honey et al., 2009; Shen, Hutchison, Bezgin, Everling, & McIntosh, 2015).

Interestingly, recent animal studies from different laboratories found that firing sequences of the HPC place cells during pre-navigation rests can "pre-play" the novel routes that the animals were going to navigate (Dragoi & Tonegawa, 2010, 2013b; Gupta et al., 2010; Pfeiffer & Foster, 2013). These observations led researchers to hypothesize that the neural activity among the HPC place cells during rest may support a large repertoire of pre-existing solutions among which some can be selected and used to more efficiently direct behavior or encode new information (Dragoi & Tonegawa, 2013b). Since the HPC can also be a node of the resting default network, these intriguing findings suggest that human resting-state brain activity in general may have similar functions: It can help to maintain a brain state of "readiness" by supporting a large repertoire of prior-knowledge, such as previously learned rules, propositions, concepts, attitudes, interests, episodes, goals, associations. This "readiness" state of brain activity during rest does not necessarily reflect conscious replay of those different types of prior experience or knowledge, because brain activity in the default network has also been detected during sleep and anesthesia (Larson-Prior et al., 2009; Vincent et al., 2007). Also, in Experiment 3 of the current research, participants reported that they did not consciously rehearse the encoding task during post-encoding rests, but I found that the aTPL connectivity with the PPA/FFA positively predicted later associative memory of the famous condition only in the post-encoding rest. Therefore, although resting brain activity can in some situations reflect conscious component processing, it can also reflect physiological processes that maintain, in an easy-to-access state, the prior-knowledge related memory traces at both the representational and processing level. Indeed, recent neurobiological studies have found that maintaining prior-knowledge (i.e., long-term memories) requires persistently active protein kinase Mζ (Sacktor, 2011; Serrano et al., 2008). This way, actively maintained prior-knowledge can be quickly recruited, selected, and recombined to facilitate processes of new tasks.

This speculation is consistent with recent findings that resting brain networks, especially among multimodal association areas, overlapped considerably with active-task brain networks, and that only a small portion of extra components were recruited during active task processes (Cole, Bassett, Power, Braver, & Petersen, 2014; Krienen, Yeo, & Buckner, 2014; Mennes, Kelly, Colcombe, Castellanos, & Milham, 2013; Smith et al., 2009). Findings that the default network
brain activity during rest is related to later task performance or learning capacity (Baldassarre et al., 2012; Staresina, Fell, Dunn, Axmacher, & Henson, 2013; Tambini & Davachi, 2013; Tambini et al., 2010; Ventura-Campos et al., 2013; Zou et al., 2013), and that learning experience can in turn modify resting brain activity (Albert et al., 2009; Deuker et al., 2013; Groen et al., 2011; Hasson et al., 2009; Urner et al., 2013; Wang et al., 2012; Zou et al., 2013) lend some indirect support for this speculation. Moreover, it is possible that this readiness state also serves as neural underpinnings for Bartlett's original schema concept (Bartlett, 1932), which can facilitate or constrain new learning, i.e., making some learning more likely and others less likely (Sadtler et al., 2014). This conceptualization fits well with the recent idea that using prior information to make predictions is a fundamental way that the brain works (Bar, 2009; Bastos et al., 2012; Friston, 2010; Summerfield & Egner, 2009).

From this perspective, we can speculate that the stronger post-encoding communication between the HPC or aTPL and posterior brain regions such as the FFA and PPA in the famous condition reflects stronger processes by which newly formed associative memory information interacts or connects with activated existing memory traces to become stabilized. These post-encoding processes reflected by functional connectivity between the HPC/aTPL and FFA/PPA can be purely neurobiological, as mentioned earlier. An alternative, but not mutually exclusive interpretation, is that these processes can also consist of conscious-level cognitive activity that contributes to memory formation. For example, it is possible that during the post-encoding rest of the famous condition (Experiment 3), participants may retrieve or process semantic or episodic information indirectly (i.e., not obviously) related to the famous people whose faces the participants had just processed. Although participants were not aware of the connections between what they processed during the post-encoding rests and what they did during the memory task, those cognitive processes or their contents can lead to retrieval or cueing effects that facilitated associative memory of the famous condition. Future studies that carefully probe post-encoding cognitive processes or manipulate post-encoding conscious or attentional states can help to test these speculations and reveal to what extent post-encoding brain activity reflects conscious cognitive or basic neurobiological processes and how these processes can differentially affect later memory.
5.4 Memory consolidation

In Experiment 2, I found that the HPC connectivity with the vmPFC played a more important role in the famous than nonfamous condition. In Experiment 3, I found that during post-encoding rest, the connectivity of the aTPL and HPC with FFA and PPA was positively related to later associative memory performance in the famous condition. These results indicated that when prior-knowledge was involved, neocortical regions seemed to play a more important role in both the initial memory formation and later memory reactivation, compared to the situations where no prior-knowledge was involved. From these results, I speculate that the involvement of the neocortical regions may be related to the faster memory consolidation under schema effects found by previous studies (Tse et al., 2007, 2011).

Moreover, recent proposals on memory systems consolidation have posited that some of the original perceptually rich episodic memory, supported mainly by the HPC, can be transformed into gist-like semantic memory during consolidation processes and supported by neocortical regions (Moscovitch, Nadel, Winocur, Gilboa, & Rosenbaum, 2006; Nadel & Moscovitch, 1997; Winocur & Moscovitch, 2011). Based on the findings of the current and previous studies (van Kesteren, Fernández, et al., 2010; van Kesteren, Rijpkema, et al., 2010), we can further hypothesize that the interaction between prior-knowledge and new memory processing is an important mechanism by which episodic memory is transformed into semantic or gist-like memory. As found in Experiment 2 and 3, prior-knowledge can trigger strong non-perceptual processes, such as evaluative or semantic processes supported by the vmPFC and aTPL. Compared to situations with no prior-knowledge, these additional processes can reconfigure the landscape of memory processing among different brain or cognitive systems and increase the weight of those higher level cognitive components, such as evaluative and semantic processes, at both the representational and processing levels. Consequently, if detailed perceptual information of the original episodic memory is degraded during consolidation, gist-like non-perceptual information supported by neocortical regions can still be available or become salient, which can be utilized in retrieving some aspects of the original memory information.

Although the current research was not designed to directly test the above-mentioned hypotheses, the findings of Experiment 2 and 3 that the vmPFC and aTPL played a more important role in associative memory processing when prior-knowledge was involved, compared to no prior-
knowledge condition, provided some indirect support for this proposal from a functional neuroanatomy perspective. At the behavioral level, I found that prior-knowledge mainly strengthened associative recollection, not familiarity, of the face and house stimuli (Experiment 1). This finding, however, does not necessarily contradict the proposed facilitative role of prior-knowledge in memory transformation during consolidation, because associative memory formed in the current studies likely had not completed the consolidation process. After a long enough time delay when detailed face-house associative memory fades away, according to this proposal, non-perceptual gist-like memory traces contributed by prior-knowledge related evaluative or semantic processing can still facilitate the retrieval of some face-house associations in the famous condition. Future studies that investigate the proposed facilitation effects of prior-knowledge on memory transformation are likely to shed new light on our understanding of how memory changes with time.

5.5 Limitations and future directions

In this research project, I took advantage of the recent face processing literature and designed the face-house associative memory task in which famous faces were used to elicit multiple component prior-knowledge. Although the manipulation of prior-knowledge was successful and the experiments produced results that supported many of my hypotheses, there are also shortcomings that need to be addressed in future investigations.

First, participants' prior-knowledge related to those famous people evoked by their face pictures can be rather idiosyncratic and, therefore, not well controlled. Although at the group level, stronger activation in those hypothesized brain regions, such as the HPC and vmPFC, has been observed, it is less clear to what extent these brain activities really reflect the cognitive processes or representations that I intended to probe. To remediate this problem, I asked participants to rate all famous faces along different dimensions and used these ratings in some analyses. However, these measures and analyses are correlational in nature and difficult to separate effects of different aspects of prior-knowledge. Because prior-knowledge was not well controlled across participants, similar brain activation in different participants may not reflect the same cognitive processes. The not-well-controlled prior-knowledge manipulation can also lead to some uncertainty in how this type of prior-knowledge was used during new memory processing. Thus, future studies should experimentally manipulate the different components of prior-knowledge.
and examine their effects on new learning. For example, we can train participants to acquire different types of prior-knowledge associated with face stimuli. Perceptual prior-knowledge, such as perceptual familiarity, can be created by presenting face images to participants before the main associative memory task was administered. We can also pre-expose participants with novel faces paired with information of people's names, vocations, hobbies, or social relations to create prior semantic knowledge. To create social emotional prior-knowledge, we can ask participants to learn novel faces with descriptions of personality traits or social political attitudes. This way, we can be more certain about the types of prior-knowledge that participants have. By isolating effects of different types of prior-knowledge, we can test the specificity of different brain systems in their contribution to prior-knowledge effects. Moreover, since face and house information can be processed differently in the brain (Kanwisher, 2010), different experimental manipulation of prior-knowledge should also be applied to house stimuli. Using this strategy, we can understand better the specific effects of different prior-knowledge components during associative processing at both the behavior and brain level.

Second, in addition to providing better control of prior-knowledge manipulation, we also need to understand better how different types of prior-knowledge are used in new associative processing. In the current studies, although I found that the activation of the aTPL, HPC, and vmPFC was modulated by emotion and episodic memories associated with famous faces, we can only infer that prior semantic, episodic, and social evaluative information was used in new encoding. To confirm this is indeed the case, future investigations should use more refined probes to obtain information regarding how these types of prior-knowledge are activated and used during online and offline processing of new memories. For example, we can ask participants to report in more detail how they make the associations between the face and house stimuli. We can also instruct participants to use different types of associative methods, such as evaluation-based vs. perception-based processing, in different experimental conditions. Alternatively, we can use other objective measures such as eye movements to obtain more detailed information about how prior-knowledge can modulate spatial sampling (e.g., saccade scan path) or temporal processing (e.g., gaze dwelling time) of associated visual stimuli.

Finally, in the current research project, I only investigated how prior-knowledge affected associative encoding and post-encoding rest. However, the literature has also shown that prior-knowledge can affect new learning at both the encoding and retrieval phase (Kim et al., 2012;
Poppenk, Köhler, et al., 2010; Reder et al., 2013; van Kesteren, Fernández, et al., 2010; van Kesteren, Rijpkema, et al., 2010). Thus, whether and how the type of prior-knowledge manipulated in the current studies can affect associative memory retrieval is not clear. One hypothesis would be that during retrieval, the anterior brain regions such as the aTPL and vmPFC play a more important role in the retrieval of associations in which prior-knowledge is involved, compared to no prior-knowledge condition. Testing this hypothesis in experiments with long encoding-retrieval delay can also help to clarify previous speculation that prior-knowledge can facilitate memory consolidation through stronger involvement of these anterior brain regions. Therefore, although some findings of this dissertation research project has extended the existing literature, they are best considered as a starting point of a systematic investigation for prior-knowledge effects on new associative processing.

5.6 Conclusions

In this dissertation, I conducted three experiments to investigate how prior-knowledge could affect associative memory processing at both the behavioral and neural level. In the behavioral study (Experiment 1), a face-house paired-associate task was developed in which prior-knowledge was manipulated by using famous and nonfamous faces. This study showed that prior-knowledge can enhance associative recollection, but not associative familiarity. This behavioral task was then used in the following two fMRI studies to investigate prior-knowledge effects at the brain level. I hypothesized that prior-knowledge can trigger additional evaluative, semantic, or episodic-binding processing, mainly supported by the vmPFC, aTPL, and HPC, respectively, that could facilitate new memory processing during both encoding and post-encoding rest. Indeed, the results (Experiment 2) showed that during encoding, the HPC, vmPFC and aTPL played a more important role in the face-house associative processing when prior-knowledge was involved. During the post-encoding rests (Experiment 3), the HPC-FFA and aTPL-FFA/PPA connectivity positively predicted later associative memory in the famous condition. This indicates that when prior-knowledge is involved in the preceding encoding task, brain regions that support prior episodic and semantic memories continue to interact with the posterior perceptual brain regions during the post-encoding rest to facilitate off-line processing of the newly formed memory. Taken together, the findings of these studies contributed to our understanding of how prior-knowledge can affect on new associative learning at both the
behavioral and brain level, and showed that prior-knowledge effects can be effectively investigated from brain systems perspective.
References


Fox, M. D., & Raichle, M. E. (2007). Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging. *Nat Rev Neurosci, 8*(9), 700–711. doi:10.1038/nrn2201


