Examination of Emotion-Modulated Processing Using Eye Movement Monitoring and Magnetoencephalography

by

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A thesis submitted in conformity with the requirements for the degree of Doctor of Philosophy
Psychology
University of Toronto

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Abstract

Research shows that emotional items are associated with enhanced processing and memory. However, emotional memories are composed of not only memory for the specific emotion-eliciting item, but also other items associated with it, as well as memory for how these items are related. The current thesis utilized verbal report, eye movement monitoring and magnetoencephalography in order to examine how emotions may influence online processing and memory for associated information. It was found that while emotions influenced attention to both the emotion-eliciting item and associated information during the encoding stage, this was not related to subsequent memory performance as indexed by verbal report. It was also found that while emotions impaired detailed memory for associated information, it did not affect the ease or speed at which those memories could be accessed. In using MEG, it was found that emotions may modulate not only how participants’ view associated information, but it may also modulate the type of representation formed. Together, findings from the current work suggests that: (1) emotions influence online processing and memory for associated information; (2) emotions modulate memory for associated information via routes other than overt attention; (3) encoding and retrieval may occur in stages; and (4) memory exerts early influences on processing. The current work shows that emotions modulate online processing of associated
neutral information in a top-down manner, independent of differences in its physical properties. Work from this thesis encourages a reconceptualization of emotion, memory and perception and how they relate to one and another. Rather than viewing them as independent modular processes, they may, in fact, be more widely distributed in the brain and interact more closely than previously described. This may be evolutionarily adaptive allowing us to quickly and efficiently form memories for emotional events/scenes that can later guide perception and behaviour.
Acknowledgments

I owe my deepest gratitude to my advisor, Dr. Jennifer D. Ryan. She has exceeded what an ideal supervisor should be. Dr. Ryan has taught me how to think, write and speak like a scientist. She has provided me with the perfect balance of challenge and support. She has an infectious passion for science and inexhaustible attention to detail. Although we are still arguing over appropriate spelling conventions (note the British/Canadian spelling throughout), she has influenced me in immeasurable ways. I would like to thank her for inspiring me and always pushing me to be better. She is truly a Great, and I hope to do her proud.

Many thanks to my thesis committee, Dr. Adam K. Anderson and Dr. Bernhard Ross, for their invaluable insight, guidance, and support.

I am also honoured to have been taught and mentored by Drs. Morris Moscovitch, Sandra N. Moses, Anthony T. Herdman, Takako Fujioka, and Timothy Bardouille. They have lent me their years of expertise and patiently taught me the basic fundamentals of science and neuroimaging.

I would like to thank my amazing lab mates and Rotman colleagues who were always there for moral support and in-depth discussions of science, puppies, and food. I am especially grateful to Christina Richardson for her unwavering loyalty and friendship, for always helping me step back and see the bigger picture, and for teaching me how to use pivot tables. I would also like to thank future Dr. Mark Chiew, a python wizard who babysat my bike rides to and from work, wrote countless scripts for my experiments (2.5), and kept me sane and entertained during innumerable hours at the library writing. Our bond is like Valyrian steel.

I am grateful for all the wonderful collaborators, research assistant and students who have helped me with my research projects: Douglas A. McQuiggan, Norman Farb, Daniel Lee, Ella Pan, Amy Oziel, Helen Dykstra, and Lisa Bolshin.

I would also like to thank my surrogate Toronto families: the Mrazs, Kings and Godris. They welcomed me into their homes, fed me, and taught me the essential life skills that I did not even realize that I would need. I would like to thank Vera Mraz especially for always being so positive and enthusiastic about my research, and for being the best mother-in-law one could hope for.
Special thanks to my bridesmaids/best friends for their years of cheerleading and “bad” influence: Danielle King, Christina Richardson, Krystal Godri, Yu Gu and Christina Sinopoli.

I am extremely grateful to all the institutions and persons who funded my graduate career and rockstar lifestyle: Natural Sciences and Engineering Research Council, Ontario Mental Health Foundation, Jack & Rita Catherall Fund and Men’s Services Group at Baycrest Hospital, Jennifer D. Ryan Fund, The Richard Mraz Foundation, Alpha Gamma Delta Foundation, The Riggs Family, and University of Toronto.

Many, many thanks to my fabulous family who have always supported me and encouraged me in every way. They instilled in me a great love of learning, reading and science, and they have only themselves to blame that I did not grow up to be rich and famous.

I am deeply indebted (literally and figuratively) to my new husband, Richard Mraz, who has been exceptionally loving and surprisingly patient throughout this entire process. I love him more than I could ever adequately express and feel extremely fortunate to have him in my life.
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Chapter 1
Background and Rationale
1 Background and rationale

1.1 Introduction

The durability of emotional memories is verified not only by personal experience, but also by empirical evidence (e.g. Christianson & Loftus, 1987; Heuer & Reisberg, 1990; Cahill et al., 1996; Phelps, LaBar, & Spencer, 1997). From an evolutionary perspective, it is very adaptive, and often crucial, to remember emotional information that is appetitive (the best place for foraging) or aversive (the dwelling of a predator). An extreme example of emotion-enhanced memory is called ‘flashbulb memory’. According to Brown and Kulik (R. Brown & Kulik, 1977), flashbulb memories are formed when something emotionally intense happens and have the following characteristics: richly detailed and very complete, accurate, and immune to forgetting. This led some researchers to suggest that emotionally arousing memories are indelible (LeDoux, 1992). However, it has since been shown that although greater emotional intensity is associated with greater memory confidence, it is not necessarily associated with higher memory accuracy (Talarico & Rubin, 2003). Indelible or not, and for better or worse, emotional memories often endure longer and contain more vivid details than non-emotional memories.

However, in order to remember an event, one needs to remember not only the individual details, but also be able to bind them into a coherent whole. For example, if one were the eyewitness to an armed robbery, it would be important to not only remember seeing a weapon (e.g. a gun), but to also associate the weapon with other aspects of the event such as what the person holding the gun looked like, what s/he was wearing, and who else may be involved. While there is an abundance of research focused on examining how emotion may influence memory for the emotion-arousing item (i.e. the gun), there is a lack of research focused on how emotion may modulate memory for associated information that may not be emotional in and of themselves (e.g. what kind of clothes the perpetrator was wearing). In other words, it is unclear how emotions may affect our ability to process the surrounding neutral information and bind various bits of information together into a coherent and lasting episode. Such an examination may help us better understand the interaction between emotions and memory. Specifically, do emotions enhance memory for all aspects of an event, or only some aspects of an event? If emotions only enhance some aspects of an event, how does this occur? Such an examination may also have
clinical relevance and lead to insights for understanding how neutral information may be altered and become imbued with emotional significance in disorders such as post-traumatic stress disorder (PTSD).

In studies examining how emotions may influence memory, most have assessed memory directly via either recognition (i.e. has this stimulus been presented before?) or recall (i.e. tell me what you remember) tasks (e.g. Adolphs, Cahill, Schul, & Babinsky, 1997; Adolphs, Denburg, & Tranel, 2001; Anderson, Wais, & Gabrieli, 2006; Buchanan, Denburg, Tranel, & Adolphs, 2001; Cahill et al., 1996). However, verbal reports represent the final output of a long chain of processes that occur prior to it and emotions may influence memory by modulating any, or all of those processes. Emotions may modulate how much attention we may direct to a stimulus, thereby influencing what kind of information we get into memory in the first place (encoding). Emotions may also influence how quickly we may be able to access memory representations and/or the way in which we evaluate those stored representations, thereby influencing what kind of information we get out of memory (retrieval). In order to assess how emotions may influence these processes, one must go beyond verbal report and take advantage of technologies that are able to reveal aspects of online processing, such as eye movement monitoring and neuroimaging techniques such as magnetoencephalography (MEG).

The current thesis utilizes verbal report, eye movement monitoring and MEG in order to address the following questions: (1) How do emotions influence attention to both the emotion-eliciting item (e.g. a gun) and associated information (e.g. what the person holding the gun looked like) during the encoding stage and what we get into memory; and (2) how do emotions influence the retrieval of both the emotion-eliciting item and associated information and what we may be able to get out of memory? In this chapter, background information relevant to addressing the above questions is reviewed including: emotion-enhanced memory for items, differences between memory for items and memory for associated information, emotion-modulated memory for associated information. The use of eye movement monitoring and MEG, and how they may be utilized to outline aspects of memory is also reviewed. Finally, an overview of methods and specific project objectives are outlined.
1.2 Emotion-Enhanced Memory for Items

The bulk of the literature examining emotion-modulated memory has focused on how emotion influences memory for single items such as words and faces. In this literature, studies consistently showed that emotional items are remembered better than neutral items whether memory is tested immediately after encoding or after a longer delay, i.e. more than 24 hours (for reviews see: Dolan, 2002; LaBar & Cabeza, 2006). Research has shown that special neural and hormonal processes exist to enhance emotional, but not nonemotional memories. The brain region most implicated for emotion processing is the amygdala (for reviews see: Dolan, 2002; LaBar & Cabeza, 2006; McGaugh, 2000; Phelps, 2004; Zald, 2003). For example, patients with amygdala lesions did not show emotion-enhanced memory (e.g. Adolphs et al., 1997; Anderson & Phelps, 2001) and amygdala lesions or infusions of beta-adrenergic receptor antagonists into the amygdala blocked the memory modulating/enhancing effects of epinephrine and glucocorticoids on consolidation (McGaugh, 2004).

Although most research on the amygdala’s role in emotion-enhanced memory have focused on its effects during consolidation, a period in which a memory trace is stabilized after initial encoding, which can take days (McGaugh, 2000, 2002), it has also been shown that the amygdala may also enhance memory during the encoding stage. For example, it has been found that even when memory was tested immediately, the amount of amygdala activity during encoding was positively correlated with subsequent memory for the emotional items (e.g. Kensinger & Schacter, 2006; Richardson, Strange, & Dolan, 2004). It is suggested that in addition to its role during consolidation, the amygdala may also enhance memory by modulating attention, i.e. the active processing of specific information in the environment (LaBar & Cabeza, 2006), and sensory processing, i.e. the construction of a coherent representation regarding sensory input (Armony & Dolan, 2002; Carretie, Hinojosa, Martin-Loeches, Mercado, & Tapia, 2004; Phelps, 2004; Williams, Mathews, & MacLeod, 1996), both of which have been shown to be significant factors in enhancing memory (Craik, Govoni, Naveh-Benjamin, & Anderson, 1996; Phelps, 2004; Talmi, Anderson, Riggs, Caplan, & Moscovitch, 2008). In other words, emotions may enhance memory by increasing the amount of attention one may direct to the emotion-eliciting item and/or by enhancing the visual representation of that item in the brain.
Another way in which the amygdala may enhance memory is through direct modulation of mnemonic structures in the medial temporal lobe. The amygdala has connections to many regions involved in memory such as the caudate nucleus, the rhinal cortex and the hippocampus (Pikkarainen, Ronkko, Savander, Insausti, & Pitkanen, 1999; Pitkanen, Pikkarainen, Nurminen, & Ylinen, 2000). Via these projections, the amygdala is able to enhance different forms of memory. For example, it has been shown that while infusions of amphetamine into the hippocampus and caudate nucleus enhanced memory for spatial and cued training, respectively, infusions of amphetamine into the amygdala enhanced memory for both types of memory (Packard & Cahill, 2001; Packard, Cahill, & McGaugh, 1994).

As mentioned previously, although there is ample research showing emotion-enhanced memory for items such as faces and words, there is less research that examines the effects of emotion on memory for neutral information associated with the emotional item. One may be tempted to argue that since emotions enhance memory for items, it may also enhance memory for information that is associated with the emotional items. After all, when people report on the contents of their memory for emotional events (e.g. an armed robbery), they do not only report on the emotional item (e.g. the gun), but also other neutral items associated with the event (e.g. what the perpetrator was wearing). However, as mentioned at the beginning of this chapter, research has shown that such reports were not always accurate (Talarico & Rubin, 2003). Further, there is evidence to suggest that the same conditions that promote memory for items may not promote memory for associated information, and that these two forms of memory may rely on different neural regions (e.g. Craik, Luo, & Sakuta, 2010; Litman & Davachi, 2008). Therefore, just because emotions enhance memory for the emotion-eliciting item, it does not necessarily mean that emotions also enhance memory for information associated with the item.

In the next section, differences between item memory and associative memory are outlined within a larger framework of memory systems.

### 1.3 Memory Systems

In 1953, a patient underwent a bilateral medial temporal-lobe resection for the relief of incapacitating non-focal seizures. Subsequent to the operation, although the patient’s seizure episodes decreased, he now suffered from profound anterograde amnesia – an inability to form new memories. Importantly, this memory deficit was not accompanied by other intellectual or
motor skill deficits (Corkin, 1968, 2002). The patient is now famously known as H.M. (Scoville & Milner, 1957, 2000) and led to the discovery that memory depends on the integrity of medial temporal brain regions, and specifically the hippocampus (e.g. Scoville & Milner, 2000; Squire & Zola-Morgan, 1991; Zola-Morgan, Squire, & Amaral, 1986). This is corroborated by cross-species studies (for review see Squire, 1992) and set the stage for current cognitive and neuroscientific theories.

One of the most important ideas to emerge in the last few decades is that memory is not a unitary system, but divided into subsystems supported by different regions in the brain. In 1980, Cohen and Squire (N. J. Cohen & Squire, 1980) proposed that declarative memory, defined as the long-term memory for events, depends on medial temporal regions of the brain, especially the hippocampus, and is compromised in amnesia. On the other hand, procedural memory, defined as memory for skills and measured by tasks of motor skills (Corkin, 1968), classical conditioning (Warrington & Weiskrantz, 1982; Weiskrantz & Warrington, 1979), priming (Warrington & Weiskrantz, 1968) and perceptual skills (Milner, Corkin, & Teuber, 1968), depend on cortical regions of the brain and is spared in amnesic patients.

While almost all researchers agree that memory is not a unitary system, and that loss of hippocampal function is associated with impaired declarative memory and preserved procedural memory, there is intense debate regarding what ‘declarative memory’ encompasses (for reviews see: N. J. Cohen, Poldrack, & Eichenbaum, 1997; Squire, 2004; Tulving, 1987). Some researchers argue that declarative memory encompasses memory for information that is consciously or explicitly accessible such as memory for facts and events, as opposed to memory for skills such as riding a bike which would be considered a procedural memory. Under this definition, declarative memory is synonymous with explicit or conscious memory, and the critical role of the hippocampus is to form and retrieve memories that are available to conscious introspection (Graf & Schacter, 1985; Schacter, 1987; Squire & Zola, 1997). This is referred to as the “explicit account” and under this definition, conscious memory for both singular items (e.g. a face) and the relations between multiple items (e.g. a face within a particular scene) will rely critically on the integrity of the hippocampus. Supporting this, it has been found that amnesic patients with damage to the hippocampus are impaired when they have to recall or recognize items (e.g. words) and associative information (e.g. word pairs; for reviews see: N. J. Cohen et al., 1999; Mayes, Montaldi, & Migo, 2007; Squire, 2009). In view of this, it could then
be reasoned that since memory for items and memory for associations rely on the same neural region, and research clearly shows that emotions enhance memory for items (Section 1.1), then one can reasonably conclude that emotions may also enhance memory for associations as well.

In contrast to the explicit account, some researchers use declarative memory to describe relational memory. Relational memory is defined as the formation of relations/associations among items within a scene or an event into a lasting representation, and relies critically on the integrity of the hippocampus (N. J. Cohen et al., 1997; N. J. Cohen et al., 1999). This is referred to as the “relational account” and under this definition, memory for the relations between items depends critically on the hippocampus, irrespective of conscious awareness (Chun & Phelps, 1999; Ryan, Althoff, Whitlow, & Cohen, 2000; Ryan & Cohen, 2004), and memory for items do not depend on the hippocampus. For example, it has been reported that the more complex a stimulus is and the more associations that are required to memorize it, the greater the hippocampal activity observed (Henke, Weber, Kneifel, Wieser, & Buck, 1999; Kirwan & Stark, 2004; Montaldi et al., 1998; Stern et al., 1996). Critically, it has been shown that while amnesics can express memory for items (e.g. faces), they do not show memory for the relations between items irrespective of whether memory was assessed directly via verbal report or indirectly via eye movement monitoring without requiring participants to explicitly comment on the contents of their memory (Ryan et al., 2000; Ryan & Cohen, 2004). This suggests that relational memory can be decoupled from conscious awareness and that memory for items and memory for the relations between items is supported by different regions in the brain. In view of this, it could be argued that just because emotions enhance item memory (Section 1.1), this does not necessarily mean that emotions would also enhance relational memory.

It should be clear from the above that not only do proponents of the explicit and relational account of declarative memory disagree on what encompasses ‘declarative memory’ and what the critical role of the hippocampus is, but these accounts also lead to potentially different predictions as to the way in which emotions may influence relational memory. However, it is important to note that although proponents of the explicit versus relational account may disagree on the critical role of the hippocampus, most researchers would agree that the hippocampus plays an important role in relational memory. In further support of this, there is a growing body of literature showing that not only is the hippocampus specialized for relational memory, but other regions within the medial temporal lobe may be specialized for other types of memory as well.
(e.g. Henson, 2005; see also: Squire, Stark, & Clark, 2004). For example, results from rat studies show a functional dissociation such that lesions to the hippocampus led to impaired responding on tasks requiring relational memory, whereas lesions to the perirhinal cortex led to impaired responding on tasks requiring item memory (e.g. Moses, Cole, Driscoll, & Ryan, 2005). In a study by Wan and colleagues (Wan, Aggleton, & Brown, 1999), neuronal activity in rats was measured using immunohistochemistry for the protein products of c-fos while the rats viewed familiar and novel pictures simultaneously. It was found that when the rats had to distinguish between familiar and novel items, activity in the perirhinal cortex was significantly higher for novel as compared to familiar objects. However, when rats had to distinguish between objects in a familiar versus novel arrangements, activity in the hippocampus was significantly higher for novel as compared to familiar arrangements.

Similar results as those reported for rats have also been observed with humans using neuroimaging techniques such as functional magnetic resonance imaging (fMRI). Specifically, memory with an associative component (i.e. item + contextual information) tends to elicit more activity in the hippocampus, whereas memory for single items tends to elicit more activity in the perirhinal cortex (M. W. Brown & Aggleton, 2001; Davachi, Mitchell, & Wagner, 2003; Dougal, Phelps, & Davachi, 2007; Ranganath et al., 2004). For example, in an fMRI study of item and relational memory (Davachi et al., 2003), participants were presented with a list of adjectives and were instructed to either read the word backwards (“Read”) or to form a mental imagery of the word (“Image”). After 20 hours, participants’ item (i.e. is the word old or new?) and source/relational memory (i.e. was the word studied in the Read or Image condition?) was examined. It was found that the level of activity in the perirhinal cortex predicted later item recognition, but it did not predict later source memory. On the other hand, the level of activity in the hippocampus predicted subsequent success in recalling the condition in which the word was studied (source memory), but it did not predict subsequent item memory.

In light of the above, there are a couple important points worth highlighting. First, if the relational account is correct and relational memory can be decoupled from conscious awareness, then an examination of how emotions may influence relational memory should include both direct (verbal report) and indirect methods (e.g. eye movement monitoring) of measuring relational memory. This would not only provide convergent evidence, but it may also reveal aspects of online processing that cannot be accessed by probing participants’ conscious memory.
alone. Second, if different subregions of the medial temporal lobe underlie item and relational memory, it can be argued that just because emotions may enhance item memory via the perirhinal cortex, this does not necessarily imply that it must also enhance relational memory via the hippocampus. Thus, the aim of the current thesis is to examine how emotions may influence relational memory by utilizing direct and indirect methods to assess memory formation and retrieval. However, before describing the specific methods in detail, a review of the relevant literature concerning emotion-modulated relational memory is described in the next section.

1.4 Emotions and Relational Memory

The literature is mixed and somewhat unclear as to whether emotions may enhance or impair relational memory. There are two main theories that have emerged concerning the effects of emotion on relational memory and I examine each in turn: (1) emotion enhances relational memory; and (2) emotion enhances memory for the emotion-eliciting item, but impairs relational memory.

1.4.1 Emotion Enhances Relational Memory

MacKay and colleagues (Hadley & Mackay, 2006; MacKay & Ahmetzanov, 2005; MacKay et al., 2004) have proposed that emotional arousal may enhance relational binding by acting as the ‘glue’ that preferentially binds features within the emotional item as well as between it and its experimental context (e.g. information regarding when and where the experiment occurred). These studies examined differences in memory for taboo versus neutral words. For example, participants were presented with taboo words and neutral words typed in different font colours and were instructed to ignore the meaning of the word and name the colour of the font. In a surprise memory test, it was found that not only were the participants more accurate in recalling the taboo words as compared to the neutral words, they were also more accurate in remembering the colour in which the taboo words were presented (MacKay et al., 2004). However, remembering the colour of the font in which a word was typed represents enhanced memory for specific details of the word, or in other words, enhanced memory for specific details of an item. Thus, this type of memory is not considered relational memory, but rather item memory and likely relies on the perirhinal cortex rather than the hippocampus (Section 1.3).
Similar results have also been reported by D’Argembeau and Van der Linden (D’Argembeau & Van der Linden, 2004, 2005) examining the effects of emotion on associated information such as spatial location and temporal order. In one of these studies (D’Argembeau & Van der Linden, 2004), the researchers presented participants with positive, negative and neutral words in a 4×4 grid and found that participants were better able to identify the spatial location in which the emotional as compared to where the neutral words had been presented. In a separate study, the researchers also examined the influence of emotions on associated temporal information (D’Argembeau & Van der Linden, 2005). Here, participants were presented with three separate lists composed of negative, positive and neutral complex visual scenes. Memory for associated temporal information was examined by asking participants to recall in which list a certain scene had originally been presented during the encoding phase. As expected, memory for temporal information was more accurate for negative versus neutral pictures.

The above studies show that emotions enhanced memory for not only the emotional item, but also for contextual details associated with the item such as its spatial location and its temporal position. However, it is unclear how emotions may enhance memory for such relations. D’Argembeau and Van der Linden (D’Argembeau & Van der Linden, 2004; D’Argembeau & Van der Linden, 2005) suggested that emotional items may capture and hold one’s attention to a greater extent, thereby facilitating memory for both the item and information associated with it. However, this has not been examined directly. And perhaps even more problematically, emotion-modulated attention is also cited as the reason for the opposite pattern of results as those reported above, namely, emotions lead to impaired relational memory. These studies are reviewed in the next section.

1.4.2 Emotion Impairs Relational Memory

Returning briefly to the scenario of being a witness in an armed robbery (Section 1.1), some studies have shown that contrary to the results reported above (Section 1.4.1), people actually have worse memory for information associated with the emotional event such as what the perpetrator looked like. It is suggested that while emotions enhance memory for the emotion-eliciting item (e.g. gun), the cost of this memory enhancement is impaired memory for associated information. In other words, emotions may enhance item memory at the cost of impaired
relational memory. This is commonly referred to as the central/peripheral tradeoff effect in memory (for review see Christianson, 1992).

In a classic study by Loftus and colleagues (E. F. Loftus, Loftus, & Messo, 1987), participants were shown a slide sequence depicting a man (target) holding a gun or a bill to the cashier at a fast food restaurant line-up. Later, participants completed a 20-item recognition test and attempted to identify the target man from a 12-person line-up as well as other aspects of the scenes presented. The researchers found that when participants viewed the slide sequence with the gun, they performed better in identifying the gun but more poorly in identifying the man holding the gun as compared to when the man was holding a bill. This showed the purported central/peripheral tradeoff effect in memory and similar results have been reported in numerous studies (e.g. Jurica & Shimamura, 1999; Kensinger, Piguet, Krendl, & Corkin, 2005; Kramer, Buckhout, & Eugenio, 1990; Levine & Pizarro, 2004; Pickel, 1998). Using a different paradigm, Brown (J. M. Brown, 2003) also reported similar results. Specifically, Brown utilized the contextual reinstatement (CR) procedure in which he used peripheral information to cue memory and found that while CR enhanced memory in the neutral and unusual conditions, it did not enhance memory in the emotionally arousing condition. This was likely the result of the fact that participants’ memory representations did not contain information pertaining to the periphery and/or the relation between the peripheral and central information.

It is suggested that the central/peripheral tradeoff effect in memory is the consequence of differences in attention allocation during encoding. Specifically, it is reasoned that when an arousing stimulus is present, participants spend most of their time focusing on it, which then results in better encoding and memory for the emotion-eliciting item, but impaired encoding and memory for the associated information (Armony & Dolan, 2002; J. M. Brown, 2003; Easterbrook, 1959; Kensinger et al., 2005; E. F. Loftus et al., 1987; Wessel & Merckelbach, 1997). According to Easterbrook’s (Easterbrook, 1959) hypothesis, this attention narrowing effect occurs because emotional arousal leads to a restricted focus on the emotion-eliciting item and as a consequence of that, fewer resources are available for processing associated information in the periphery. This bias in the attention systems seems to be evolutionarily adaptive. A major function of attention is to ignore irrelevant and select relevant stimuli in the environment (Lavie, Hirst, de Fockert, & Viding, 2004) and this ability is especially important in the selective appraisal of appetitive and aversive stimuli in order to guide approach and avoidance behaviour.
However, although there is an abundance of studies showing that emotions preferentially capture and sustain attention (e.g. Anderson, 2005; Anderson & Phelps, 2001; Armony & Dolan, 2002; Calvo & Lang, 2005; E. F. Loftus et al., 1987; Nummenmaa, Hyona, & Calvo, 2006; Ohman, Flykt, & Esteves, 2001; Ohman & Mineka, 2001), there has not been a successful attempt to directly examine whether such differences in attention allocation during the encoding period are related to differences in subsequent relational memory performance.

In summary, some lines of research show that emotions enhance relational memory while other lines of research show that emotions impair relational memory. Further, while both camps suggest that these emotion-modulated differences in memory are the result of emotion-modulated differences in attention during the encoding stage, this has not been successfully examined. In the next section, I highlight some of the issues within this body of literature and the questions that still remain.

1.4.3 Questions Remaining

As mentioned in the previous section, although many researchers have suggested that emotion-modulated differences in relational memory may be the result of differences in attention during the encoding stage, this has not been successfully examined. Now, as mentioned in the introduction (Section 1.1), emotion may modulate relational memory at different stages, during not only the encoding stage via differences in attention, but also during the retrieval stage. Thus, in addition to questions regarding how emotions may modulate relational memory via attention (above), it is also unclear how emotions may modulate relational memory during the retrieval stage. Such questions cannot be addressed by using direct measures of memory such as recall and recognition. Therefore, experiments within the present thesis also used eye movement monitoring and MEG. Each methodology is reviewed in the next sections.

1.5 Eye Movement Monitoring

1.5.1 Measures of Attention

It is often reasoned that emotions may modulate relational memory via differences in attention during the encoding period. The study of attentional processes has typically been explored with the use of behavioral tasks such as the dot probe paradigm (e.g. Karin Mogg & Bradley, 1999, visual search task (e.g. Fox et al., 2000; Ohman, Flykt, et al., 2001; Ohman, Lundqvist, &
Esteves, 2001; Tipples, Atkinson, & Young, 2002) and the exogenous cueing task (Fox, Russo, & Dutton, 2002; Koster, Crombez, Van Damme, Verschuere, & De Houwer, 2004; Rowe, Hirsh, & Anderson, 2007; Yiend & Mathews, 2001). However, these reaction time based studies are not suitable for the research aims of the present thesis for the following reasons: First, they cannot reveal how emotion may influence attention to information associated with emotional versus neutral stimuli. Second, they cannot reveal qualitative differences in attention. Third, they cannot reveal how emotion may influence processes during the retrieval period. In contrast, an examination of eye movement behaviour can begin to reveal how emotions may influence the above aspects of attention and retrieval.

The human visual system is structured in such a way that detailed information is primarily discerned by directly fixating on the region of interest. This is because we have a high-resolution central fovea and lower resolution visual surround (Henderson, Williams, Castelhano, & Falk, 2003). In this way, eyes are continually active and sampling the visual world all around us in order to gather relevant information and to guide subsequent behaviour. The way in which we view the world (i.e. where we look, how long we may look at it) is driven not only by stimulus bound characteristics such as colour and movement, but also internal cognitive processes such as goals, semantic knowledge and memory (for review see: Hannula et al., 2010). Eye movement monitoring takes advantage of these revealing characteristics of eye movement behaviour, thus making it an excellent tool to study processes related to a variety of cognitive processes, including attention and memory, and the effects of emotion on both processes. In the sections below, I outline how researchers have used eye movement monitoring to reveal attention and memory processes, and how emotions may modulate them.

1.5.2 Eye Movement Monitoring and Attention

One of the ways in which eye movement monitoring has been used to study emotion-modulated attention is to assess whether emotions lead to orienting or engagement of attention and whether this process is obligatory or not. Specifically, eye movement monitoring can differentiate between attention orientation and attention maintenance via differences in early versus later viewing, respectively (e.g. Ryan & Cohen, 2004). Further, eye movement monitoring can also yield insights into whether a certain process is obligatory or not by assessing whether the eye movement effects are affected by task instructions, i.e. if the process is obligatory, then it should
not be affected by task instructions (Ryan, Hannula, & Cohen, 2007). Taking advantage of these characteristics, the use of eye movement monitoring has shown that the presence of an emotionally arousing stimulus led to faster orienting and enhanced maintenance of attention, and some of these effects occurred in an obligatory fashion. For example, when participants viewed emotional and neutral stimuli simultaneously, they were more likely to direct their first fixation and subsequent viewing to the emotional versus neutral stimuli (e.g. Calvo & Lang, 2004; Calvo & Lang, 2005; Caseras, Garner, Bradley, & Mogg, 2007; K. Mogg, Millar, & Bradley, 2000; Nummenmaa et al., 2006). It has been suggested that participants continued to view emotional stimuli more than neutral stimuli because it was difficult to disengage attention from the emotional qualities of the stimulus (Fox, Russo, Bowles, & Dutton, 2001). Further, Nummenmaa and colleagues (Nummenmaa et al., 2006) found that regardless of whether participants were instructed to direct their first gaze to the emotional or to the neutral picture, they were more likely to direct their first gaze to the emotional picture. This suggests a bias in attentional orienting that may be automatic and/or obligatory.

In addition to providing a measure for the amount of attention directed to a stimulus of interest, eye movement monitoring has also been used to reveal differences in the manner of viewing directed to neutral versus emotional stimuli. Differences in the manner of viewing may represent qualitative differences in attention and/or differences in perception (i.e. the construction of a coherent representation regarding sensory input). Specifically, researchers have used eye movement monitoring to examine how eye movement patterns may differ for viewing faces in a neutral expression versus those expressing emotions such as anger, fear or happiness (e.g. Bate, Haslam, & Hodgson, 2009; Calder, Young, Keane, & Dean, 2000; M. L. Smith, Cottrell, Gosselin, & Schyns, 2005; Wong, Cronin-Golomb, & Neargarder, 2005). It has been found that viewing of threat-related versus non-threat-related (neutral) facial expressions is characterized by an overall increase in the number of fixations directed to the face and number of regions sampled within the face (Bate et al., 2009), an increase in sampling of internal features of the face, and an extensive or “vigilant” style of scanning, i.e. long durations between fixations (Green, Williams, & Davidson, 2003a). Eye movement patterns have also been found to distinguish between more specific facial expressions. For example, expressions of anger and fear elicit focusing on the eyes, and expressions of disgust and happiness elicit focusing on the mouth (Aviezer et al., 2008; Calder et al., 2000; M. L. Smith et al., 2005; Wong et al., 2005).
In summary, previous studies have shown that emotions modulate not only the amount of attention directed to emotionally arousing items, but also the manner in which such items were viewed. In other words, emotion may lead to both quantitative and qualitative differences in attention. Given these differences, it is possible that the presence of an emotional stimulus may also lead to quantitative and/or qualitative differences in the processing of associated information during the encoding stage. Further, eye movement monitoring can be utilized to outline such emotion-modulated changes in attention. Eye movement monitoring can be used to characterize several different aspects of attention such as what was attended, how quickly attention was directed to a certain item of interest, how long attention was sustained and the manner in which visual stimuli were viewed. Further, such eye movement behaviours can be quantified and correlated with subsequent memory performance. In the next section, I review how eye movement monitoring has been used as a measure of memory.

1.5.3 Eye Movement Monitoring and Memory

In addition to the use of eye movement monitoring as a measure of attention during encoding, it can also be used as an indirect measure of memory during retrieval because it does not require participants to explicitly comment on the contents of their memory (for review see: Hannula et al., 2010). In contrast, more traditional means of measuring memory through recall and recognition accuracy require participants to explicitly comment on the contents of their internal memory representations which can be problematic or impossible for some populations such as those without adequate language skills, e.g. babies and animals. Further, while verbal reports are the end product of a long chain of processes that occur prior to it, eye movement monitoring can reveal those aspects of online processing that may ultimately culminate in the explicit verbal response, such as how quickly memories may be accessed and which aspects of a scene are important in guiding that decision. Based on eye movement effects of memory, Parker (Parker, 1978) proposed that there may be four different stages that contribute to recognition memory: 1) information regarding the gist of a scene is acquired; (2) the acquired information is compared with expectations and stored memory representations; (3) there is an evaluation of whether or not there is a mismatch between the external stimulus and one’s internal memory representation, and if so, whether this is sufficient for a response; and (4) if the mismatch is sufficient, eyes are then guided to the region of mismatch in order to gather more information. Given these different stages of retrieval, it is possible that if emotion influences retrieval processes, it may even have
differential effects on the different stages of retrieval. Although the use of eye movement monitoring has not been used to study the influence of emotion on the retrieval process, it has been used by multiple labs as an indirect measure of memory for neutral information (for review see Hannula et al., 2010).

In using eye movement monitoring to assess memory, there are two commonly reported effects: the repetition effect and the manipulation effect. The repetition effect describes a phenomenon in which participants direct significantly fewer fixations (i.e. a discrete pause in eye movements – the absence of a saccade or blink) to a stimulus that is familiar and that one has a strong memory representation for (e.g. a famous face) as compared to a stimulus that is novel (e.g. Althoff & Cohen, 1999; Ryan et al., 2000; Ryan, Hannula, et al., 2007). This ‘repetition’ effect in eye movement behaviour may be akin to the ‘repetition suppression’ effect observed in neural activity for priming studies (Schacter & Buckner, 1998) and may represent a ‘sharpening’ of one’s representation. In other words, as a stimulus becomes more familiar, one would direct fewer fixations to it because most of its details are already committed to memory.

On the other hand, the manipulation effect describes the phenomenon in which eye movements to a region of a scene that has undergone a change (e.g. adding an object, deleting an object, or moving an object’s spatial location) as compared to a region of a scene that has not been manipulated is characterized by faster orienting (e.g. Parker, 1978), longer fixation durations and increased number of fixations (Ryan et al., 2000). It is reasoned that if participants had successfully bound the different element within the scene into a coherent and lasting memory representation, then they would be able to detect the subsequent manipulation, whether directly via verbal report and/or indirectly as measured by eye movement monitoring. Critically, it has been reported that this manipulation effect is absent in amnesic patients suggesting that such relational processes are supported by the hippocampus (e.g. Ryan et al., 2000; Ryan & Cohen, 2004).

Now, if emotions enhance relational memory, then this would lead to a stronger and/or more stable memory representation for stimuli paired with emotional information as compared to those paired with neutral information. From the above, it can be seen that eye movement monitoring provides a powerful tool by which to examine such emotion-modulated differences in memory, as well as attention. By using this technique, we can reveal not only aspects of how emotions
may influence relational memory (i.e. via differences in attention), but also describe how emotions may modulate different stages of the retrieval process. In this way, eye movement monitoring has the potential to shed light on the nature of memory formation and retrieval, how malleable such processes may be, and also how extensive the effects of emotions are.

However, although eye movement monitoring is a powerful tool in revealing how relational memory processes may occur behaviourally, a comprehensive account of emotion-modulated relational memory should also include an examination of how such processes are supported in the brain, i.e. which neural regions/networks drive these changes in viewing? As mentioned in the previous sections, the amygdala and the hippocampus have been found to play an important role in emotion processing and relational memory, respectively. Thus, the use of neuroimaging may shed light how these two regions and/or other neural networks may interact to support emotion-modulated relational memory. In the next section, I review the neuroimaging technique of magnetoencephalography (MEG) and outline reasons for which why this was the ideal tool to address the question of how emotions may modulate relational memory.

1.6 Magnetoencephalography

In exploring the neural regions underlying emotions and relational memory, many researchers have utilized fMRI. In convergence with neuropsychological data, this has revealed an important role of the amygdala in emotion processing (Section 1.2), and of the hippocampus in relational memory (Section 1.3). However, the temporal resolution of fMRI is on the order of seconds whereas cognitive operations occur within hundreds of milliseconds. An understanding of the precise temporal dynamics underlying neural activity is crucial to the understanding of not only how different neural regions may interact and modulate each other, but it may also allow us to answer questions regarding the nature of memory (e.g. is memory retrieval an obligatory process?) and emotion-modulated cognitive processes (e.g. how quickly do emotions influence relational binding?).

Precise temporal dynamics underlying neural activity can be recorded directly during surgery by inserting microelectrodes into a particular region. However, this has the obvious drawback that one can only study the ‘damaged’ brain as opposed to the ‘healthy’ brain. Another method that can be applied to the study of precise neural dynamics is electroencephalography (EEG), which is a measurement of electric potential differences on the scalp. Although this is widely used in
the study of various cognitive operations, including memory (for review see, Rugg, 1995b), electric signals measured from the scalp is greatly influenced by various inhomogeneities in the head, making accurate localization of neural activity within the brain very difficult (Hämäläinen, Hari, Ilmoniemi, Knuutila, & Lounasmaa, 1993). In contrast, magnetoencephalography (MEG) is a noninvasive neuroimaging technique that is similar to EEG in that both methods measure signals generated by synchronized neural activity in the brain. The major difference between the two methods is that whereas EEG measures electric potential differences that are affected by various inhomogeneities in the head, MEG measures the magnetic field differences produced by population of neurons that are largely unaffected by various inhomogeneities (Hämäläinen et al., 1993; Hari, Levanen, & Raij, 2000). Thus, MEG provides recording of neural activity with temporal resolution on the order of milliseconds and spatial resolution comparable to that of fMRI (Miller, Elbert, Sutton, & Heller, 2007).

Taking advantage of the precise temporal resolution of MEG, researchers have been able to better elucidate the functional networks mediating cognitive processes, including the processing of emotions (Cornwell et al., 2008; Garolera et al., 2007; Hung et al., 2010; Luo, Holroyd, Jones, Hendler, & Blair, 2007; Moses et al., 2007; Salvadore et al., 2009; Streit et al., 1999). For example, based on animal studies, it has been proposed that there are two routes by which threat-related information gains access to the amygdala: via a fast subcortical route (thalamus-amygdala) and a slower cortical route (thalamus-sensory cortex-amygdala (LeDoux, 1996). This implies that the presentation of a threat stimulus should elicit an early and a later peak of activity in the amygdala. Due to limitations in its temporal resolution, fMRI cannot be used to characterize neural activity related to the subcortical and cortical route by which emotional information may gain access to the amygdala. However, MEG can be successfully utilized to characterize such timing differences. In a MEG study examining neural signal changes to faces expressing fear as compared to faces with a neutral expression (Hung et al., 2010), researchers found two significant peaks of activity within the amygdala: viewing of faces with a fearful versus neutral expression elicited significantly higher activity within the right amygdala at 100 ms and then again at 165 ms after stimulus onset.

From the above, it can be seen that MEG has been utilized to examine the temporal dynamics underlying emotion processing and that such activity has been successfully localized to the amygdala. Thus, it seems that MEG would be an ideal tool with which to examine the questions
of the current thesis, namely, do emotions modulate the processing of associated information and if so, how is this process supported in the brain? However, there is considerable debate with regards to whether MEG can be reliably used to localize deeper sources such as the hippocampus, which is a critical structure in any examination of relational memory (Section 1.3). For this reason, it was critical to first establish the reliability of MEG in characterizing neural activity from deep sources such as the hippocampus before it can be used to assess how emotions may modulate relational memory. With this in mind, the next section will outline all of the specific objectives of the current thesis and provide an overview of the methods.

1.7 Objectives

The purpose of this thesis was to examine how the presence of emotion may affect relational memory. Specifically, (1) How does the presence of emotional information influence the amount of attention to different aspects of an event/scene and how is this related to subsequent memory; (2) how does association with emotional versus neutral information change the manner in which participants view certain stimuli and how is this related to subsequent memory; and (3) how might association with emotional versus neutral information manifest during different stages of retrieval.

A convergent methods approach was utilized such that attention was assessed via eye movement monitoring and/or MEG, and memory was assessed both directly via verbal report and indirectly via eye movement monitoring. As mentioned previously, eye movement monitoring can provide a reliable measure of differences in eye movement scanning that occur during encoding of information associated with negative versus neutral information; and it can also provide an indirect measure of the different stages that may occur during retrieval (Section 1.5). The use of MEG provided information regarding which neural regions were involved in emotion-modulated processing of associated information and allowed us to address more specific questions regarding how this process may occur. This is discussed in more detail below. However, in contrast to eye movement monitoring, the use of MEG to study emotion-modulated relational memory may be more controversial because there is some doubt as to whether MEG can localize neural activity to deep sources such as the hippocampus, a critical structure implicated in relational memory (Section 1.3). Thus, a corollary aim of the current thesis was to examine whether MEG can be
successfully used to characterize neural activity from the hippocampus before using MEG to assess how emotions may influence relational processing.

Thesis Overview

The next sections provide a brief outline of the different chapters contained within this thesis and the main question that it sought to address.

Do emotions modulate relational memory via differences in the amount of attention during encoding (Chapter 2)?

It is commonly argued that emotions may modulate memory for associated information via differences in the amount of attention directed to that item during the encoding stage (Section 1.4). However, this has not been successfully examined. The experiment in Chapter 2 used eye movement monitoring and verbal report in order to address the following questions: (1) does the presence of an emotional stimulus influence the amount of attention directed to associated neutral information during the encoding phase; (2) do emotions modulate one’s ability to remember the associated neutral information; and (3) if there are differences in the amount of attention directed to information paired with emotional versus neutral stimuli, are these differences related to subsequent memory performance?

Do emotions modulate relational memory via differences in the retrieval process (Chapter 3)?

As mentioned previously, emotions may modulate relational memory at the encoding and/or retrieval stage. Thus, Chapter 3 utilized eye movement monitoring in order to assess whether emotion influenced different stages of retrieval. Specifically, it is possible that emotion may have differential effects on different stages of retrieval (Section 1.5.2). For example, it is possible that the presence of emotionally arousing information may make associated information easier to retrieve. Alternatively, it is possible that while early stages of memory retrieval occur in an obligatory fashion and are uninfluenced by the effects of emotion, the subsequent and more evaluative stages of retrieval may be modulated by emotion.
Can MEG be reliably used to characterize neural activity from the hippocampus (Chapter 4)?

Before moving on to address issues concerning which neural regions support emotion-modulated relational memory, the feasibility of using MEG to study relational memory, or more specifically, to localize hippocampal activity, was examined. To this aim, the experiment in Chapter 4 measured participants’ brain activity using MEG during a recognition memory paradigm, which has been shown to elicit hippocampal activity from a variety of other neuroimaging techniques such as fMRI and PET (for reviews see: Cabeza & Nyberg, 2000; Henson, 2005; Lepage, Habib, & Tulving, 1998). Further, three different localization methods were applied to the MEG data in order to provide convergent evidence and also a more comprehensive description of hippocampal activity relating to spectral frequency and precise onsets.

Do emotions modulate relational memory via the manner in which associated information is perceived (Chapter 5)?

In order to examine whether emotions led to differences in processing associated neutral information, we utilized both eye movement monitoring and MEG. The use of eye movement monitoring and MEG allowed us to assess how emotions may modulate differences in the manner of viewing and neural activity, respectively, to associated neutral information during the encoding stage. Specifically, emotions may modulate the manner in which participants view associated neutral information by changing the nature of the neutral stimulus itself such that it takes on ‘emotional’ qualities and perception is changed. Alternatively, association with emotional information may not change perception per se, but participants may process it differently due to the associated emotional information. In other words, do emotions change perceptual processing of associated information or is the emotional information activated following perceptual processing? One way in which we sought to address this question was to examine the precise temporal neural dynamics underlying emotion-modulated viewing of associated neutral information by using MEG. If emotion changes the way in which associated information is perceived, then one may expect to see differences when viewing information associated with emotional versus neutral items within the first 200 ms after stimulus onset, a time frame typically associated with perception of externally presented stimuli (e.g. Ryan et al., 2008;
Tsivilis, Otten, & Rugg, 2001). On the other hand, if emotion does not change perceptual processing of associated information, then one would not expect to see differences in viewing information associated with emotional versus neutral items within the first 200 ms after stimulus onset.

**Conclusion (Chapter 6)**

The last chapter of the thesis provides a summary of the findings as a whole, discusses the results in context of previous work and provides suggestions for future work. It is anticipated that work from the current thesis will contribute to the growing literature on emotion-modulated memory. By examining how emotion may modulate relational memory, it will lead to greater insight into the different ways in which emotions may influence our ability to process and bind various bits of information into a coherent whole and later retrieve them from memory. This may have implications for understanding a variety of phenomena such as eye witness testimony, emotional autobiographical memory and how neutral experiences may be altered in clinical disorders such as depression, anxiety and post-traumatic stress disorder.

Work from this thesis also makes a more general contribution to the field of cognitive neuroscience by advancing the use of tools such as eye movement monitoring and MEG. Specifically, the use of eye movement monitoring can reveal aspects of online processing that cannot be gleaned from verbal report alone, thus shedding light on aspects of memory that cannot be captured by using more traditional measurements such as recall and recognition. Further, MEG can reveal precise temporal dynamics underlying brain activity that cannot be answered by more traditional neuroimaging techniques such as fMRI and PET, allowing one to address questions regarding the nature of cognitive processes such as memory (e.g. Is memory retrieval obligatory?) and interaction between ‘different’ processes such as emotion, attention, perception and memory (e.g. Do emotions change perception?).
Chapter 2
The Role of Overt Attention in Emotion-Modulated Memory


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2 The role of overt attention in emotion-modulated memory

2.1 Abstract

The presence of emotional stimuli results in a central/peripheral tradeoff effect in memory: memory for central details is enhanced at the cost of peripheral items. It has been assumed that emotion-modulated differences in memory are the result of differences in attention, but this has not been tested directly. The present experiment used eye movement monitoring as an index of overt attention allocation and mediation analysis to determine whether differences in attention were related to subsequent memory. Participants viewed negative and neutral scenes surrounded by three neutral objects and were then given a recognition memory test. The results revealed evidence in support of a central/peripheral tradeoff in both attention and memory. However, contrary with previous assumptions, whereas attention partially mediated emotion-enhanced memory for central pictures, it did not explain the entire relationship. Further, although centrally presented emotional stimuli led to decreased number of eye fixations toward the periphery, these differences in viewing did not contribute to emotion-impaired memory for specific details pertaining to the periphery. These findings suggest that the differential influence of negative emotion on central versus peripheral memory may result from other cognitive influences in addition to overt visual attention or on post-encoding processes.

2.2 Introduction

It is well-noted that presence of an emotional element may result in a central/peripheral tradeoff effect in memory: memory for central, emotional aspects of an event is enhanced, and memory for peripheral, nonemotional aspects of an event is impaired (e.g., Adolphs, Tranel, & Buchanan, 2005; J. M. Brown, 2003; Christianson, 1992; E. F. Loftus, 1979; E. F. Loftus et al., 1987; Reisberg & Heuer, 2004). It is argued that the process underlying this tradeoff effect in memory is attentional narrowing (e.g., Kensinger, Gutchess, & Schacter, 2007; Kensinger et al., 2005; Wessel & Merckelbach, 1997) such that when an emotionally arousing stimulus, specifically a negative stimulus, is present (Derryberry & Tucker, 1994; see also Gable & Harmon-Jones, 2008; Harmon-Jones & Gable, 2009), attention will “narrow” like a spotlight and be focused primarily on it (Easterbrook, 1959; Posner, 1980), resulting in better encoding and subsequent
memory (e.g., Craik et al., 1996) for the central emotional object and impaired encoding and subsequent memory for the neutral objects in the periphery. In support of this, there is an abundance of literature showing that when emotionally arousing and neutral stimuli are simultaneously presented, arousing stimuli preferentially capture and sustain attention (e.g., Anderson, 2005; Anderson & Phelps, 2001; Armony & Dolan, 2002; Bradley, 1994; Calvo & Lang, 2005; E. F. Loftus et al., 1987; Nummenmaa et al., 2006; Ohman, Flykt, et al., 2001; Ohman & Mineka, 2001; Stormark, Nordby, & Hugdahl, 1995). However, whereas there is evidence showing that highly arousing and negatively valenced emotions lead to attention narrowing and that a central/peripheral tradeoff effect occurs in memory, the co-occurrence of both effects does not necessarily imply that the former mediates the latter.

Only two studies have examined the relationship between emotion-modulated attention and the central/peripheral tradeoff effect in memory within the same experiment (Christianson, Loftus, Hoffman, & Loftus, 1991; Wessel, van der Kooy, & Merckelbach, 2000). In both studies, researchers used eye movement behavior as a measure of overt attention during encoding and found evidence in support of attention narrowing, specifically, participants spent longer looking at the central details of the critical slide if it was negatively arousing than if it was neutral and less time looking at the peripheral details of the slide when it appeared in a negative context than when it appeared in a neutral context. In a subsequent test phase, both studies reported higher recall and recognition accuracy for central negative versus neutral details, but contrary to the notion that more attention results in better memory, Christianson and colleagues (1991) found that those who directed more viewing to the central aspects of the scene did not have higher recognition memory scores than those who directed less viewing. Wessel and colleagues (2000) did not directly examine the relationship between eye movement measures recorded during the encoding phase and recall memory at the test phase. However, since neither study found a difference in memory for peripheral details, it is not known whether attention narrowing results in a central/peripheral tradeoff in memory per se. As such, it is possible that the relationship between attention narrowing and the central/peripheral tradeoff in memory is not a unitary phenomenon, that is, differences in attention may mediate differences in memory for peripheral details but not central details or vice versa.

To address the extent to which the central/peripheral tradeoff effect in memory is caused by attention narrowing, we performed a mediation analysis (Baron & Kenny, 1986; MacKinnon,
Fairchild, & Fritz, 2007) to examine the relationship between overt attention, as measured by eye movement monitoring (EMM), and subsequent memory performance in a paradigm that elicited both emotion-enhanced memory for central negative pictures and emotion-impaired memory for peripheral items. A mediation analysis allowed us to examine the observed relationship between an independent (emotion) and dependent (measure of memory) variable via the inclusion of a third or mediator variable (measure of attention). The use of EMM can reveal differences in overt attention allocation and scanning patterns during encoding which reveals not only what was attended, but also how extensively it was attended.

In the present experiment, participants’ eye movements were monitored while they studied a central picture that was either neutral or negatively arousing, surrounded by three neutral everyday objects in the periphery. It is important to note that the central picture and the peripheral objects did not overlap in space or meaning (see Reisberg & Heuer, 2004). After a brief delay, memory for central pictures and peripheral objects was assessed separately in the test phase in which previously viewed and novel central pictures and previously viewed, manipulated and novel peripheral objects were presented. To the extent that the emotion-modulated central/peripheral tradeoff effect in memory is related to differences in overt attention allocation, measures of attention should mediate the relationship between emotion and memory. On the other hand, if differences in attention do not mediate the relationship between emotion and memory, then this would suggest that emotion affects memory via mechanisms other than attention. This may include direct modulation as well as indirect modulation via mechanisms such as differences in postencoding influences on memory formation.

2.3 Method

2.3.1 Participants

Twenty-four undergraduate students (mean age = 19.17 years, 3 males1 left-handed) from the University of Toronto participated for course credit. All participants had normal neurological histories and had normal or corrected-to-normal vision.

2.3.2 Stimuli and Design

The materials used to create the experimental displays consisted of 48 pictures taken from the International Affective Picture System (IAPS), of which 24 had a negative valence and 24 were
of neutral valence (Lang, Bradley, & Cuthbert, 1999) and 192 neutral objects (Hemera Photo Objects). Each display consisted of one picture in the center and three objects randomly placed in the periphery. The everyday objects were judged by the authors (LR and DM) and two independent raters to be neutral and nonarousing. All pictures chosen from the IAPS set included people. The negative pictures had a more negative valence ($t = -17.03, p < .001$) and were more arousing ($t = 14.02, p > .0001$) than the neutral pictures. The complexity of the pictures was assessed in terms of the number of bytes of the image files in JPEG format, that is, more complex images should have a larger file size (Boudo, Sarlo, & Palomba, 2002; Nummenmaa et al., 2006). We found that there were no differences between the negative and neutral set of pictures used ($t(46) = .63, p > .1$). Each display was divided equally into a 3 X 3 grid (not presented to the participants), and the central picture was always placed in the center cell with the three objects randomly placed in the periphery. The three objects in the periphery did not overlap in physical space or semantic meaning with the central element but were always distinct and not relevant to the meaning of the central scene (Burke, Heuer, & Reisberg, 1992; Reisberg & Heuer, 2004). A manipulated version was constructed for each display in which one of the three peripheral objects was replaced with a novel object. In the test blocks, the central pictures and peripheral objects were presented separately. Central pictures were either previously presented (repeated) or entirely new (novel). Peripheral objects contained the same three objects presented during the study phase (repeated), two previously studied objects, and one novel object (manipulated) or three novel objects that were not presented during the study phase (novel). Peripheral objects in the repeated and manipulated displays were presented in the same spatial location as seen during the study phase. For all displays of peripheral objects in test block, a black box was placed in the location previously occupied by the central picture so that judgments of repetition/manipulation/novelty could only be based on the peripheral objects rather than the central picture. Counterbalancing of the display occurred such that each version of the display appeared equally often in each experimental condition (repeated/novel for central pictures, repeated/manipulated/novel for peripheral objects) and paired with each emotion (negative, neutral) across participants.

2.3.3 Procedure

Eye movements were measured throughout the study and test phases with a SR Research Ltd. Eyelink 1000 eye-tracking desktop monocular system and sampled at a rate of 1000 Hz with a
spatial resolution of 0.1°. A chin rest was used to limit head movements. A 9-point calibration was performed at the start of the experiment followed by a 9-point calibration accuracy test. Calibration was repeated if the error at any point was more than 1°. Participants studied 32 randomly presented displays (16 negative, 16 neutral) once in each of two study blocks. The displays were 1024 X 768 pixels in size and subtended approximately 33.4 degrees of visual angle when seated 25” from the monitor. Consistent with previous procedures in which a central/ peripheral tradeoff was observed (e.g., Kensinger et al., 2007; Kensinger et al., 2005), each display was presented for 2 s followed by a 3-s interstimulus interval (Figure 2.1). Participants were instructed to freely view the entire display, and they were not told that there would be a subsequent memory test. After a 10-min delay (approximately) in which participants completed a background information form, participants’ memory for the peripheral objects and central pictures was assessed separately across four test blocks. The first two test blocks involved passively viewing 16 previously studied, 16 manipulated and 16 novel peripheral object displays, and 32 previously studied and 16 novel pictures. Eye movement data from this test phase is not presented in the present paper but is discussed elsewhere (Riggs et al., 2010). In the final two test blocks, the same materials were presented again following procedures as in our previous work (e.g., Ryan et al., 2000). Participants were informed that they would be seeing the last two blocks of pictures again but now they had to indicate whether a set of peripheral objects was exactly the same as during the study sessions (“repeated”), had changed in some way (“manipulated”), or had not been viewed during the study session (“novel”). In the last test

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1 In designing the present experiment, we had two aims: to explore the relationship between emotion-modulated attention and memory (current paper) and to examine whether a tradeoff in memory performance can be observed and the retrieval process outlined using eye movement monitoring (Riggs, McQuiggan, Anderson, & Ryan, 2010). Previous eye movement studies of memory have reported significant differences in viewing novel versus repeated stimuli only after multiple exposures (e.g., Althoff et al., 1998; Ryan, Hannula, et al., 2007). Therefore, since we planned to measure memory using both eye movement monitoring and verbal reports, we presented all of the stimuli twice across two study blocks and assessed memory first indirectly by eye movement monitoring and then directly via verbal reports. Indirect assessment of memory via eye movement monitoring always occurred before the direct measure of memory via verbal reports because previous eye movement studies of memory have reported memory effects in eye movement behavior during free viewing of the stimuli when participants were not explicitly instructed to perform a memory task (e.g., Ryan et al., 2000).
block, participants had to indicate whether a central picture was the same ("repeated") or different ("novel") from what they had seen during the study blocks.

Figure 2.1 Experimental procedure.

Participants viewed negative and neutral central pictures paired with 3 everyday objects; each display was randomly presented once in each of two study blocks (A). During the test for peripheral objects, the central picture was blacked out so that only the peripheral objects were visible (B). Participants freely viewed repeated (3 previously presented objects), manipulated (2 previously presented and 1 novel object) and novel (3 never previously presented objects) peripheral objects. In the test for memory of central pictures, only the central picture was visible (C). This block consisted of repeated and novel pictures.

2.3.4 Analysis

To examine the role of attention on subsequent memory, measures derived from EMM were used to quantify the amount of overt attention allocated to the central and the peripheral objects in each display. Previous research shows that during the encoding phase, it is the number of eye fixations, rather than duration of viewing, that predicts subsequent memory performance (e.g., G. R. Loftus, 1972). In the present experiment, the number of fixations was used to characterize eye movement behavior and provide an index of the amount of viewing/overt attention directed
within a particular region during the study phase. A fixation was defined as the absence of any saccade (e.g., the velocity of two successive eye movement samples exceeds 22°/s over a distance of 0.1°) or blink (e.g., pupil is missing for three or more samples) activity. Each fixation is separated by a saccade. Analysis of eye movements was performed with respect to the experimenter-drawn interest areas corresponding to the location of central picture and peripheral objects. During the test phase, evidence of memory was obtained via verbal reports of recognition. Recognition accuracy was measured as the proportion of correct responses to novel and repeated central pictures and novel, repeated, and manipulated peripheral objects. Reported hits for central pictures were corrected for false alarms. Reported hits to repeated and manipulated peripheral objects are presented uncorrected for false alarm rates, because we were interested in how processing and memory of peripheral objects are modulated by emotion, and novel peripheral objects were never paired with either emotional or neutral pictures.

To address the question of whether the central/peripheral tradeoff effect is related to the amount of overt attention at study, we performed a mediation analysis (Baron & Kenny, 1986) using a bias-corrected bootstrap method (standard Monte-Carlo algorithm) for assessment of indirect effects built into AMOS (MacKinnon, Lockwood, & Williams, 2004; Preacher & Hayes, 2004). Specifically, viewing as indexed by the number of fixations during study blocks 1 and 2 was included in the mediation analysis as a measure of overt attention. Viewing during both study blocks was included in the analysis because subsequent memory performance cannot be attributed to a single study block only. Emotion and memory for each trial were entered as binary variables with 1 representing negative pictures and 0 representing neutral pictures and with 1 representing a correct response and 0 representing an incorrect response, respectively. The degrees of freedom for the regression analysis were 24. This allowed us to determine whether the relationship between emotion and memory was (1) indirectly mediated by attention either fully or partially or (2) direct and not mediated by attention. By “direct” we mean that the path between emotion and memory remained statistically significant even after controlling for attention. A significant direct effect may be the result of the influence of emotion on memory via mechanisms other than overt attention, including direct modulation as well as other unquantified third variable factors.
2.4 Results

2.4.1 Study Blocks

The extent to which participants directed more viewing to the central picture (and, as a consequence, less viewing to the peripheral objects) when it was negative versus when it was neutral was considered to provide evidence for emotion-modulated attention narrowing. Analyses of variance (ANOVA) were conducted on the number of fixations\(^2\) directed to particular regions of interest using emotion (negative, neutral), region type (central, peripheral), and block (block 1, block 2) as within-subject factors. All possible interactions were evaluated.

Differences in viewing were evident in significant main effects for region type such that participants directed more fixations to the central pictures versus peripheral objects (F(1, 23) = 29.28, p < .0001, d = .56). The main effect of emotion was also significant; participants sampled the entire display with more fixations when the central picture was negative compared with when it was neutral (F(1, 23) = 6.64, p < .05, d = .22). A significant main effect of block was also observed (F(1,23) = 10.10, p < .01, d = .31), there was a decrease in the number of fixations across study blocks. A significant three-way interaction was found between emotion, region type, and block (F(1, 23) = 31.99, p < .0001, d = .58) (Figure 2.2), and follow-up t tests were used to explore this interaction.

\(^2\) The same pattern of results was obtained when we examined eye movement measures of duration of viewing and proportion of fixations, that is, the number of fixations directed to a particular region of interest relative to the total number of fixations directed to the entire visual display.
Participants initially directed more fixations to central scenes when they were negative compared to when they were neutral and fewer fixations to peripheral objects when they were paired with negative versus neutral central pictures. In the second study block, viewing to negative central pictures decreased, which likely resulted in a corresponding increase in viewing the associated peripheral objects.

Consistent with the attention-narrowing hypothesis, in the first study block, participants directed significantly more fixations to negative relative to neutral central pictures ($t(23) = 5.54, p < .0001$), and significantly fewer fixations to peripheral objects that were paired with negative than neutral pictures ($t(23) = -7.61, p < .0001$). During the second study block, there were no significant differences in the number of fixations directed to negative versus neutral central pictures ($t(23) = .89, p > .1$). This change of viewing across study blocks was the result of decreased fixations to negative central pictures ($t(23) = 4.03, p < .01$). There were no significant changes in the number of fixations to neutral central pictures across study blocks ($t(23) = .32, p > .1$). For peripheral objects, participants continued to direct more fixations to peripheral objects that were paired with neutral versus negative central pictures ($t(23) = -2.28, p < .05$).
In summary, the presence of an emotional central stimulus led to an initial tradeoff in attention, such that more overt attention was allocated to a negative versus a neutral central picture and less attention was allocated to peripheral objects when they were paired with negative versus a neutral central picture. Further, although this attention-narrowing effect was significantly attenuated in the second study block, there was still evidence of emotion-modulated tradeoff in attention allocation for peripheral objects. Below, we examine whether emotion also led to a tradeoff in memory as measured by verbal report.

### 2.4.2 Test Blocks

**Verbal recognition reports.** Consistent with the notion that emotion enhances memory for central details, participants were more accurate (hits minus false alarms) in identifying repeated central pictures when they were negative compared to when they were neutral ($t(23) = 2.86, p < .01$). Accuracy for repeated peripheral objects did not differ by emotionality, but participants were less accurate in identifying manipulated peripheral objects if they were previously paired with a negative central picture versus a neutral central picture ($t(23) = -2.19, p < .05$). All relevant means and standard errors are presented in Table 2.1.

#### Table 2.1. Mean responses and standard errors for peripheral objects and central pictures.

<table>
<thead>
<tr>
<th>Response Type</th>
<th>Peripheral Objects</th>
<th>Central Pictures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Neutral</td>
<td>Negative</td>
</tr>
<tr>
<td>“Novel”</td>
<td>.43 (.05)</td>
<td>.17 (.03)</td>
</tr>
<tr>
<td>“Manipulated”</td>
<td>.26 (.03)</td>
<td>.28 (.03)</td>
</tr>
<tr>
<td>“Repeated”</td>
<td>.31 (.04)</td>
<td>.55 (.04)</td>
</tr>
</tbody>
</table>

Accuracy for central pictures (corrected) was calculated as hits minus false alarms.

### 2.4.3 Mediation Analysis

In the current study, emotion-modulated tradeoffs in overt attention to central and peripheral elements as measured by EMM and tradeoffs in recognition memory for central pictures and manipulated peripheral objects were observed. However, it is not known whether the tradeoffs
in memory performance were a result of the tradeoffs in the allocation of attention. The number of fixations to central and peripheral elements was used as an index of overt attention in the mediation analysis. This allowed us to examine whether the amount of fixations to central pictures was predictive of subsequent memory for central pictures and whether the amount of fixations to peripheral objects was predictive of subsequent memory for peripheral objects.

In examining the total relationship between emotion and accuracy, a regression analysis revealed that negative emotion contributed significantly to higher accuracy for central pictures (β = .24, p < .01) and lower accuracy for manipulated peripheral objects (β = -.09, p < .05). Consistent with the behavioral results, emotion did not contribute significantly to accuracy for repeated peripheral objects (β = .004, p > .1), therefore, we did not examine this relationship further. In examining the relationship between emotion and attention, it was found that emotion was associated with enhanced sampling, that is, more fixations of central pictures (β = .14, p < .05) and decreased sampling of manipulated peripheral objects (β = -.09, p < .05).

Having established a significant relationship between emotion and memory performance, it was critical to ascertain whether this relationship was fully, partially, or not at all mediated by attention. To do this, we conducted mediation analyses separately for central pictures and manipulated peripheral objects. For central pictures, the indirect path between emotion and memory, with attention as a mediator, was significant (path a * path b: β = .02, p < .05) (Figure 2.3), suggesting that attention may mediate the relationship between emotion and memory. However, it was also found that even when attention was fixed, the direct path (path c) between emotion and accuracy remained significant (β = .23, p < .05). In other words, attention only partially mediated emotion-enhanced recognition memory for central pictures. For manipulated peripheral objects, the indirect path was not statistically significant (β = -.0004, p > .1), and the direct path between emotion and accuracy for manipulated peripheral objects remained significant even when the variable of attention was fixed (β = -.09, p < .05). Thus, the results

3 A potential concern with using the raw number of fixations as an overt measure of attention is that there may be significant between-subjects variance in the total of fixations directed. One way to control for these individual differences is to use the measure of proportion of fixations. When we performed the mediation analysis using the proportion of fixations as the measure of overt attention, the same pattern emerged as was found using number of fixations.
suggest that although emotion led to decreased viewing of peripheral objects, these changes did not play a significant role in reducing one’s ability to identify changes in the periphery.

Figure 2.3 A mediation model with emotion, attention (number of fixations) and memory.

In summary, emotion led to tradeoffs in attention. Participants directed more overt attention to negative versus neutral central pictures and less attention to peripheral objects paired with negative versus neutral central pictures. Emotion also led to a central/peripheral tradeoff effect in memory. Recognition was more accurate for negative versus neutral central pictures and less accurate for manipulated peripheral objects previously paired with negative versus neutral central pictures. However, the mediation analysis revealed that differences in emotion-modulated memory, especially memories of the details in the periphery, cannot fully be explained by differences in attention allocation during the encoding phase. Rather, the current analysis suggests that factors other than overt attention may mediate the relationship between emotion and the central/peripheral tradeoff effect.

2.5 Discussion

The presence of emotional stimuli has typically resulted in a central/peripheral tradeoff effect in memory. It has been suggested that these memory differences are the result of attention
narrowing during encoding (e.g., Kensinger et al., 2007; Kensinger et al., 2005; Wessel & Merckelbach, 1997). However, the relationship between attention narrowing and the central/peripheral tradeoff effect in memory has not been directly examined in a study where emotion was found to modulate memory for both central and peripheral items. In the current study, it was found that consistent with previous research, emotion enhanced attention toward, and memory for, centrally placed pictures. Specifically, participants directed more attention to, and were more accurate in identifying, repeated negative versus neutral central pictures. Emotion also led to decreased attention to objects in the periphery and less accurate memory for identifying manipulations in the periphery that were both spatially and conceptually distinct from the central picture. The present work addressed whether attention narrowing was related to the central/peripheral tradeoff in memory through mediation analysis. The results here revealed that differences in overt attention during the study phase cannot fully account for subsequent memory performance. Specifically, although attention mediated some of emotion’s effects on memory, it did not mediate the entire relationship. This suggests that cognitive mechanisms other than attention are involved in modulating the relationship between emotion and the central/peripheral tradeoff effect in memory. In the next sections, we discuss our results in light of previous findings regarding the central peripheral tradeoff in attention and memory and how the current work may inform theories regarding the influence of emotion on attention and memory.

2.5.1 Attention Narrowing

The preferential allocation of attention toward emotional stimuli is typically regarded as an adaptive function allowing one to prioritize the detection and processing of potentially threatening and/or important information (Whalen et al., 1998). Consistent with this notion, here, participants directed more viewing to the central picture and less viewing to the surrounding peripheral objects when the central picture was negative compared to when it was neutral. This attention-narrowing effect occurred despite the fact that participants were instructed to freely view the presented displays. This supports the hypothesis that emotional pictures engage more attention (e.g., Calvo & Lang, 2005; Nummenmaa et al., 2006) and leads to attention narrowing (Easterbrook, 1959), in particular for negatively valenced events (Schmitz, De Rosa, & Anderson, 2009). These findings are also consistent with previous studies showing that when emotional and neutral stimuli are presented simultaneously, attention is biased toward the emotional stimuli (e.g., Calvo & Lang, 2004; Christianson et al., 1991;
Nummenmaa et al., 2006; Wessel et al., 2000). In the present study, this attention-narrowing effect was present during the first study block but was mitigated in the second study block. This suggests that whereas negatively arousing pictures may attract increased amounts of overt attention initially, this response may habituate upon subsequent presentations, leaving participants more time and resources for the processing of peripheral objects (Harris & Pashler, 2004; Nummenmaa et al., 2006). Further, it has also been shown that participants direct less viewing to repeated versus novel stimuli (e.g., Althoff & Cohen, 1999; Althoff et al., 1998; Ryan et al., 2000; Ryan, Hannula, et al., 2007). Thus, the decrease in viewing to negative, but not neutral, central scenes across the study blocks may reflect the influence of more detailed and/or stable memory representations on viewing behavior. In other words, the results may suggest more efficient memory encoding of negative pictures during initial presentation. All together, a significant emotion-modulated attention-narrowing effect was observed that dissipated after the first presentation of the displays, suggesting rapid formation of stable memory representations and thus rapid habituation of emotional capture of overt attention.

2.5.2 Central/Peripheral Tradeoff in Memory and Attention

Consistent with the eye movement data from the study phase, recognition accuracy from the test phase showed that memory for central negative pictures was more accurate than memory for central neutral pictures, and memory for manipulated peripheral objects was less accurate for those that were previously paired with negative versus neutral pictures (e.g., J. M. Brown, 2003; Kensinger et al., 2005; Pickel, French, & Betts, 2003; Wessel & Merckelbach, 1997). However, compared to previous studies (e.g., Kensinger et al., 2007; Kensinger et al., 2005), we observed that accuracy for recognizing novel central pictures was relatively lower than expected. This is likely a result of the fact that when participants had to make an explicit judgment regarding whether the central pictures were novel or previously presented, all of the test stimuli had already been presented during the eye movement test phase. Therefore, participants had to make relative novelty judgments. Further, contrary to previous studies (e.g., Kensinger et al., 2007; Kensinger et al., 2005), no emotion-modulated effects were observed for recognition of repeated peripheral objects. One important methodological difference is that whereas previous studies have presented the stimuli once during the encoding phase (e.g., Christianson, 1992; Kensinger et al., 2007; Kensinger et al., 2005; E. F. Loftus & Christianson, 1989), we presented the stimuli twice over two study blocks. Thus, it is possible that by repeating the stimuli, the central/peripheral
tradeoff effect in memory was not as robust as it would have been had the stimuli only been presented once. Therefore, an emotion-modulated effect in the repeated peripheral objects did not manifest. There is some indication in the literature that the central/peripheral tradeoff effect in memory is sensitive to methodological parameters such as the duration of exposure to the stimuli, specificity of the information interrogated during the test phase, and the length of time between encoding and retrieval (e.g., Burke et al., 1992; Christianson, 1992; Steblay, 1992). However, despite having presented the stimuli twice during the study blocks, we still observed an influence of emotion on the memory for the manipulated peripheral objects. The correct identification of manipulated peripheral objects may require a more detailed memory representation than the correct identification of repeated objects. This increase in difficulty was reflected in the lower accuracy of the verbal report data. Thus, the current results suggest that emotion may predominantly impact memory for the specific details in the periphery (Adolphs et al., 2001; Adolphs, Tranel, et al., 2005; Denburg, Buchanan, Tranel, & Adolphs, 2003).

Contrary to the attention-narrowing hypothesis (e.g., Easterbrook, 1959; Kensinger et al., 2007; Kensinger et al., 2005; Wessel & Merckelbach, 1997), the amount of overt attention (i.e., eye movements) directed to central pictures versus peripheral objects did not fully account for the subsequent central/peripheral tradeoff seen in memory. Specifically, through mediation analysis, it was found that even when differences in overt attention to central pictures were fixed, the relationship between emotion and recognition memory remained significant. Further, even though the presence of negative central pictures led to decreased attention directed to peripheral objects, this change in attention allocation was not significantly related to the memory impairment observed. One possibility is that because very little attention was directed toward the peripheral objects during the encoding phase, emotion-modulated differences in attention were not large enough to affect subsequent memory performance. Another possibility is that because participants viewed all stimuli twice across two study blocks, this may have attenuated the effects of emotion-modulated attention on subsequent memory. However, despite viewing the stimuli twice, participants continued to direct fewer fixations to objects paired with negative central pictures than those paired with neutral pictures.

Taken together, the current results suggest that the presence of emotion enhanced memory for central emotional information via overt attention and additional mechanisms. Further, it was also found that emotion impaired memory for neutral information in the periphery via
mechanisms other than overt attention. Given that the attention-narrowing account does not fully explain the central/peripheral tradeoff observed, below, we consider some alternate mechanisms.

2.5.3 Mechanisms Underlying Emotion-Enhanced Memory

One factor that has often been invoked to explain emotion-modulated memory is the factor of distinctiveness. It has been shown that when an item is relatively distinct from its surroundings (e.g., unique features, location, color, etc.), memory for that item is enhanced, likely at the expense of memory for other items (Schmidt, 1991; Talmi, Schimmack, Paterson, & Moscovitch, 2007). However, previous studies that controlled for distinctiveness still found a significant effect of emotion above and beyond distinctiveness (Anderson, 2005; Anderson et al., 2006). In other studies, it has been shown that memory for central and peripheral details of unusual pictures did not differ and resembled that of neutral pictures (Christianson et al., 1991; Wessel et al., 2000). Here, distinctiveness is unlikely to account for the emotion-modulated differences in recognition of peripheral objects because those were counterbalanced across emotional conditions. However, because the central pictures were not counterbalanced across emotional conditions, it is possible that differences in the distinctiveness of negative versus neutral pictures contributed to not only memory for central pictures but also the peripheral objects with which they were presented.

In addition to distinctiveness, another mechanism that may underlie the emotion-modulated central/peripheral tradeoff effect is the amount of covert attention allocated, which can be decoupled from overt attention as measured by EMM (e.g., Posner, 1980; Rowe et al., 2007). However, although eye fixations and attention can be dissociated under explicit instructions, they are closely related in real world situations, because a covert shift of visual attention is reliably and quickly followed by an overt gaze shift to the attended spatial location (Findlay & Gilchrist, 2003; Hoffman, 1998; Reichle, Pollatsek, Fisher, & Rayner, 1998). Despite this, it is unknown whether emotion would impact the correlation between overt and covert attention, and any contributions from the covert allocation of attention cannot be ruled out as a factor underlying the emotion-modulated central/peripheral tradeoff in memory.

Another possible mechanism underlying the central/peripheral tradeoff may be the direct modulation of memory processes through emotional arousal. Hadley and MacKay (Hadley & Mackay, 2006) have proposed that emotional arousal may act as a “glue” that preferentially
binds features within an emotional item, as well as between the emotional item and its experimental context (e.g., information regarding when and where the experiment occurred), thereby facilitating the subsequent retrieval of the emotional item. At the same time, this binding of the emotional item interrupts the encoding of surrounding nonemotional items, making the nonemotional items more difficult to retrieve later (Miu, Heilman, Opre, & Miclea, 2005; Most, Chun, Widders, & Zald, 2005). On this view, the central/peripheral tradeoff effect occurs because participants preferentially encode elements within the central negative picture that interfere with the encoding of the surrounding peripheral objects. Although the theory by Hadley and MacKay refers specifically to rapidly presented stimuli (<200 ms), there is some evidence to suggest that even at longer presentation times, there are qualitative differences between the encoding of negative versus neutral stimuli (e.g., Kensinger, Garoff-eaton, & Schacter, 2006; Takahashi, Itsukushima, & Okabe, 2006). In the present experiment, central negative pictures may have received prioritized processing, increased perceptual processing (Anderson & Phelps, 2001; Lim, Padmala, & Pessoa, 2009), deeper semantic processing, and/or poststimulus elaboration, leading to the disruption of the processing of the peripheral objects. In other words, when it comes to memory, it is not necessarily how long one spends viewing an item, but rather how one processes it (e.g., Craik, 2002). Thus, even when participants were attending to the peripheral objects, they may have still been elaborating and/or rehearsing information associated with the negative central picture. This may also explain why overt attention during the study phase was not a significant mediating factor for memory of manipulated peripheral objects.

Consistent with the idea that there are qualitative differences in encoding emotional and neutral information, research shows that special neural and hormonal processes exist to enhance emotional, but not neutral, memories. For example, results from human and nonhuman animal studies (Cahill & McGaugh, 1998) reveal amygdala activation is significantly correlated with subsequent memory performance (e.g., Dolcos, LaBar, & Cabeza, 2004; Kensinger & Corkin, 2004b; Packard & Cahill, 2001; Talmi et al., 2008). Critically, the amygdala may mediate enhanced processing of emotional information that is separate from any increases in attention (Anderson & Phelps, 2001). In addition, given the amygdala’s critical role in post encoding modulation of memory consolidation (Adolphs, Tranel, & Denburg, 2000; Cahill & McGaugh, 1998; McGaugh, 2000), and in mediating the central-peripheral tradeoff (Adolphs et al., 2001;
Adolphs, Tranel, et al., 2005), it is possible that amygdalar modulatory influences during consolidation may also play a role. Further, consistent with the notion that the central/peripheral tradeoff effect in memory cannot be fully explained by emotion-modulated differences in attention during encoding, Payne and colleagues (Payne, Stickgold, Swanberg, & Kensinger, 2008) found that after a 12-hr sleep period, the central/peripheral tradeoff effect was even more pronounced than it was when memory was tested immediately or after a 12-hr wake period, because sleep led to a preservation of central emotional details within a scene and decay of peripheral details within a negative scene and all aspects of neutral scenes. In view of this, it is possible that results from the current study would have been even more robust after a 12-hr sleep period than they were at immediate testing.

Taken together, the present results suggest that, contrary to some previous assumptions, the central/peripheral tradeoff effect in memory is not entirely a result of differences in overt attention allocation. Rather, this memory effect may be related to altered covert attention, and/or may be the result of the direct influence of emotion on memory processes through cognitive mechanisms such as depth of processing, and/or specialized neuromodulatory mechanisms such as the direct modulation of the amygdala on medial temporal regions, leading to enhanced processing of emotionally arousing items at the cost of impaired processing of surrounding peripheral objects; these accounts remain to be tested in future research. Attention and memory may be independent processes to the extent that the amount of overt attention directed to an item may not predict subsequent memory performance. This may allow emotion to enhance memory for significant stimuli even when there is limited time or attentional resources to devote to the encoding of such stimuli.

2.5.4 Limitations and Future Directions

In addition to examining how emotion may modulate memory via cognitive and specialized neuromodulatory mechanisms, it may also be important to examine the relationship between emotion, attention, and memory under more “real-life” circumstances. The stimuli used in the present experiment delineated between central and peripheral details both spatially and conceptually. However, this may be less ecologically valid than previous studies that have examined central and peripheral details within one cohesive scene. Although it is possible that the central/peripheral tradeoff effect in attention and memory reported in the current study was
more exaggerated than in previous studies given that the peripheral details were clearly irrelevant for the understanding of the central details, this is unlikely because we did not find evidence of emotion-impaired memory for repeated peripheral objects as reported in previous work (e.g., Kensinger et al., 2007; Kensinger et al., 2005). Thus, although the findings here suggest that differences in overt attention during the encoding phase do not fully explain emotion-impaired memory for specific details in the periphery that are spatially distinct and conceptually unrelated to the central details, future studies could explore whether this is also true for central and peripheral details within a cohesive and more ecologically valid paradigm.

In the present study, IAPS pictures were used to elicit negative emotion. However, rather than depicting the range of negative emotions (e.g., anger, fear, disgust), the negative pictures from IAPS are mostly associated with fear and disgust. Studies show that not only may different negative emotions result in different degrees of memory impairment for peripheral details (Talarico, Berntsen, & Rubin, 2009), but there are different viewing patterns and perhaps different cognitive processes engaged when viewing faces depicting anger, fear, and disgust (e.g., Aviezer et al., 2008; Lerner, Gonzalez, Small, & Fischhoff, 2003; Susskind et al., 2008). In a similar vein, there may be differences in viewing patterns to stimuli that elicit different emotions (e.g., fear, disgust, anger) in the viewer. For example, although disgust is associated with sensory rejection, fear is associated with enhanced sensory acquisition (Susskind et al., 2008). Thus, fear may result in a stronger central/peripheral tradeoff effect in attention and/or memory than disgust. In view of this, it would be important for future studies to explore how these discrete negative emotions may differentially affect attention, memory, and the relationship between attention and memory.

2.6 Acknowledgments

We thank Ella Pan for her assistance. This work was supported by funding to JDR from Natural Sciences and Engineering Research Council of Canada (NSERC), Canada Research Chairs Program, and Canadian Foundation for Innovation (CRC/CFI), to AKA from NSERC, and a postgraduate scholarship to LR from NSERC.
Chapter 3
Eye Movement Monitoring Revealed Differential Influences of Emotion on Memory


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Eye movement reveals differential influences of emotion on memory

2.7 Abstract

Research shows that memory for emotional aspects of an event may be enhanced at the cost of impaired memory for surrounding peripheral details. However, this has only been assessed directly via verbal reports which reveal the outcome of a long stream of processing but cannot shed light on how/when emotion may affect the retrieval process. In the present experiment, eye movement monitoring (EMM) was used as an indirect measure of memory as it can reveal aspects of online memory processing. For example, do emotions modulate the nature of memory representations or the speed with which such memories can be accessed? Participants viewed central negative and neutral scenes surrounded by three neutral objects and after a brief delay, memory was assessed indirectly via EMM and then directly via verbal reports. Consistent with the previous literature, emotion enhanced central and impaired peripheral memory as indexed by eye movement scanning and verbal reports. This suggests that eye movement scanning may contribute and/or is related to conscious access of memory. However, the central/peripheral tradeoff effect was not observed in an early measure of eye movement behavior, i.e., participants were faster to orient to a critical region of change in the periphery irrespective of whether it was previously studied in a negative or neutral context. These findings demonstrate emotion’s differential influences on different aspects of retrieval. In particular, emotion appears to affect the detail within, and/or the evaluation of, stored memory representations, but it may not affect the initial access to those representations.

2.8 Introduction

For years, researchers have noted that emotionally arousing events are remembered better than neutral events (Cahill & McGaugh, 1998). However, emotion-enhanced memory does not always extend to all aspects of an event. Rather, emotion, or specifically negative emotion, may result in a central/peripheral tradeoff effect in memory: memory for central, emotional aspects of an event is enhanced, and memory for peripheral, non-emotional aspects of an event is impaired (for review, see Levine & Edelstein, 2009; Steblay, 1992). In other words, emotion affects the nature of one’s memory representations for how a particular scene/event is remembered. While
there are many studies showing the influence of emotion during encoding and consolidation (e.g., Cahill & McGaugh, 1998), it is unclear which aspects of retrieval are modulated by emotion. For example, in addition to the quality and/or the amount of details that are stored in memory, emotion may also affect the ease or speed at which such memories can be accessed and, further, whether such representations are subsequently available for conscious introspection.

Evidence in support of the central/peripheral tradeoff effect in memory has been derived exclusively from verbal reports (e.g., Christianson, 1992; Kensinger et al., 2007; Kensinger et al., 2005; E. F. Loftus, 1979; E. F. Loftus et al., 1987; Reisberg & Heuer, 2004), which provides a direct measure of the end product of a long stream of memory processing, but it cannot reveal processing differences online. Previous studies show that online indices of memory, such as those garnered by eye movement monitoring (EMM), do not necessarily correspond to verbal reports memory (e.g., Laloyaux, Devue, Doyen, David, & Cleeremans, 2008; Ryan et al., 2000; Ryan & Cohen, 2004; Thornton & Fernandez-Duque, 2000; Thornton & Fernandez-Duque, 2002). Further, retrieval may occur in stages, therefore it may be useful to have a measure of memory that can evaluate retrieval throughout the process. The first stage of retrieval may reflect initial access to stored representations in memory. We have previously argued that access to memory representations occurs very early (within the first few fixations) and in an obligatory fashion, such that it is not affected by changes in task demands (e.g., Althoff & Cohen, 1999; Ryan, Hannula, et al., 2007). Subsequent stages of retrieval may reflect a more evaluative process that depend critically on the quality of stored memory representation; this evaluative process allows for repetition and/or changes in the environment to be detected and may ultimately result in conscious access of the information (e.g., Hannula, Ryan, Tranel, & Cohen, 2007; Ryan & Cohen, 2004; Ryan, Hannula, et al., 2007). On this view, emotion-impaired memory for peripheral information may be the result of difficulties in the initial access of memory, and/or differences in the amount of detail contained within those representations that are retrieved (e.g., Adolphs et al., 2001; Adolphs, Tranel, et al., 2005; Denburg et al., 2003). This would contribute to a more comprehensive understanding of how malleable the processes related to memory retrieval are, and how extensively emotion may influence memory, i.e., does it modulate seemingly “obligatory” processes during retrieval in the same manner as processes that are considered more evaluative?
In order to gain a more comprehensive understanding of the effect of emotion on memory, we employed measures derived from EMM as well as verbal reports to characterize retrieval processing differences as a function of emotion. In contrast to verbal reports, EMM can reveal aspects of mnemonic processing such as what aspects of a scene were subsequently remembered, and when this information was retrieved. Specifically, previous studies show that even when participants were not cued or instructed to make recognition memory judgments, the rate of overall sampling decreased for repeated versus novel scenes (repetition effect); and further, sampling increased for critical regions within a scene that had undergone a change in manipulated scenes compared to unchanged regions of repeated scenes (manipulation effect; e.g., Ryan et al., 2000; Ryan & Cohen, 2004). This shows that eye movement scanning behavior can be altered by prior experience, and by outlining where eye movements are attracted to within a scene that has undergone a change, it can reveal how detailed the memory representation is.

Further, differences in eye movement behavior due to prior experience have been found to occur very early during processing (Althoff & Cohen, 1999; Ryan, Hannula, et al., 2007; Ryan, Leung, Turk-Browne, & Hasher, 2007) and in advance of explicit responding (Hannula et al., 2007), suggesting that EMM can reveal the time at which memories are initially accessed. Additionally, eye movement indices of memory may reveal that information has been retained in memory that is unavailable for conscious introspection (e.g., Althoff & Cohen, 1999; Althoff et al., 1998; Hollingworth & Henderson, 2002; Hollingworth, Williams, & Henderson, 2001; Laloyaux et al., 2008; Ryan et al., 2000; Ryan & Cohen, 2004; Thornton & Fernandez-Duque, 2000; Thornton & Fernandez-Duque, 2002).

To address how emotion may affect the nature of, and access to memory representations for the central emotional and peripheral neutral information, we adapted an experimental paradigm which has been shown to elicit the central/peripheral tradeoff effect in memory when measured via verbal reports (Kensinger et al., 2007). During the study phase, participants studied a central picture that was either neutral or negatively arousing surrounded by three neutral everyday objects. After a brief delay, memory for central pictures and peripheral objects was assessed separately in the test phase in which previously viewed and novel central pictures, and previously viewed, manipulated, and novel peripheral objects were presented. Here, memory for the central pictures and peripheral objects was indexed by verbal reports and through changes in eye movement patterns as a function of prior exposure. Since the aim of the current study was to
examine how emotion may affect what is retrieved from memory and when, we focus only on the results obtained during the retrieval phase of the experiment.

As shown in previous studies, evidence of a central/peripheral tradeoff in memory would be indexed by: (1) more accurate recognition, as measured via verbal reports, in identifying previously viewed negative versus neutral central pictures, and (2) conversely, more accurate recognition of peripheral objects that had been previously paired with neutral versus negative central pictures. Further, if emotion leads to retrieval advantages for the central negative versus neutral pictures, this would lead to a larger repetition effect (overall sampling decreases for previously viewed versus novel scenes) for central negative pictures. On the other hand, if emotion leads to retrieval disadvantages for the surrounding neutral information due to difficulties in access and/or less detailed memory representations, this would be manifested as: (1) faster orienting to a region of change among the peripheral objects previously paired with a neutral versus negative picture and/or (2) increased viewing of manipulated versus repeated peripheral objects (manipulation effect) previously paired with neutral, but not negative pictures, respectively.

2.9 Materials and Methods

2.9.1 Participants

Twenty-four undergraduate students (mean age = 19.17 years, three males; one left-handed) from the University of Toronto participated for course credit. All participants had normal neurological histories and normal or corrected-to-normal vision.

2.9.2 Stimuli and Design

The materials used to create the experimental displays consisted of 48 pictures taken from the International Affective Picture System (IAPS), of which 24 had a negative valence and 24 were of neutral valence (Lang et al., 1999), and 192 neutral objects (Hemera Photo Objects). The everyday objects were judged by the authors (Lily Riggs and Douglas A. McQuiggan) and two independent raters to be neutral and non-arousing. All pictures chosen from the IAPS set included people. The negative pictures had a more negative valence \( (t = -17.03, p < 0.001) \) and were more arousing \( (t = 14.02, p < 0.0001) \) than the neutral pictures. Each display consisted of one picture in the center and three objects randomly placed in the periphery, which did not
overlap in physical space or semantic meaning with the central element, but were always distinct and not relevant to the meaning of the central scene. A manipulated version was constructed for each display in which one of the three peripheral objects was replaced with a novel object. Each set of peripheral objects was counterbalanced across participants such that it was presented as paired with negative and neutral pictures equally. In the test block, the central pictures and peripheral objects were presented separately. Central pictures were either previously presented (repeated) or entirely new (novel). Peripheral objects contained the same three objects presented during the study phase (repeated), two previously studied objects and 1 novel object (manipulated) or three novel objects that were not presented during the study phase (novel). For all displays of peripheral objects in test block, a black box was placed in the location previously occupied by the central picture so that judgments of novelty/repetition could only be based on the peripheral objects rather than the central picture. Counterbalancing of the display occurred such that each version of the display appeared equally often in each experimental condition (repeated/novel for central pictures; repeated/manipulated/novel for peripheral objects) across participants.

2.9.3 Procedure

Eye movements were measured throughout the study and test phases with a SR Research Ltd. Eyelink 1000 eye-tracking desktop monocular system and sampled at a rate of 1000 Hz with a spatial resolution 0.1°. A chin rest was used to limit head movements. A nine-point calibration was performed at the start of the experiment followed by a nine-point calibration accuracy test. Calibration was repeated if the average gaze error was greater than 1° and if the error at any single point was more than 1.5°. Participants studied 32 randomly presented displays (16 negative, 16 neutral) once in each of two study blocks. The stimuli were repeated across two study blocks because previous EMM studies have shown that significant differences in viewing novel versus repeated stimuli manifested only after multiple exposures in which the trial duration was longer than in the current work (Althoff & Cohen, 1999; Ryan et al., 2000; Ryan, Leung, et al., 2007). The displays were 1024 × 768 pixels in size and subtended approximately 33.4° of visual angle when seated 25 inches from the monitor. Each display was presented for 2 s (e.g., Kensinger et al., 2007; Kensinger et al., 2005) followed by a 3-s inter-stimulus interval. Participants were instructed to freely view the scene. After a 10-min delay (approximately) in which participants completed a background information form, participants’ memory for the
peripheral objects and central pictures was assessed separately across four test blocks. Further, during the study phase, the stimuli were repeated across two blocks because previous EMM studies have shown that significant differences in viewing novel versus repeated stimuli manifested only after multiple exposures in which the trial duration was longer than in the current work (e.g., Althoff & Cohen, 1999; Ryan et al., 2000; Ryan, Leung, et al., 2007). Test blocks using indirect measures of memory were always assessed first, followed by test blocks that elicited direct verbal reports of memory. This was done in an effort to reduce the effect of verbal reports on eye movement responses (Ryan et al., 2000; Yarbus, 1967). To indirectly assess memory for the peripheral objects, participants were shown 16 previously studied, 16 manipulated, and central pictures was assessed indirectly via EMM by presenting 32 previously studied and 16 novel pictures and asking participants subjects to engage in free viewing while eye movements were monitored (Figure 2.1). Memory for the central pictures was assessed indirectly via EMM by presenting 32 previously studied and 16 novel pictures and asking participants subjects to engage in free viewing. The same materials presented during the EMM test phase were repeated during the verbal response test phase. During the verbal response test blocks, participants were informed that they would be seeing the last two blocks of pictures again. In the first test block, participants had to indicate whether a set of peripheral objects was exactly the same as during the study sessions (“old”), had changed in some way (“manipulated”) or was completely novel (“new”). In the second test block, participants had to indicate whether a central picture was the same (old) or different (new) from what they had seen during the study blocks.

2.9.4  Analysis

Eye movements were measured during the study and test phase. From the test phase, our analyses focused on the results from the repeated and manipulated peripheral objects as they were a direct test of emotional influences on memory (Kensinger et al., 2007). Analysis of eye movements was performed with respect to the experimenter-drawn interest areas corresponding to the location of central picture and peripheral objects. Eye movement measures of interest included the time of first fixation and the number of fixations into a region of interest. A fixation is defined as the absence of any saccade (e.g., the velocity of two successive eye movement samples exceeds 22°/s over a distance of 0.1°), or blink (e.g., pupil is missing for three or more samples) activity. The time of first fixation indicates how quickly overt attention was directed to
a particular region of interest and provides an index of how quickly memory representations are accessed. The number of fixations indicates the amount of viewing directed within a particular region and provides a measure of the detail contained within the memory representation. Both EMM measures of time of first fixation and number of fixations provide an indirect measure of memory, as these measures can be collected without having participants simultaneously comment on the contents of their memories.

Evidence of memory during the test phase for the central pictures would be revealed as a decrease in the sampling of previously presented versus novel pictures (e.g., Althoff & Cohen, 1999; Althoff et al., 1998; Ryan et al., 2000). It is important to note that for central pictures, we examined eye movement differences between novel and repeated negative pictures and eye movement differences between novel and repeated neutral pictures. In other words, evidence of memory is manifested as changes in viewing between novel and previously viewed pictures, and not between negative and neutral pictures. Since participants always began each trial fixated in the center of the screen and the central region was the only filled region present on the screen, we examined only the number of fixations for central pictures. For the peripheral objects, a comparison of repeated versus novel/manipulated peripheral objects provided evidence for the time at which memory representations may be accessed and the quality of those stored representations (e.g., Ryan & Cohen, 2004). This was examined as a proportion of difference in viewing the critical object in repeated and manipulated arrays with reference to viewing of the critical object in novel arrays as a baseline. The critical object in novel object arrays was never associated with a neutral or negative central picture and served as a baseline to correct for individual differences in viewing. Evidence of impaired access to peripheral objects as a result of emotion would be manifested by slower orienting to the critical object (the novel object among two repeated objects) in manipulated displays versus the exact same “critical” object in repeated displays which had not undergone a change, for peripheral objects that had been paired with negative versus neutral pictures. Evidence of a less detailed memory representation as a result of emotion would be manifested by a lack of difference in the number of fixations directed to the critical object in manipulated versus repeated displays for those peripheral objects that had been paired with a negative, but not neutral, picture. In order to control for stimulus specific effects, the critical object appeared as a novel object within a manipulated display, as a repeated object within a repeated display, and as a novel object within a novel display across participants.
Additionally, the presentation of central pictures as novel or previously viewed was counterbalanced across participants, thus any differences in viewing was the result of the participants’ prior viewing history (Ryan et al., 2000; Ryan, Leung, et al., 2007).

Recognition accuracy was measured as the proportion of correct responses to novel and repeated central pictures, and novel, repeated and manipulated peripheral objects. Reported hits for central pictures were corrected for false alarms. Reported hits to repeated and manipulated peripheral objects are presented uncorrected for false alarm rates as novel peripheral objects were not presented with emotional/neutral images.

2.10 Results

2.10.1 Central Pictures

2.10.1.1 Eye movement measures

Eye movements were analyzed with respect to the interest area corresponding to the location of the central picture. The raw means and standard errors for the number of fixations made to the central pictures are presented in Table 3.1. Differences in the number of fixations directed to novel versus repeated pictures were calculated using novel pictures as the baseline. We then used paired-sample t-tests to determine whether this difference in viewing was significantly different from 0 and modulated by emotion (negative versus neutral). Consistent with the notion that emotion enhances memory, differences in viewing novel versus repeated pictures was significantly different from 0 when the pictures were negative ($t(23) = 3.01, p < 0.01$), but not when they were neutral ($t(23) = 1.38, p = 0.18$). Specifically, participants directed fewer fixations to repeated versus novel pictures only when they were negative. A direct comparison of viewing of negative and neutral central pictures was not significant ($t(23) = 0.37, p = 0.72$).
Table 0.1 Means and standard errors for eye movement measures for viewing of the critical object in the periphery and central scenes during test session.

<table>
<thead>
<tr>
<th>Measures</th>
<th>Critical Peripheral Object</th>
<th>Central Pictures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Neutral</td>
<td>Novel</td>
</tr>
<tr>
<td>Time of first fixation (ms):</td>
<td>895.25 (44.18)</td>
<td>800.83 (49.07)</td>
</tr>
<tr>
<td>Number of fixations (#):</td>
<td>2.06 (.09)</td>
<td>2.25 (0.14)</td>
</tr>
</tbody>
</table>

Central Pictures

<table>
<thead>
<tr>
<th></th>
<th>Neutral</th>
<th>Repeated</th>
<th>Novel</th>
<th>Repeated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of fixations (#):</td>
<td>6.68 (.21)</td>
<td>6.45 (.23)</td>
<td>7.39 (.28)</td>
<td>6.94 (.25)</td>
</tr>
</tbody>
</table>

2.10.1.2 Verbal recognition reports

Verbal recognition for the central pictures was analyzed using a paired-sample t-test examining accuracy for repeated negative and neutral pictures. When hit rates were corrected by false alarms, participants were more accurate in identifying repeated pictures when they were negative versus when they were neutral (t(23) = 2.86, p < 0.01). All relevant means and standard errors are presented in Table 3.2.

Table 0.2 Mean responses and standard errors for peripheral objects and central pictures.

<table>
<thead>
<tr>
<th></th>
<th>Peripheral Objects</th>
<th>Central Pictures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Neutral</td>
<td>Negative</td>
</tr>
<tr>
<td></td>
<td>Novel</td>
<td>Manipulated</td>
</tr>
<tr>
<td>Accuracy (SEM)</td>
<td>.43 (.05)</td>
<td>.28 (.03)</td>
</tr>
</tbody>
</table>

Central Pictures

|                                 | Neutral | Repeated | Repeated (Corrected) | Negative |
|                                 | Novel   | Repeated | Repeated (Corrected) |
| Accuracy (SEM)                  | .64 (.07) | .74 (.04) | .56 (.03) | .54 (.08) | .92 (.02) | .69 (.04) |

In summary, when memory was measured indirectly via EMM at the test phase, eye movement patterns distinguished between repeated and novel pictures when they were negative, but not when they were neutral pictures. Consistent with this, emotion was also found to enhance recognition memory for repeated central pictures when measured directly via verbal reports.
2.10.2 Peripheral Objects

2.10.2.1 Eye movement measures

Eye movements were analyzed with respect to the interest area corresponding to the location of the critical object which was the novel object among two repeated objects in the manipulated arrays and the corresponding object in the repeated and novel object arrays. Proportion of difference in viewing of the critical object between manipulated and repeated displays relative to novel displays reveals the extent to which information regarding the peripheral objects was retained in memory (Ryan et al., 2000; Ryan & Cohen, 2004).

Eye movement measures to the critical object were analyzed using separate 2 × 2 repeated measures ANOVA using emotion (negative, neutral) and object array type (manipulated, repeated) as within-subject factors. All relevant raw means and standard errors are presented in Table 3.1. Consistent with the notion that EMM measures are sensitive to prior experience, there was a significant main effect of object array type (both measures: $F(1,23) = 7.47, p = 0.01, d = 0.25$). Participants were faster to fixate, and directed more viewing to the critical object when it appeared in a manipulated versus a repeated display, regardless of whether that set of peripheral objects had been previously paired with a negative or neutral central picture. The main effect of emotion on eye movement behavior was not significant (time of first fixation: $F(1,23) = 0.16, p = 0.69, d = 0.01$ number of fixations: $F(1,23) = 0.11, p = 0.75, d = 0.004$). There was a significant interaction for the number of fixations ($F(1,23) = 4.11, p = 0.05, d = 0.15$; Figure 3.2); participants directed more fixations to the critical object when it appeared in a manipulated compared to a repeated array if the objects had been previously paired with a neutral central picture ($t(23) = 2.94, p = 0.007$), but not when it had been paired with a negative central picture ($t(23) = 1.23, p = 0.23$). The interaction between emotion and type was not significant for the time of first fixation ($F(1,23) = 0.58, p = 0.46, d = 0.02$), suggesting that while emotion affected the overall quality (i.e., number of fixations) of memory for peripheral objects, it did not affect access to, and early indicators of, memory for detecting which peripheral object had been altered, which occurred approximately 800 ms following stimulus onset.4

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4 It should be noted that the same pattern of results was found when we examined the raw values resulting from the EMM measures.
Participants directed more fixations to the critical object in manipulated versus repeated object arrays for objects previously encoded in a neutral, but not in a negative context.

2.10.2.2 Verbal recognition reports

Verbal recognition accuracy was analyzed with repeated measures ANOVA using emotion (negative, neutral) and peripheral object array type (manipulated, repeated) as within-subject factors. For accuracy, the main effect of object type was significant ($F(1,23) = 61.14$, $p < 0.0001$, $d = 0.73$). In other words, participants were more accurate in identifying repeated versus manipulated object arrays. The main effect of emotion was marginally significant ($F(1,23) = 3.59$, $p = 0.07$, $d = 0.14$); participants were more accurate in classifying peripheral objects as
either repeated or manipulated if they had been previously paired with a neutral central picture rather than a negative central picture. Planned contrasts revealed that participants were significantly more accurate in identifying manipulated peripheral objects if they were previously paired with a neutral central picture versus a negative central picture (t(23) = 2.19, p < 0.05). Emotion did not modulate accuracy for repeated peripheral objects (t(23) = 0.30, p = 0.77). All relevant means and standard errors are presented in Table 3.2.

In summary, indirect measures of memory as indexed by EMM revealed that early eye movement patterns distinguished between manipulated and repeated object arrays irrespective of whether they were previously paired with a negative or neutral picture. In contrast, viewing of the periphery was modulated by emotion and only distinguished between manipulated and repeated object arrays of those previously paired with a neutral picture. Consistent with this, emotion was also found to impair recognition memory, as indexed by verbal reports, for detecting a change in the periphery.

2.10.3 Relation between Verbal reports and Eye Movement Data

In further support of the finding that there may be a dissociation between memory measured by verbal reports versus EMM, we also examined EMM for half of the participants who showed the strongest emotion-modulated effect in verbal memory, i.e., those who showed the largest difference in correctly identifying peripheral objects previously paired with negative (M = 0.11, SEM = 0.03) versus neutral pictures (M = 0.34, SEM = 0.03; t(11) = 5.14, p < 0.0001). Despite this strong tradeoff effect in memory as measured by verbal reports, the same tradeoff effect was not observed in EMM measures. Specifically, a repeated measures ANOVA using emotion (negative, neutral) and object type (manipulated, repeated) did not reveal significant main effects of emotion for either of the EMM measures (time of first fixation: F(1,11) = 0.43, p > 0.1, d = 0.04; number of fixations: F(1,11) = 1.43, p > 0.1, d = 0.12) nor did it reveal a significant interaction between emotion and object type (time of first fixation: F(1,11) = 0.66, p > 0.1, d = 0.06; number of fixations: F(1,11) = 1.67, p > 0.1, d = 0.13). However, consistent with previous results, there was a significant main effect of object type for time of first fixation (F(1,11) = 6.35, p < 0.05, d = 0.37) such that participants were quicker to fixate on manipulated versus repeated objects regardless of whether the objects were previously paired with neutral or negative central pictures. The main effect of type was not significant for the number of fixations (F(1,11) = 2.87,
p > 0.1, d = 0.21). This suggests that the strongest dissociation between verbal reports and EMM may be observed in measures of early viewing such as the time of first fixation, which is modulated by prior experience, but not emotion.\footnote{Since accuracy for central pictures was at ceiling, there was not enough variability to conduct the same type of analysis to examine the relation between verbal reports and eye movement behavior for central pictures.}

2.11 Discussion

The presence of emotional stimuli results in a central/peripheral tradeoff effect in memory (e.g., Kensinger et al., 2007; Kensinger et al., 2005; Wessel & Merckelbach, 1997). Prior work suggests that emotions change the nature of memory representations for the emotion-eliciting stimulus and surrounding neutral information. However, this has only been explored using explicit verbal reports which reveal the end product of what is held in memory and cannot speak to how quickly one may be able to access stored representations. Using measures derived from EMM and verbal reports, the present work examined whether the presence of emotional stimuli led to differences in the speed at which memory representations could subsequently be accessed at retrieval, and whether there were differences in the details maintained within those representations. To the best of our knowledge, the present study is the first to examine these issues regarding the influence of emotion on distinct aspects of retrieval. In the next section, we discuss our results in light of prior findings regarding the central peripheral tradeoff in memory, and how the current work may inform theories regarding the influence of emotion on memory.

The use of EMM allows for the examination of how early viewing may be modulated by prior experience and whether this was influenced by the emotional context in which the information was originally encoded. Consistent with previous research, the current results showed that an early indicator of memory (i.e., time of first fixation to an altered region) was modulated by prior experience (e.g., Althoff & Cohen, 1999; Henderson et al., 2003; Ryan & Cohen, 2004). Specifically, participants were approximately 105 ms faster to fixate on the peripheral critical object when it was manipulated compared to when it was repeated which suggests that participants were able to encode, store, and at least to some degree, access information about these peripheral objects during the test phase such that early eye movement behavior was altered.
The difference in the time of first fixation occurred as early as 800 ms, which is rapid considering that participants did not know which object arrays would be manipulated and where the critical object would appear. Critically, this early indicator of memory differentiated between manipulated and repeated object arrays irrespective of the emotional context in which the objects were originally encoded. Thus, contrary to the notion that emotion impairs memory for information in the periphery, the current results show that emotion did not modulate early access of memory when measured indirectly via EMM.

In addition to examining an early indicator of memory via EMM, the current study also examined viewing patterns during the entire presentation period, i.e., number of fixations. Consistent with the central/peripheral tradeoff effect in memory, viewing patterns showed that emotion-enhanced memory for central pictures and impaired memory for peripheral objects. Specifically, it was found that viewing of central pictures was characterized by a repetition effect, i.e., a decrease in the number of fixations in viewing repeated versus novel scenes (e.g., Althoff & Cohen, 1999; Althoff et al., 1998; Ryan et al., 2000; Ryan, Leung, et al., 2007) for negative, but not neutral central pictures. Previous studies have shown that significant differences in viewing novel versus repeated stimuli largely occur only after multiple exposures in which the trial duration was longer than in the current work (e.g., Althoff & Cohen, 1999; Ryan et al., 2000; Ryan, Leung, et al., 2007). Thus, it is likely that the EMM metric did not distinguish between novel and repeated neutral central pictures because more repetitions were required before such differences in eye movement behavior could manifest. Despite this, eye movement behavior did distinguish between novel and repeated negative pictures, which suggests that emotion does not only enhance the probability that the picture will later be remembered, it also suggests that emotion may enhance the speed at which a lasting memory representation is formed. It is important to note that the repetition effect found in the eye movement behavior for viewing negative central pictures may represent the contributions of perceptual fluency rather than (or in addition to) declarative/relational memory. For example, repetition effects have been demonstrated in amnesic patients who have compromised medial temporal lobe systems (e.g., Althoff et al., 1998; Ryan et al., 2000), and intact repetition effects have been observed in healthy older adults in whom compromised medial temporal lobe function has been implicated (Driscoll et al., 2003; Ryan, Leung, et al., 2007).
For peripheral objects, participants directed significantly more fixations to the critical object of manipulated versus repeated displays (manipulation effect) if the objects were previously studied with a neutral central picture, but not when the peripheral objects were studied with a negative central picture. The finding that more fixations were directed to the manipulated versus repeated critical object is consistent with previous eye movement studies that have reported an increase in viewing for regions of change (e.g., Ryan et al., 2000; Ryan & Cohen, 2004; Ryan, Leung, et al., 2007). Such effects have been reported irrespective of task demands and have been found to precede behavioral responding, which suggest that such eye movement behaviors may ultimately culminate in the conscious access of previously learned information. It is possible that it is only through an increase in the amount of viewing to, and investigation of, a region of change that allows one to not only notice a change, but also be able to explicitly identify what had been changed and how. Further, on this view, it is likely that a manipulated versus repeated scene may require a more extensive comparison process between the presented external stimulus and the internal memory representation, leading to an increase in viewing (see Ryan & Cohen, 2004, for further discussion). In addition, such an increase in viewing may also represent the re-binding and/or the updating of memory representations. Thus, although early access to memory was not modulated by emotion, the quality and/or the amount of details contained within the memory, as indexed by the amount of sampling, was modulated by the emotional history of the retrieved information. This suggests that although emotion may lead to a more impoverished memory representation for information in the periphery, it may not impair one’s ability to access that information during the retrieval phase, however poor in quality those representations may be. In contrast to the repetition effect found for viewing of novel and repeated central pictures, the manipulation effect found for viewing of manipulated versus repeated peripheral objects likely reflects the influence of emotion on the representations that are declarative/relational in nature; as eye movement indices of detection of a manipulation are impaired in amnesic patients (Ryan et al., 2000) and older adults who presumably have a compromised medial temporal lobe system (Ryan, Leung, et al., 2007). Altogether, it would appear that emotion affects the formation of (detail contained within) multiple memory representations, including those that would contribute to perceptual fluency and those that are declarative/relational in nature and which support identification of a change by the eyes. However, it does not appear that emotion affects the speed with which such representations are accessed.
Consistent with the notion that measures of sampling of the critical region may contribute and/or are related to the final output of memory processing, direct measures of memory obtained through verbal reports showed that emotion-enhanced memory for central pictures and impaired memory for peripheral objects. Specifically, participants were more accurate to identify repeated negative versus neutral central pictures, and less accurate to detect a change in the periphery if the peripheral objects were previously studied with a negative compared to a neutral picture (e.g., J. M. Brown, 2003; Kensinger et al., 2005; Wessel & Merckelbach, 1997). Interestingly, while emotion impaired participants’ ability to detect a change in the peripheral objects, it did not modulate their ability to identify repeated peripheral objects (see: Kensinger et al., 2007; Kensinger et al., 2005). A possible reason for this is that whereas previous studies have presented the stimuli once during the encoding phase, the present study presented the stimuli twice across two study blocks. It is possible that by repeating the stimuli, the central/peripheral tradeoff effect in memory was not as robust as it would have been had the stimuli only been presented once. There is some indication in the literature that the central/peripheral tradeoff effect in memory is sensitive to methodological parameters such as the duration of exposure to the stimuli, specificity of the information interrogated during the test phase and the length of time between encoding and retrieval (e.g., Burke et al., 1992; Christianson, 1992; Steblay, 1992). However, despite having presented the stimuli twice during the study blocks, we still observed an influence of emotion on the memory for the peripheral objects. Detection of a manipulation within the peripheral objects may require a more detailed declarative/relation memory representation as participants need to be able to identify a critical novel object among two previously viewed objects. Thus, the current results may suggest that memory for specific details in the periphery is more sensitive to emotional modulation than memory for the gist of information (Adolphs et al., 2001; Adolphs, Tranel, et al., 2005; Denburg et al., 2003).

The results of this study showed that while emotion (here, negative emotion) did not modulate early indicators of, or access to memory, it led to a central/peripheral tradeoff in memory as indexed by sampling of the stimulus and by verbal reports. These differences in the influence of emotion may be due to differences in what such changes in eye movement measures and verbal reports represent; specifically, the early online use of memory versus the quality of stored memory representations, and subsequent conscious access to those representations. An important question that remains is how emotion may influence the quality and/or amount of
details stored in memory. It is often argued such differences in memory are the result of emotion-modulated differences during the encoding phase. However, there has not been a complete examination of whether such differences in attention during the encoding phase are related to subsequent memory (see: Christianson et al., 1991; Wessel et al., 2000). In a recent paper by Riggs and colleagues (Riggs, McQuiggan, Farb, Anderson, & Ryan, 2011), the researchers used EMM as an index of overt attention allocation, and mediation analysis to determine whether differences in attention were related to subsequent memory. It was found that contrary to previous assumptions, differences in attention during the encoding phase did not fully explain the central/peripheral tradeoff effect in verbal reports memory. These findings suggest that the differential influence of negative emotion on central versus peripheral memory may result from other cognitive influences in addition to visual attention, or on post-encoding processes. Alternatively, it could also be argued that while EMM provides a reliable measure of overt attention, it cannot capture processes related to covert attention which can be decoupled from overt attention (e.g., Posner, 1980; Rowe et al., 2007). Future studies can more systematically differentiate between these two contributing factors.

In summary, the current findings suggest that emotion does not modulate all aspects of retrieval. Access to previously formed memory representations occurred early, without regard to the nature of the information that is contained therein. Together, with our previous work that suggests initial access to memory occurs despite differences in task demands (e.g., Ryan, Hannula, et al., 2007), and even when such information is not relevant for the task at hand (Ryan, Hannula, et al., 2007), we propose that retrieval of previously stored memory representations occurs in an obligatory fashion, despite the valence of the stored information. By contrast, emotion impacts the detail and/or amount of information that is maintained in memory and the likelihood that there will be conscious access to that information. Thus, the more evaluative components of memory (formation and) retrieval are impacted by emotional valence.

2.12 Acknowledgments

This work was supported by funding from the Natural Sciences and Engineering Research Council of Canada (Jennifer D. Ryan, Adam K. Anderson), the Canada Research Chairs Program (Jennifer D. Ryan), the Canadian Foundation for Innovation (Jennifer D. Ryan), and a
Postgraduate Scholarship from the Natural Sciences and Engineering Research Council of Canada (Lily Riggs).
Chapter 4
A Complementary Analytic Approach to Examining Medial Temporal Lobe Sources Using Magnetoencephalography

3 A complementary analytic approach to examining medial temporal lobe sources using magnetoencephalography

3.1 Abstract

Neuropsychological and neuroimaging findings reveal that the hippocampus is important for recognition memory. However, it is unclear when and whether the hippocampus contributes differentially to recognition of previously studied items (old) versus novel items (new), or contributes to a general processing requirement that is necessary for recognition of both types of information. To address this issue, we examined the temporal dynamics and spectral frequency underlying hippocampal activity during recognition of old/new complex scenes using magnetoencephalography (MEG). In order to provide converging evidence to existing literature in support of the potential of MEG to localize the hippocampus, we reconstructed brain source activity using the beamformer method and analyzed three types of processing-related signal changes by applying three different analysis methods: (1) Synthetic aperture magnetometry (SAM) revealed event related and non-event-related spectral power changes; (2) Inter-trial coherence (ITC) revealed time-locked changes in neural synchrony; and (3) Event-related SAM (ER-SAM) revealed averaged event-related responses over time. Hippocampal activity was evident for both old and new information within the theta frequency band and during the first 250 ms following stimulus onset. The early onset of hippocampal responses suggests that general comparison processes related to recognition of new/old information may occur obligatorily.

3.2 Introduction

Since Scoville and Milner's (Scoville & Milner, 1957) discovery that excision of the hippocampus and surrounding cortex leads to profound and pervasive memory deficits, memory research has focused on the functional significance of this medial temporal lobe region (N. J. Cohen & Eichenbaum, 1993; N. J. Cohen et al., 1999; Eichenbaum & Cohen, 2001; Squire, 1992). Early neuropsychological studies revealed that damage to the hippocampus leads to severe deficits in memory for facts and events, as typically assessed using recall and recognition tasks in which participants have to either retrieve previously studied items or distinguish
previously studied items from novel items, respectively (N. J. Cohen & Squire, 1980; Corkin, 1968, 1992; Manns, Hopkins, Reed, Kitchener, & Squire, 2003).

With the advent of functional neuroimaging techniques such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI), researchers have studied the contribution of the hippocampus to memory in the healthy brain, often by using recognition memory tasks. Consistent with the neuropsychological data, neuroimaging findings revealed that the hippocampal region is involved during recognition memory tasks compared to control tasks that require simple visual processing/discrimination (e.g., Kapur, Friston, Young, Frith, & Frackowiak, 1995; Schacter et al., 1995; Squire, 1992).

With further advances in technology and analysis, researchers used event-related fMRI to interleave trial types that required different cognitive demands and/or to separate trials based on participants’ response (Greenberg et al., 2005; Kensinger, Clarke, & Corkin, 2003; Yonelinas, Otten, Shaw, & Rugg, 2005) to determine whether the hippocampus contributes specifically to successful retrieval of stored information or whether the hippocampus has a more general role during the retrieval stage. While some studies found that the hippocampus was preferentially recruited during the successful recognition of previously studied (old) information, others found that it was recruited to a similar extent (or even more) for novel (new) information (see Henson, 2005, for review). This suggests that the critical role of the hippocampus during memory retrieval may not reflect successful access to a stored representation per se, but instead may reflect a more general processing requirement that is common for both previously studied and novel information (N. J. Cohen et al., 1999). However, it is also possible that the hippocampus contributes differentially to the recognition of old/new information in ways that are not reflected in the amount of changes in metabolism as measured using PET and fMRI. Specifically, to the extent that different processes are invoked to support the recognition of old versus new information, the hippocampus may be recruited at a different time and/or in a different manner, as reflected in time course and spectral frequency of electromagnetic brain activity. PET and fMRI techniques do not have the adequate temporal resolution to outline the time course by which the hippocampus may come online during the recognition of different types of information, therefore, we require a neuroimaging method that can localize the hippocampus and outline its precise temporal dynamics.
Precise temporal dynamics underlying neural activity can be observed using electroencephalography (EEG) or event-related potentials (ERPs). For years, ERP studies of recognition memory have described what is thought of as hippocampally-mediated neural activity associated with viewing of previously studied and novel stimuli (for review, see Rugg, 1995a). This is known as the late positive component (LPC) of the ERP and is typically observed over medial and posterior sensor sites and begins around 500–600 ms after stimulus onset (e.g. Duzel, Picton, et al., 2001; Duzel, Vargha-Khadem, Heinze, & Mishkin, 2001; Rugg, Schloerscheidt, Doyle, Cox, & Patching, 1996; M. E. Smith & Halgren, 1989). This seems to suggest that different types of information recruit hippocampal processing in the same temporal manner. However, it is not known to what extent the late ERP components reflect the contribution from the hippocampus versus other sources. The spatial localization of EEG is compromised by volume conduction and therefore the signals likely reflect multiple underlying neural regions, thereby making it difficult to outline the temporal dynamics of the hippocampus specifically. Moreover, even if the temporal dynamics of hippocampal activity for previously studied versus novel information is similar during later processing (N500 ms), it is not known whether they are similar during earlier stages of recognition memory (b500 ms).

Magnetoencephalography (MEG) is a noninvasive neuroimaging technique that estimates neuronal activity based on recordings of the magnetic flux outside of the head (Hämäläinen et al., 1993; Hari et al., 2000). MEG has the same temporal resolution as EEG, but magnetic fields are less susceptible to attenuation by skull and tissue, therefore, its spatial localization is more precise than EEG. MEG provides recording of neural activity with temporal resolution on the order of milliseconds and spatial resolution comparable to that of fMRI (Miller et al., 2007). These properties make MEG an ideal tool for studying the dynamics of brain function. However, there is some debate of whether MEG can be reliably used to detect signals from deep neural structures such as the hippocampus (Mikuni et al., 1997). First, it has been argued that the specific shape of the hippocampus prevents any signal from being detected by MEG sensors (Mikuni et al., 1997). Specifically, it has been speculated that the “spiral” shaped hippocampal formation may lead to cancellation of all detectable signal from this region (Baumgartner, Pataaraia, Lindinger, & Deecke, 2000; Mikuni et al., 1997; Stephen, Ranken, Aine, Weisend, & Shih, 2005). However, complete cancellation would require simultaneous activation of dentate and cornu ammonis (CA) fields with equal signal intensity. Contrary to this, it has been argued
that the hippocampus is laminated, thus, signals tend to summate rather than cancel (Nishitani et al., 1999). Moreover, anatomical and electrophysiological asymmetries in the hippocampus (Duvernoy, 1988; Yeckel & Berger, 1990) suggest that cancellation will be incomplete and at least some portion of the signal will be visible to MEG (for an in depth discussion, see Stephen et al., 2005).

Second, it has been argued that signals from the hippocampus would be too weak to be detectable by MEG sensors because the magnetic field decreases with the square of distance between neural source and the MEG sensor (Baumgartner et al., 2000; Hämäläinen et al., 1993; Hillebrand & Barnes, 2002). Since the hippocampus is situated deep within the brain, detecting hippocampal activity at the scalp surface is challenging. Under the assumption that deep structures do not contribute to the recorded signal, some source analysis programs constrain the localization of neural activity to the cortex excluding all subcortical structures including the hippocampus (Berg & Scherg, 1994; Gonsalves, Kahn, Curran, Norman, & Wagner, 2005; Jerbi et al., 2004). However, the development of modern whole-scalp MEG sensor arrays has increased the sensitivity for deep structures (Ahonen et al., 1993) by capturing magnetic flux signals across the entire head. Advanced data analysis methods make use of information obtained by all sensors and support volumetric source analysis, e.g. standardized low resolution brain electromagnetic tomography (sLORETA) (Pascual-Marqui, 2002), L1 minimum-norm current estimate (MCE) (Tesche, 1996; Uutela, Hamalainen, & Somersalo, 1999), synthetic aperture magnetometry (SAM) (Fawcett, Barnes, Hillebrand, & Singh, 2004; Gaetz & Cheyne, 2003; Herdman et al., 2004; Herdman et al., 2003; Hirata et al., 2002; Luo et al., 2007; Robinson & Vrba, 1999; Schulz et al., 2004), and event-related SAM (ER-SAM) (Cheyne, Bakhtazad, & Gaetz, 2006; Cheyne, Bostan, Gaetz, & Pang, 2007; Hämäläinen et al., 1993; Herdman & Ryan, 2007; Itier, Herdman, George, Cheyne, & Taylor, 2006; Schulz et al., 2004). Our group contributed to these tools with a new source analysis approach using inter-trial coherence (ITC) (Bardouille & Ross, 2008).

Third, there is some question as to whether MEG is sensitive enough to differentiate activity between the hippocampus and parahippocampal gyrus. It has been reported that at the depth of these sources (5–6 cm), spatial resolution ranges from 25 mm to 40 mm, making it difficult to distinguish activity originating in the hippocampus from those originating in the parahippocampal region (D. Cohen et al., 1990; Mosher, Spencer, Leahy, & Lewis, 1993).
However, in a study that examined the precision of localization using simulated MEG activity presented with real background brain activity, Stephen and colleagues (Stephen et al., 2005) showed that MEG is able to correctly localize activity to either the hippocampus or the parahippocampal gyrus when activity in these two regions did not overlap in time. When these two regions did overlap in time and were simultaneously active, MEG was unable to differentiate between them and modeled the activity to a single source. However, this is not a problem for localizing the hippocampus per se, rather, this suggests that when both regions are active, activity localized to one region cannot be said to be completely independent of the other, and may reflect simultaneous activity from both regions.

Based on previous literature, it is clear while the localization of deep sources, such as the hippocampus, using MEG remains a challenging task, it is by no means an impossible one. In fact, numerous studies have lent support to the notion that hippocampal activity can be detected by MEG using a variety of experimental paradigms such as sensory oddball tasks (Hamada, Sugino, Kado, & Suzuki, 2004; Ioannides et al., 1995; Nishitani, Nagamine, Fujiwara, Yazawa, & Shibasaki, 1998; Tesche, Karhu, & Tissari, 1996), conditioning (Kirsch et al., 2003), mental calculation (Tesche, 1997), and motor reaction to an auditory cue (Tesche & Karhu, 1999). Of the MEG studies that examined memory, several have reported observable responses from the hippocampus for tasks of prospective memory (T. Martin et al., 2007), working memory (Campo, Maestu, Ortiz, et al., 2005; Tesche & Karhu, 2000), and transverse patterning (Hanlon et al., 2003; Hanlon et al., 2005). However, despite the theoretical and empirical link between the hippocampus and long-term memory, and the prevalent use of recognition memory paradigms in neuropsychological, PET, fMRI, and ERP studies, only very few MEG studies have examined hippocampal activity within this framework (Breier, Simos, Zouridakis, & Papanicolaou, 1998, 1999, 2000; Gonsalves et al., 2005; Papanicolaou et al., 2002; Tendolkar et al., 2000).

The MEG studies that have looked at hippocampal activity during a recognition memory task have been inconclusive. In a recent MEG study of visual memory by Osipova and colleagues (Osipova et al., 2006), it was found that correctly recognized old items elicited stronger theta oscillations than correctly rejected new items. The authors suggested that this theta oscillation may derive from hippocampal activity, but were not able to localize the activity to any region in the brain due to insufficient signal-to-noise ratio. In a MEG study of verbal recognition,
magnetic evoked activity localized to the right medial temporal region was reported (Tendolkar et al., 2000). However, because the MEG data had not been co-registered with participants’ structural MRIs, it is not clear whether the activity originated from the hippocampus or surrounding cortex. In a combined MEG and fMRI study that also examined neural activity during a verbal recognition task, significant left medial temporal lobe (MTL) activity was localized to the perirhinal and parahippocampal cortex predominantly during the 150–450 ms time interval following stimulus onset (Gonsalves et al., 2005). However, since the MEG sources had been constrained to the cortex only, it is unclear whether the hippocampus was also involved. When researchers incorporated co-registration of MEG and structural MRI and did not constrain the MEG localization to cortical sources, activity was localized to the medial temporal lobe, including the hippocampus and parahippocampal gyrus using both visual and verbal recognition tasks (Breier et al., 1998, 1999, 2000; Papanicolaou et al., 2002). However, Papanicolaou and colleagues (2002) only examined the time course of medial temporal lobe activation in general, and while Breier and colleagues (Breier et al., 1998, 1999, 2000) localized the activity specifically in the hippocampus and parahippocampal gyrus and found them to be active between 200–800 ms post-stimulus onset, the exact time course of activity in the hippocampus was not outlined. Altogether, all of the MEG studies examining recognition memory of which we are aware reported medial temporal activation when there was sufficient signal-to-noise ratio for brain localization and when source analysis had not been constrained to the cortical surface, (Breier et al., 1998, 1999, 2000; Gonsalves et al., 2005; Papanicolaou et al., 2002; Tendolkar et al., 2000). Furthermore, activity in the hippocampus can be detected when using precise co-registration of MEG and structural MRI (Breier et al., 1998, 1999, 2000; Papanicolaou et al., 2002).

While the above studies have examined hippocampal activity during recognition memory using MEG, questions remain regarding precisely when peak hippocampal activity occurs and whether the manner of activity changes depending on the nature of the stimulus (old/new). For example, hippocampal activity associated with the recognition of previously studied versus novel items may peak at the same/different times and/or oscillate in the same/different frequency range. The purpose of the present study was to provide converging evidence for the earlier work described above, which outlines the potential of using MEG for localizing hippocampal activity, and to expand upon it both methodologically and theoretically. We adapted an experimental paradigm
in which participants first studied a series of scenes and scrambled versions of the scenes (Kirchhoff, Wagner, Maril, & Stern, 2000). Immediately following, participants had to distinguish previously studied from novel scenes.

To expand upon prior work methodologically, we provide a comprehensive examination of electromagnetic activity from the hippocampus by analyzing multiple aspects of processing-related signal changes in the observed signals. The three analysis methods used were variations of the beamformer approach (Robinson & Vrba, 1999): Synthetic Aperture Magnetometry (SAM), Inter-Trial Coherence (ITC) of brain source activity, and Event Related SAM (ER-SAM). The beamformer approach to MEG data analysis is a two-step procedure: the first step uses the beamformer as spatial filter for reconstructing source activity, and in the second step, a signal statistic is derived from the source activity and mapped volumetrically. While the three analysis methods in our study use the same beamformer, each method uses different statistics and varies in their degree of specificity for particular aspects of the data such as spectral and temporal information. SAM examines the changes in signal power in a certain frequency band between a specified control and active time window for each volume element. The signal power statistics include both the phase-locked event-related activity and changes in signal power induced by the stimulus but not strictly phase-locked. ITC is a normalized measure of neural synchrony across multiple trials. ITC reveals the time and frequency range in which high coherence between stimulus and brain activity occurs and provides complementary information to the signal power statistics in SAM. ER-SAM averages waveforms of source activity across all trials and examines event-related, time-locked neural responses. Unlike modeling the MEG data with a small number of equivalent current dipoles (ECD), the beamformer analysis does not require a priori assumptions about the number of active sources. Also, beamformer algorithms take advantage of the high dimensionality of the signal space offered by multi-channel MEG in order to reduce correlations in the data and suppress interactive sources (Cheyne et al., 2006). Specifically, the entire brain volume is covered by a grid, and at each grid node, the beamformer maximizes sensitivity for the signal from that node and suppresses the signal from other nodes (Huang et al., 2004). It should be noted that while the proposed analyses vary in their degree of specificity for particular aspects of the data such as spectral and temporal information, the observed measures may not be completely independent because they are affected by properties of the commonly applied beamformer. Further, the methods of examining the averaged evoked
response with ER-SAM and ITC are asymptotically equivalent for a large number of trials. However, two important differences exist between ITC and ER-SAM. First, ITC uses the normalized amplitude of neural activity, which makes the statistics more homogeneous across the whole brain than ER-SAM. This is important for localizing deep sources, which likely have lower signal amplitudes than more superficial sources. Second, ITC provides information about synchrony at a specific frequency, while ER-SAM provides precise timing information. With the three complementary analysis methods we will give an exhaustive description of relevant electromagnetic brain activity as expressed in changes in spectral signal power, time course of event-related activity and changes in signal coherence. To the best of our knowledge, the application of multiple analysis methods to characterize the different aspects of neural activity from hippocampus with the same set of MEG data has not been previously attempted.

To expand upon prior work theoretically, through our multi-method approach, we are able to outline the precise time courses and spectral frequencies of hippocampal activity during recognition of old and new items. This will provide insights into the nature of recognition memory, namely, when does the hippocampus begin to participate in recognition memory of, and does it participate similarly for, old/new information? Such an analysis may speak to questions regarding the functional role of the hippocampus in distinguishing the familiar from the novel.

3.3 Method

3.3.1 Participants

Thirteen adults (6 males, 28.1 years of age, 1 left-handed) from the Toronto community with normal neurological histories and normal or corrected-to-normal vision participated in the study. The study was approved by the local ethics committee and the rights and privacy of the participants were observed. All participants gave informed consent before the experiment and received monetary compensation.

3.3.2 Stimuli

Visual stimuli consisted of 200 pictures of indoor scenes, 200 of outdoor scenes, and 400 scrambled scenes. The resolution of all pictures was 1024 by 768 pixels. The 400 indoor and outdoor scenes were created from a set of 200 scenes (100 indoor, 100 outdoor) taken from a repository of scenes in CorelDraw. Each scene was divided into two unique non-overlapping
images to create a set of target scenes and a set of foil images. In this manner, sets of targets and foils were similar for color, luminance and complexity. Targets were presented during the encoding phase and as ‘old’ images in the retrieval phase; foils were presented as ‘new’ images during the retrieval phase. The sets of scenes were counterbalanced such that every scene was presented equally often as a target and foil across participants. The scrambled scenes were random patterns generated from permutations of the indoor and outdoor scenes, such that each scene had a scrambled counterpart, and therefore had similar color and luminance as the original scenes. Scrambled scenes were made using Adobe Photoshop.

3.3.3 Procedure

The experiment consisted of an encoding and retrieval phase, each lasting approximately 20 min. MEG was recorded during both phases; however, only the data from the retrieval phase is presented here. During the encoding phase, participants viewed 200 indoor and outdoor scenes and 200 matched scrambled scenes. Scenes were presented for 1000 ms with an average inter-stimulus interval (ISI) of 2000 ms (range 1750–2250 ms). During the ISI a fixation cross appeared in center of the black screen (Figure 4.1). Participants were instructed to distinguish between indoor, outdoor, and scrambled scenes by pressing one of three different buttons with their right hand. Participants were also informed that there would be a subsequent memory test. The retrieval phase immediately followed the encoding phase. During retrieval, participants viewed the 200 previously studied (target) scenes and 200 novel indoor and outdoor scenes (foil images). Participants were instructed to respond whether they were highly confident that the picture had been previously studied (‘old’), if they were only somewhat confident that the picture was ‘old’, or if the picture was 'new'.
3.3.4 Data acquisition

MEG recordings were performed in a magnetically shielded room at the Rotman Research Institute, Baycrest Hospital for Geriatric Care, using a 151-channel whole head first order gradiometer system (VSM-Med Tech Inc.) with detection coils uniformly spaced 31 mm apart on a helmet-shaped array. Participants sat in upright position, and viewed the stimuli on a back projection screen that subtended approximately 31 degrees of visual angle when seated 30 in. from the screen. The MEG collection was synchronized with the onset of the stimulus by recording the luminance change of the screen. Participant’s head position within the MEG was determined at the start and end of each recording block using indicator coils placed on nasion and bilateral preauricular points. These three fiducial points established a head-based Cartesian coordinate system for representation of the MEG data.

In order to specify/constrain the sources of activation as measured by MEG and to co-register the brain activity with the individual anatomy, a structural MRI was also obtained for each participant using standard clinical procedures with a 1.5 T MRI system (Signa EXCITE HD 11.0GE Healthcare Inc., Waukesha, WI) located at Sunnybrook Health Sciences Centre. All participants’ anatomical MRIs and MEG source data were spatially normalized to the Talairach standard brain using AFNI (National Institute of Mental Health, Bethesda, MD, USA) for the SAM and ITC method and using SPM99 (Wellcome Institute of Cognitive Neurology, London, UK) for the ER-SAM method to allow for group analysis of functional data.
3.3.5 Data analysis

Analysis methods were applied to scenes that were later correctly identified as ‘new’ (correct-new) and ‘high confidence old’ (correct-old). For all analyses, the beamformer spatial filter as provided by the VSM software package was used to estimate source activity on a grid with regular spacing of 5 mm. Analyses were performed individually for each participant. Resulting individual volumetric maps of functional brain activity were then transformed into the standard Talairach space, using the same transform applied to the anatomical MR image. The resultant functional maps for each time/frequency interval were then averaged across participants. Group statistics were performed to identify which regions of brain activation were significantly different from a pre-specified control window on average across all participants. The type of group statistics applied for each analysis method is consistent with previous work, for example, permutation test for SAM (Chau, Herdman, & Picton, 2004) and pseudo-z for ER-SAM (Herdman, Pang, Ressel, Gaetz, & Cheyne, 2007). In order to ensure that significance in the group-averaged results was not driven by outliers, we also examined individual volumetric maps. The purpose of the present paper is to explore hippocampal activity in a visual recognition memory task. As such, we present and discuss only activity restricted to this region.

3.3.5.1 MEG analysis using SAM

The linearly constrained minimum variance (LCMV) beamformer algorithm (Robinson & Rose, 1992; Van Veen, van Drongelen, Yuchtman, & Suzuki, 1997) was used to estimate source activity in a wide frequency band (0–30 Hz) and specifically in the theta (4–8 Hz) frequency band (e.g. Tesche & Karhu, 2000). The control window was defined as the time interval from –500 to –250 ms before stimulus onset, and four active-windows of 250 ms duration between 0 and 1000 ms post-stimulus onset. For the two frequency bands, the differences in signal power between all active and the control window were normalized to an estimate of noise power. The resulting expression of stimulus induced relative power changes for each node was termed pseudo t-statistic, which is a normalized measure of the difference between signal power in the active and control window (Robinson & Vrba, 1999). Pseudo-t values at all nodes were compiled to generate a volumetric map of neuronal power changes for each post-stimulus interval and each frequency band. This calculation was performed for both ‘correct-new’ and ‘correct-old’ scenes. SAM volumetric maps were viewed in AFNI and only spatially distinct regions of activity overlying the hippocampus were considered. Permutation tests were applied
separately for the group-averaged volumetric maps corresponding to each time interval, frequency band, and both types of scenes in order to identify the brain regions with significant ($\alpha=0.05$) signal power changes (Chau et al., 2004).

3.3.5.2 MEG analysis using ITC

The beamformer algorithm was applied to the 0–100 Hz wide band filtered MEG data in the –1000 to 1000 ms time interval relative to stimulus onset to define a spatial filter. Source waveforms at all volume elements were obtained from spatially filtering the MEG data. Morlet wavelet transform of the source waveforms provided phase information over each 250 ms time interval between −1000 and 1000 ms and seven frequencies centered approximately around 4, 6, 9, 13, 19, 28, and 41 Hz. ITC is a statistic describing the distribution of phase values across repeated trials (Fisher, 1993). ITC is zero in the case of the phase being uniformly distributed between 0 and $2\pi$, which means that the signal does not show any stimulus-related contributions in the specific time and frequency interval. In contrast, ITC is close to 1 if the phase values are concentrated around a mean value indicating that the brain signal is strongly synchronized with the stimulus. A more detailed description of the analysis can be found in Bardouille and Ross (2008).

Volumetric calculation of ITC in time-frequency domain results in a five dimensional data set (three spatial dimensions, time, and frequency). In order to find relevant regions of interest, first the locations of right and left hippocampus were identified on each participant's MRI. ITC values for the closest grid node were compiled to generate time-frequency plots for both ‘correct-old’ and ‘correct-new’ scenes. These plots were used as a descriptive guideline to examine more specific spectral and temporal information in whole-head volumetric ITC maps and no statistics were applied. Whole-head volumetric ITC maps were generated for both types of scenes during any specific time/frequency intervals that depicted high inter-trial coherence in the hippocampus. Volumetric ITC maps were spatially normalized and group-averages were calculated as the mean ITC value across corresponding voxels. Individual and group-averaged volumetric ITC maps were visualized in AFNI using each participant's own MRI and the group-averaged MRI, respectively. In order to estimate the distribution of ITC amplitudes under the null hypothesis, we examined ITC values during the baseline period ($-500$ ms to $-750$ ms) for each participant.
and the group average, as outlined in Bardouille and Ross (2008). Only values exceeding the 95% level of this distribution were considered.

### 3.3.5.3 MEG data analysis using ER-SAM

The beamformer algorithm was used to define a spatial filter based on the MEG data in the 0–30 Hz frequency and −1000 ms to 1000 ms time interval. The spatial filter was applied to the time domain averaged MEG and normalized to a noise estimate, which resulted in time courses of a pseudo-z statistic corresponding to the amount of event-related brain activity in each volume element across the entire time interval (−1000 to 1000 ms). The pseudo-z is like the t-statistic used in SAM except that it is applied to multiple time points (every 5 ms) rather than normalized over time (i.e. 250 ms intervals), making it more appropriate for evoked and averaged data. Individual volumetric maps of the magnitude of pseudo-z values were transformed onto a normalized brain and averaged across all participants. Individual and group-averaged SAM maps were calculated for ‘correct-new’ and ‘correct-old’ scenes and the post-stimulus time interval (0–1000 ms) was examined. A distribution of the pseudo-z values under the null hypothesis was estimated from randomly sampled data in the pre-stimulus interval and thresholds for $\alpha \leq 0.05$ were obtained for all volume elements (Herdman et al., 2007). Threshold values for the group-averaged data were based on the pre-stimulus interval in the group-averaged data and threshold values for individual volumetric maps were based on the pre-stimulus interval for each participant. ER-SAM maps were thresholded accordingly and the locations of activation peaks in the remaining data were identified using a customized MATLAB procedure. This procedure, provided by the CTF software package, marks peaks in the volumetric data by first finding the voxel containing the maximum value within a 3 voxel volume of $15 \times 15 \times 15$ mm after the ER-SAM image is thresholded, and then removes all voxels in the surrounding region that are contiguous or lower in magnitude than the maximum. The next peak is found as the maximum value in the remaining volume. This procedure is repeated until the entire volume has been scanned. For individual ER-SAM maps, peaks found in or within less than 1 cm of the hippocampus were considered. Time courses of the magnitudes of event-related neural activities (pseudo-z values) were calculated for the identified locations of peak activity from the grand-averaged ER-SAM maps. In order to examine any differences in hippocampal activity between processing of ‘correct-new’ and ‘correct-old’ scenes, we also performed a contrast between the two types of scenes.
3.4 Results

3.4.1 Behavioral responses

Three participants were excluded from all analyses due to low numbers of total correct responses (below 25%). Participants were significantly more likely to correctly identify old (hit) scenes with high confidence and novel scenes (correct rejection) than would be expected by chance (old: t(9) = 2.68, p<.05; novel: t(9) = 3.03, p<.05). The incidence of hits and correct rejections did not differ significantly from each other (t(9) = 1.61, p>.1). A summary of the behavioral recognition results can be found in Table 4.1. Behavioral results are similar to those obtained in fMRI studies using similar number of stimuli (e.g. Kirchhoff et al., 2000).

Table 3.1 Average accuracy for correctly identifying a scene as ‘old’ or ‘new’

<table>
<thead>
<tr>
<th>Response:</th>
<th>Old scenes % (SEM)</th>
<th>New scenes % (SEM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High confident old</td>
<td>41.2 (3.06)</td>
<td>18.3 (3.13)</td>
</tr>
<tr>
<td>Low confident old</td>
<td>16.8 (3.58)</td>
<td>19.8 (4.29)</td>
</tr>
<tr>
<td>New</td>
<td>34.2 (5.57)</td>
<td>53.1 (6.63)</td>
</tr>
</tbody>
</table>

Standard errors of mean (SEM) are noted.

3.4.2 Signal power changes in neural responses: SAM

SAM maps for each time interval and frequency band for both ‘correct-new’ and ‘correct-old’ scenes were examined. Permutation tests performed on the group averaged activity did not reveal significant differences between the pre-stimulus control and active intervals in the hippocampus for either scene type (α=0.05). The only activity revealed to be significantly different from the control interval was within the visual cortex. However, the permutation test estimates a threshold common for all voxels in the brain and this may be too conservative for deep sources such as the hippocampus. We further explored the data by lowering the threshold limit and found spatially distinct activity in the right hippocampus for ‘correct-new’ scenes and in the parahippocampal region for ‘correct old’ scenes during the same time interval and frequency band (Figure 4.2).
Figure 3.2 Group-averaged SAM activation maps

SAM activation maps are shown for the theta frequency band during 0–250 ms post-stimulus onset. Activity is below the significance level of p=.05 for the group statistics (pseudo-t value=.49). However, when the raw data were viewed in AFNI, spatially distinct activity in the hippocampus (pseudo-t value=.15) and parahippocampal region (pseudo-t value=.15) was observed for correct-new and correct-old scenes, respectively. Black cross-hairs indicate the location of the regional peak, also reported in Talairach co-ordinates.

Coherence in neural responses: ITC

Averaged ITC values in time-frequency domain revealed stimulus-locked activation of the hippocampus during the 0–250 ms and 250–500 ms time interval following stimulus onset for the frequency bands up to 12 Hz for both ‘correct-new’ and ‘correct-old’ scenes. ITC measures in the hippocampus were specifically expressed in the first two frequency bins, which correspond with the delta (1–4 Hz) and theta frequency range (4–8 Hz), respectively (Figure 4.3).
Figure 3.3 Group-averaged time-frequency maps of ITC for the hippocampus

ITC maps represent the left and right hippocampus for scenes correctly identified as ‘new’ (left) or ‘old’ (right) with high confidence.

For the group-averaged data, volumetric maps for the theta band and the two time intervals of 0–250 ms and 250–500 ms revealed spatially distinct activity exceeding group baseline threshold values in the right hippocampus for ‘correct-new’ and ‘correct-old’ scenes across both time intervals (Figure 4.4). Theta band activity in the left hippocampus was observed as a spatially distinct activation in the hippocampus for ‘correct-old’ scenes during 250–500 ms.
**Figure 3.4 Group-averaged volumetric maps of ITC**

<table>
<thead>
<tr>
<th>Time Interval</th>
<th>Correct-New</th>
<th>Correct-Old</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-250 ms 5.8Hz</td>
<td><img src="image" alt="Correct-New" /></td>
<td><img src="image" alt="Correct-Old" /></td>
</tr>
<tr>
<td>250-500 ms 5.8 Hz</td>
<td><img src="image" alt="Correct-New" /></td>
<td><img src="image" alt="Correct-Old" /></td>
</tr>
</tbody>
</table>

Volumetric maps of ITC are shown in approximately the theta frequency band (4–8 Hz, center frequency 6 Hz) during the 0–250 ms (top) and 250–500 ms time intervals (bottom) for scenes correctly identified as ‘new’ (left) and ‘old’ (right). Whereas theta band ITC in the right hippocampus was expressed for both time intervals for both ‘correct-new’ and ‘correct-old’ scenes, ITC in the left hippocampus was found during the 250–500ms interval only for ‘correct-old’ scenes. Black cross-hairs indicate the position of the hippocampal peak, also reported in Talairach co-ordinates. All values exceeding .14 and .17 were considered significant for ‘correct-new’ and ‘correct-old’ scenes, respectively, based on threshold levels derived from the baseline period. All activity shown exceeded 95% level of the baseline distribution.

Individual volumetric maps for ITC in the theta band were examined for each participant. Consistent with group-averaged results, theta band synchrony in or within less than 1 cm of the right hippocampus exceeding the significance threshold occurred in 8 participants during 0–250 ms and 5 participants during 250–500 ms for ‘correct-new’ scenes, and 6 participants during 0–250 ms and 6 participants during 250–500 ms for ‘correct-old’ scenes. Group-averaged results also revealed theta band synchrony for ‘correct-old’ scenes during 250–500 ms in the left...
hippocampus. Significant activity was found in individual volumetric maps for 2 participants (Table 4.2). Examples of hippocampal activity found for individual participants is shown in Figure 4.5 and the averaged location of peak hippocampal activity based on individual participants’ ITC maps are shown in Figure 4.6.

Table 3.2 Source ITC values and Talairach co-ordinates for individual ITC maps showing hippocampal activity

<table>
<thead>
<tr>
<th>Subject</th>
<th>Max. ITC value for Hpc during Baseline</th>
<th>Max. ITC value during Baseline</th>
<th>Local Maxima of Hpc during 0-250 ms (Tal.)</th>
<th>Max. ITC value</th>
<th>Local Maxima of Hpc during 250-500 ms (Tal.)</th>
<th>Max. ITC value</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>.12</td>
<td>.22</td>
<td>R: 25 -14 -13</td>
<td>.58</td>
<td>R: 25 -30 -7</td>
<td>.33</td>
</tr>
<tr>
<td>S2</td>
<td>.12</td>
<td>.18</td>
<td>R: 23 -23 -5</td>
<td>.21</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>S3</td>
<td>.20</td>
<td>.27</td>
<td>L: -21 -39 0</td>
<td>.42</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>S4</td>
<td>.20</td>
<td>.34</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>S5</td>
<td>.17</td>
<td>.26</td>
<td>R: 31 -41 2</td>
<td>.73</td>
<td>R: 30 -28 -7</td>
<td>.54</td>
</tr>
<tr>
<td>S6</td>
<td>.10</td>
<td>.17</td>
<td>L: -23 -46 5</td>
<td>.51</td>
<td>R: 27 -14 -11</td>
<td>.32</td>
</tr>
<tr>
<td>S7</td>
<td>.23</td>
<td>.29</td>
<td>R: 29 -29 -10</td>
<td>.64</td>
<td>R: 22 -38 4</td>
<td>.42</td>
</tr>
<tr>
<td>S8</td>
<td>.24</td>
<td>.31</td>
<td>R: 28 -43 2</td>
<td>.49</td>
<td>L: -27 -32 -5</td>
<td>.35</td>
</tr>
<tr>
<td>S9</td>
<td>.15</td>
<td>.29</td>
<td>R: 24 -10 -18</td>
<td>.34</td>
<td>L: -24 -37 -5</td>
<td>.33</td>
</tr>
<tr>
<td>S10</td>
<td>.19</td>
<td>.23</td>
<td>L: -20 -38 0</td>
<td>.40</td>
<td>L: -18 -11 -12</td>
<td>.25</td>
</tr>
</tbody>
</table>

Average (stdev)

<table>
<thead>
<tr>
<th>Max. ITC value for Hpc during Baseline</th>
<th>Max. ITC value during Baseline</th>
<th>Local Maxima of Hpc during 0-250 ms (Tal.)</th>
<th>Max. ITC value</th>
<th>Local Maxima of Hpc during 250-500 ms (Tal.)</th>
<th>Max. ITC value</th>
</tr>
</thead>
<tbody>
<tr>
<td>.17 (.05)</td>
<td>.26 (.05)</td>
<td>L: -21 -41 2 (2 4 3)</td>
<td>.44 (.06)</td>
<td>L: -23 -27 -7 (5 14 4)</td>
<td>.31 (.05)</td>
</tr>
<tr>
<td>R: 25 -28 -6 (5 12 9)</td>
<td></td>
<td>R: 26 -31 -4 (3 16 8)</td>
<td>.44 (.20)</td>
<td>R: 26 -31 -4 (3 16 8)</td>
<td>.41 (.09)</td>
</tr>
</tbody>
</table>

Total

L: 3 participants
R: 8 participants
Either: 9 participants

L: 3 participants
R: 5 participants
Either: 7 participants
## B. Correct-Old

<table>
<thead>
<tr>
<th>Subject</th>
<th>Max. ITC value for Hpc during Baseline</th>
<th>Max. ITC value during Baseline</th>
<th>Local Maxima during 0-250 ms (Tal.)</th>
<th>Max. ITC value</th>
<th>Local Maxima during 250-500 ms (Tal.)</th>
<th>Max ITC value</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>.13</td>
<td>.31</td>
<td>R: 25 -19 -12</td>
<td>.41</td>
<td>R: 16-38 3</td>
<td>.34</td>
</tr>
<tr>
<td>S2</td>
<td>.26</td>
<td>.36</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>S3</td>
<td>.13</td>
<td>.28</td>
<td>L: -25 -41 -3</td>
<td>.42</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>S4</td>
<td>.22</td>
<td>.29</td>
<td>L: -30 -24 -15</td>
<td>.32</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>S6</td>
<td>.17</td>
<td>.32</td>
<td>L: -24 -41 0</td>
<td>.38</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>S8</td>
<td>.18</td>
<td>.33</td>
<td>R: 30 -32 -5</td>
<td>.55</td>
<td>R: 21 -29 -6</td>
<td>.34</td>
</tr>
<tr>
<td>S9</td>
<td>.22</td>
<td>.40</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>S10</td>
<td>.18</td>
<td>.24</td>
<td>L: -21 -37 0</td>
<td>.38</td>
<td>R: 26 -24 -12</td>
<td>.25</td>
</tr>
<tr>
<td>Average (stdev)</td>
<td>.18</td>
<td>.30</td>
<td>L: -24 -33 -5</td>
<td>.37</td>
<td>L: -24 -25 -10</td>
<td>.31</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(4 11 8)</td>
<td>(.06)</td>
<td>(15 14 6)</td>
<td>(.02)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>R: 30 -29 -8</td>
<td>.48</td>
<td>R: 25 -31 -6</td>
<td>.35</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(5 12 8)</td>
<td>(.14)</td>
<td>(6 5 6)</td>
<td>(.07)</td>
</tr>
</tbody>
</table>

| Total  | L: 6 participants                     | R: 6 participants            | Either: 8 participants                | L: 2 participants | R: 5 participants            | Either: 5 participants |

All reported hippocampal activity were above threshold and in or within 10 mm of the hippocampus (Hpc) for (A) 'correct-new' and (B) 'correct-old' (L = left hippocampus; R = right hippocampus).
Figure 3.5 Representative individual volumetric maps of inter-trial coherence

<table>
<thead>
<tr>
<th>A. 0-250ms, 5.8Hz</th>
<th>Correct-New</th>
<th>Correct-Old</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Left Hippocampus</strong></td>
<td>![Correct-New Image]</td>
<td>![Correct-Old Image]</td>
</tr>
<tr>
<td>![s6 Image]</td>
<td>![s4 Image]</td>
<td></td>
</tr>
<tr>
<td><strong>Right Hippocampus</strong></td>
<td>![Correct-New Image]</td>
<td>![Correct-Old Image]</td>
</tr>
<tr>
<td>![s2 Image]</td>
<td>![s1 Image]</td>
<td></td>
</tr>
</tbody>
</table>
**B. 250-500ms, 5.8Hz**

<table>
<thead>
<tr>
<th>Left Hippocampus</th>
<th>Correct-New</th>
<th>Correct-Old</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="s10.png" alt="Image" /></td>
<td><img src="s5.png" alt="Image" /></td>
<td><img src="s7.png" alt="Image" /></td>
</tr>
<tr>
<td><img src="s10.png" alt="Image" /></td>
<td><img src="s5.png" alt="Image" /></td>
<td><img src="s7.png" alt="Image" /></td>
</tr>
</tbody>
</table>

Inter-trial coherence was in approximately the theta frequency band (center frequency 6 Hz) during (A) 0-250 ms and (B) 250-500 ms (bottom) time intervals for scenes correctly identified as ‘new’ (left) and ‘old’ (right). All activity shown significantly exceeded baseline levels.
3.4.3 Averaged event related neural responses: ER-SAM

Time courses of grand-averaged ER-SAM data revealed peaks of activity in the right and left hippocampus for ‘correct-new’ scenes, which were significantly different from baseline for the group ($\alpha=0.05$) (Figure 4.7). Activity in the right hippocampus peaked at 225 ms post-stimulus onset. Two smaller peaks were also observed between 300–450 ms. Activity in the left hippocampus peaked initially at 130 ms post-stimulus onset and three smaller peaks were observed between 200–350 ms. For ‘correct-old’ scenes, significant activity was found for the left parahippocampal gyrus. Peak activity occurred 120 ms post-stimulus onset. Two smaller peaks were also found between 500–600 ms. All reported peaks were above the threshold level of $\alpha=0.05$. 

<table>
<thead>
<tr>
<th>0-250ms, 5.8Hz</th>
<th>Correct-New</th>
<th>Correct-Old</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left Hippocampus</td>
<td><img src="image1" alt="Image" /> Tal: -21 -41 2</td>
<td><img src="image2" alt="Image" /> Tal: -24 -33 -5</td>
</tr>
<tr>
<td>Right Hippocampus</td>
<td><img src="image3" alt="Image" /> Tal: 25 -28 -6</td>
<td><img src="image4" alt="Image" /> Tal: 30 -29 -8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>250-500ms, 5.8Hz</th>
<th>Correct-New</th>
<th>Correct-Old</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left Hippocampus</td>
<td><img src="image5" alt="Image" /> Tal: -23 -27 -7</td>
<td><img src="image6" alt="Image" /> Tal: -24 -25 -10</td>
</tr>
<tr>
<td>Right Hippocampus</td>
<td><img src="image7" alt="Image" /> Tal: 26 -31 -4</td>
<td><img src="image8" alt="Image" /> Tal: 25 -31 -6</td>
</tr>
</tbody>
</table>
Figure 3.7 Group-averaged time-courses of neural activity emanating from the hippocampus as revealed by the ER-SAM analysis

Consistent with group-averaged results, individual ER-SAM data revealed bilateral activity in the hippocampal region for ‘correct-new’ scenes with 7 participants showing activity in the left hippocampal region and 6 participants showing activity in the right hippocampal region. For ‘correct-old’ scenes, we found 4 participants showing activity in the left and 4 in the right hippocampal region. All peaks identified in the individual ER-SAM maps were significantly different from baseline (α=0.01) and occurred predominantly within the first 500 ms post-stimulus onset (Table 4.3). Examples of peaks found in or within less than 1 cm of the hippocampus for individual participants are shown in Figure 4.8 and the averaged location of peak hippocampal activity based on individual participants’ ER-SAM maps is shown in Figure 4.9. The contrast between ‘correct-new’ and ‘correct-old’ scenes revealed no significant differences in the hippocampus.
Table 3.3  Source ER-SAM values for individual participants within the hippocampus

<table>
<thead>
<tr>
<th>Subject</th>
<th>Local Maxima (Tal.)</th>
<th>P&lt;.01 Baseline Value (pseudo -z)</th>
<th>Time Activity Reached p&lt;.01 (ms)</th>
<th>Value of 1st Peak (pseudo -z)</th>
<th>Time of 1st Peak (ms)</th>
<th>Value of Max. peak (pseudo -z)</th>
<th>Time of Max. Peak (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>L: -29 -36 -4 R: 35 -25 -21</td>
<td>.37</td>
<td>120 95</td>
<td>.40</td>
<td>125 95</td>
<td>1.0</td>
<td>635</td>
</tr>
<tr>
<td>S2</td>
<td>R: 27 -32 -7</td>
<td>0.27</td>
<td>105</td>
<td>.35</td>
<td>110 72</td>
<td>1.6</td>
<td>150</td>
</tr>
<tr>
<td>S3</td>
<td>L: -21 -32 -7</td>
<td>0.42</td>
<td>110</td>
<td>.67</td>
<td>130 89</td>
<td>.89</td>
<td>330</td>
</tr>
<tr>
<td>S4</td>
<td>L: -33 -40 -4</td>
<td>0.57</td>
<td>150</td>
<td>.57</td>
<td>150 74</td>
<td>.74</td>
<td>460</td>
</tr>
<tr>
<td>S5</td>
<td>L: -29 -28 -8 R: 31 -13 -19</td>
<td>0.25</td>
<td>90 85</td>
<td>.45</td>
<td>95 101</td>
<td>1.01</td>
<td>205</td>
</tr>
<tr>
<td>S6</td>
<td>L: -25 -33 -14 R: 27 -17 -14</td>
<td>0.26</td>
<td>110 210</td>
<td>.33</td>
<td>115 230</td>
<td>.48</td>
<td>215</td>
</tr>
<tr>
<td>S7</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a  n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>S8</td>
<td>L: -29 -13 -19 R: 23 -2 -16</td>
<td>0.32</td>
<td>90 60</td>
<td>.32</td>
<td>90 63</td>
<td>.63</td>
<td>335</td>
</tr>
<tr>
<td>S9</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a  n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>S10</td>
<td>L: -41 -25 -15 R: 39 -21 -11</td>
<td>0.35</td>
<td>85 100</td>
<td>.58</td>
<td>90 76</td>
<td>.76</td>
<td>695</td>
</tr>
<tr>
<td>Average (stdev)</td>
<td>L: -30 -30 -10 (6 9 6) R: 30 -18 -15 (6 10 5)</td>
<td>.35 (.11)</td>
<td>139.29 (50.85)</td>
<td>.48 (.13)</td>
<td>113.57 (23.04)</td>
<td>.79 (.19)</td>
<td>410.71 (194.26)</td>
</tr>
<tr>
<td>Total</td>
<td>L: 7 participants R: 6 participants Either: 8 participants</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Correct-Old

<table>
<thead>
<tr>
<th>Subject</th>
<th>Local Maxima (Tal.)</th>
<th>P&lt;.01 Baseline Value (pseudo-z)</th>
<th>Time Activity Reached &lt; .01 (ms)</th>
<th>Value of 1st Peak (pseudo-z)</th>
<th>Time of 1st Peak (ms)</th>
<th>Value of Max. Peak (pseudo-z)</th>
<th>Time of Max. Peak (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>L: -29 -28 -8</td>
<td>.36</td>
<td>110</td>
<td>.64</td>
<td>120</td>
<td>.95</td>
<td>535</td>
</tr>
<tr>
<td>S2</td>
<td>L: -21 -13 -15</td>
<td>.36</td>
<td>125</td>
<td>.44</td>
<td>160</td>
<td>.57</td>
<td>230</td>
</tr>
<tr>
<td></td>
<td>R: 27 -24 -8</td>
<td></td>
<td>925</td>
<td>.52</td>
<td>930</td>
<td>.52</td>
<td>930</td>
</tr>
<tr>
<td>S3</td>
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<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>S4</td>
<td>L: -33 -25 -11</td>
<td>0.50</td>
<td>230</td>
<td>.51</td>
<td>230</td>
<td>.82</td>
<td>885</td>
</tr>
<tr>
<td>S5</td>
<td>L: -29 -17 -18</td>
<td>0.3002</td>
<td>130</td>
<td>.71</td>
<td>135</td>
<td>1.63</td>
<td>230</td>
</tr>
<tr>
<td></td>
<td>R: 19 -6 -19</td>
<td></td>
<td>180</td>
<td>.98</td>
<td>225</td>
<td>.98</td>
<td>225</td>
</tr>
<tr>
<td>S6</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>S7</td>
<td>R: 23 -29 -11</td>
<td>0.3392</td>
<td>60</td>
<td>.40</td>
<td>65</td>
<td>.54</td>
<td>130</td>
</tr>
<tr>
<td>S8</td>
<td>R: 27 -2 -16</td>
<td>0.4387</td>
<td>135</td>
<td>.90</td>
<td>165</td>
<td>.90</td>
<td>165</td>
</tr>
<tr>
<td>S9</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>S10</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Average (stdev)</td>
<td>L: -28 -21 -13  (5 7 4)</td>
<td>.38 (.07)</td>
<td>148.75 (54.83)</td>
<td>.58 (.12)</td>
<td>161.25 (48.71)</td>
<td>.99 (.45)</td>
<td>470 (311.80)</td>
</tr>
<tr>
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<td>R: 24 -15 -14</td>
<td></td>
<td>325.00 (403.05)</td>
<td>.70 (.28)</td>
<td>346.25 (394.72)</td>
<td>.74 (.24)</td>
<td>362.5 (380.36)</td>
</tr>
</tbody>
</table>

Total: L: 4 participants  
R: 4 participants  
Either: 6 participants

Table includes Talairach co-ordinates and time of first and maximum peak for participants showing activity above threshold in or within 1cm of the hippocampus (Hpc) for ‘correct-new’ and ‘correct-old’ in individual ER-SAM maps (L = left hippocampus; R = right hippocampus).
Figure 3.8 Representative individual time-courses of hippocampal activity

<table>
<thead>
<tr>
<th>Left Hippocampus</th>
<th>Correct-New</th>
<th>Correct-Old</th>
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<th>Right Hippocampus</th>
<th>Correct-New</th>
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</table>

Individual maps and time courses from the left and right hippocampus for ‘correct-new’ (left) and ‘correct-old’ (right) scenes as revealed by the ER-SAM analysis. Neural sources are marked with red dots in the MRIs and the Talairach coordinates are provided.

Figure 3.9 The averaged location of hippocampal activity based on individual ER-SAM maps

<table>
<thead>
<tr>
<th>Left Hippocampus</th>
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Black cross-hairs indicate the location of the hippocampal peak, also reported in Talairach coordinates.

3.5 Discussion

We studied the potential of advanced MEG approaches to localize and outline different aspects of hippocampal activity in a memory recognition task by using three different analyses: SAM for event related changes in spectral power, ITC as a measure of stimulus related coherence in neural
responses and ER-SAM as volumetric representation of the averaged event related neural response. We observed hippocampal activity predominantly in the theta frequency band and within the first 200 ms post-stimulus onset for both the successful recognition of novel (‘correct-new’) and previously studied (‘correct-old’) scenes. Analyzing multiple features of electromagnetic brain activity in conjunction with previous work, provided converging evidence for the feasibility of localizing activity from the hippocampus with MEG (Breier et al., 1998; Campo, Maestu, Capilla, et al., 2005; Hamada et al., 2004; Hanlon et al., 2003; Hanlon et al., 2005; Ioannides et al., 1995; Kirsch et al., 2003; T. Martin et al., 2007; Nishitani et al., 1998; Tesche, 1997; Tesche & Karhu, 1999, 2000; Tesche et al., 1996). Below, we summarize our findings from the different data analyses and discuss its advantages and limitations. In considering the current findings to previous work, we suggest that the functional role of the hippocampus in recognition memory may be related to general processing requirements common to recognizing both novel and previously studied information, such as comparing the externally presented stimuli with internal memory traces. Further, we argue that hippocampally-mediated processes supporting recognition memory occur rapidly following stimulus onset. The observation of early hippocampal activity has implications for theories regarding memory; namely, recognition may be an obligatory process and/or may influence perceptual processing.

3.5.1 Multiple MEG data analyses

In applying three different analysis techniques, we were able to extract unique complementary information pertaining to hippocampal activity during a recognition memory task. Specifically, information regarding the underlying spectral frequencies and temporal dynamics of hippocampal responses were outlined. When we viewed the group-averaged SAM results, no activity above threshold levels was observed in the hippocampus for either ‘correct-new’ or ‘correct-old’ scenes.

SAM analysis is based on the analysis of signal power changes between the pre- and post-stimulus time window and the signal power measure includes both time-locked evoked responses and non-phase-locked or induced activity. It is possible that the signal power changes in hippocampal activity did not reach significance threshold because it occurs predominantly as an evoked response and the inclusion of induced activity reduced its overall statistical power (but see, Gudarian & Duzel, 2005). It is also possible that the permutation test used was too
conservative. The only activity revealed to be significant after the permutation test were superficial sources within the visual cortex, even though multiple regions beyond the visual cortex, such as the parietal and frontal cortex, are thought to be involved in visual recognition (e.g. Buckner, 2003; Buckner, Wheeler, & Sheridan, 2001; Tulving, Markowitsch, Craik, Habib, & Houle, 1996; Weis, Klaver, Reul, Elger, & Fernandez, 2004). However, when we further examined the data by lowering the threshold, we found spatially distinct activity in the right hippocampus for ‘correct-new’ scenes and near the right hippocampus or parahippocampal gyrus for ‘correct-old’ scenes, in the theta frequency band during the 0–250 ms time interval. This suggests that hippocampal activity may include some signal power changes in the theta frequency band that is not strictly phase-locked, but this was not strong enough to reach statistical significance. The permutation test estimates a threshold value common for all voxels in the brain, but the distribution is likely not homogeneous across the brain volume. Further, the level at which neural activity is determined to be significantly different from baseline depends on the number of neurons active, the amplitude of activity, and the amount of synchrony among neural assemblies. While the amount of neural synchrony does not change with distance from the sensors, amplitude of activity becomes weaker farther away from the sensors, making it very difficult for deep source activity to reach threshold levels. Altogether, this suggests that the permutation test may be too conservative for an examination of deep source activity and/or the dominant feature of the hippocampal response in a recognition memory task is not induced.

With ITC analysis we found high levels of bilateral hippocampal coherence in the theta frequency range during the 0–500 ms post-stimulus onset time interval for both ‘correct-new’ and ‘correct-old’ scenes. In examining the group-averaged volumetric maps, spatially distinct sources of activity could be seen in the right hippocampus across the entire time interval and for both types of scenes. This was confirmed in the individual participant analysis. However, from the ITC maps, it can be seen that hippocampal theta band activity was most synchronous during the first 250 ms after stimulus-onset (Fig. 3 and Fig. 4), and became less phase-locked to the stimulus over time. Group-averaged results also revealed theta band synchrony in the left hippocampus during 250–500 ms for ‘correct-old’ scenes. This was confirmed in individual analyses for two participants. Likely, hippocampal synchrony in most participants was below the threshold for individual analyses, but averaging data from all of the participants increased statistical power. The ITC statistic is bound between 0 and 1, thus it is unlikely that single
individual data had skewed the group results toward significance. Despite this, it is important to note that theta band synchrony in the right hippocampus was consistently found in both the group-averaged and the individual data.

Using ER-SAM, we found significant bilateral hippocampal activity for ‘correct-new’ scenes in the group-averaged data. This was confirmed for the majority of participants in the individual analysis. Group-averaged data also revealed significant left parahippocampal activity for ‘correct-old’ scenes, which was found for 4 participants in the individual analysis. It is important to note that the individual analysis was completed at $\alpha=.01$ whereas the group-averaged results were viewed at $\alpha=.05$. This more conservative criterion for the individual analysis may have resulted in smaller than expected number of participants showing activity in the hippocampal region. In the group-averaged data, hippocampal activity was found during the 100–150 ms post-stimulus period for both ‘correct-new’ and ‘correct-old’ scenes (Breier et al., 1998; Gonsalves et al., 2005; Guderian & Duzel, 2005).

While SAM is an amplitude-based analysis method, ITC, in contrast, measures the degree of neural synchrony, and thus provides a more homogeneous statistic across the brain volume. Thus, ITC may be a more appropriate analysis method for the examination of deep sources in the presence of activity from other more superficial sources. However, ITC improves the signal-to-noise ratio for the synchrony measure by integrating over relatively long (e.g. 250 ms) time windows (Bardouille & Ross, 2008). ER-SAM, in contrast, can determine the latency of the maximal evoked response with millisecond precision. These two methods can be used in a complementary fashion to understand the temporal and spectral dynamics of evoked responses. In applying three complementary analysis methods to the same set of data, we were able to consistently localize hippocampal activity in two of the three methods. Below, we explore the similarities and differences in findings from ITC and ER-SAM.

### 3.5.2 Consistency across the data analyses

Both ITC and ER-SAM revealed time-locked hippocampal activity within the first 250 ms of viewing ‘correct-new’ and ‘correct-old’ scenes. Frequency analysis (ITC) also revealed that this hippocampal activity consistently oscillated within the theta frequency band. While the obtained results were consistent in terms of temporal dynamics and frequency of hippocampal activity, there were some differences in the findings that should be discussed.
For ‘correct-new’ scenes, group-averaged results revealed significant neural synchrony (ITC) in the right hippocampus and significant increases in evoked activity (ER-SAM) in bilateral hippocampi. This is consistent with previous studies showing that whereas verbal information tends to elicit activity in the left hippocampus, visual information, such as that used in the present experiment, tends to elicit activity in either the right or bilateral hippocampi (Breier et al., 1998; Golby et al., 2001; Gonsalves et al., 2005; Kelley et al., 1998; A. Martin, Wiggs, & Weisberg, 1997; Stern et al., 1996). It is possible that activity in the left hippocampus failed to reach significance in the ITC analysis.

For ‘correct-old’ scenes, ITC localized activity to the hippocampus and ER-SAM showed that the peak of activity was within the parahippocampal gyrus. It is possible that both the hippocampus and parahippocampal gyrus were activated (Gonsalves et al., 2005; Kapur et al., 1995; Nyberg, McIntosh, Houle, Nilsson, & Tulving, 1996; Rombouts, Barkhof, Witter, Machielsen, & Scheltens, 2001; Stark & Okado, 2003), but in the ER-SAM analysis, the peak of activity was placed within the parahippocampal gyrus. As mentioned earlier, if the hippocampus and parahippocampus are active simultaneously, MEG tends to place the peak of activity within a single source (Stephen et al., 2005). It is also possible that the signal-to-noise ratio for ‘correct-new’ scenes was higher than that for ‘correct-old’ scenes since the average number of trials was greater. A higher signal-to-noise ratio allows for greater power and sensitivity to the localization of functional MEG data, and thus greater ability to localize deeper sources (Hämäläinen et al., 1993).

While both ITC and ER-SAM analyses identify brain activity that is time locked to the stimulus event, ITC is more specific in frequency information, and ER-SAM is more specific in temporal information. However, an evoked response will generate high coherence values at low frequencies (i.e. delta and theta) over sub-second time intervals. Thus, it is difficult to differentiate between an evoked response and synchronous oscillatory activity in this case. Given that ITC and ER-SAM examine different aspects of hippocampal activity, it may not be surprising that differences in laterality and precise localization are observed. This makes clear that claims about hippocampal activity have to consider the specific observed feature of brain activity.
The present study, in conjunction with previous MEG studies, shows that hippocampal activity can be successfully localized using MEG, and that it is characterized by different aspects pertaining to evoked- versus induced-response, frequency, and time. Further, depending on which aspect of the hippocampal activity one is interested in, it is important to select the appropriate analysis method. In the present experiment, we found that hippocampal responses occurred predominantly as a time-locked or evoked response, in the theta frequency band and within 200 ms following stimulus onset during recognition of previously studied and novel stimuli. Critically, we found no significant differences in the hippocampus between ‘correct-new’ and ‘correct-old’ scenes using ER-SAM. This suggests that the functional role of the hippocampus may be related to general memory processing requirements common for both the viewing of new and old information (N. J. Cohen et al., 1999). Below, we focus on the theoretical implications for the functional role of the hippocampus in light of the present results.

3.5.3 Theoretical implications

A general processing requirement for viewing new and old information in a recognition task is the comparison of the external stimulus that is represented in the sensory cortices with internal memory traces that may be stored within multiple neural assemblies (Ryan et al., 2008). This ‘comparison’ process (James, 1983; Ryan & Cohen, 2004) is thought to rely not only on the hippocampus (Hannula, Federmeier, & Cohen, 2006; Rugg et al., 1996; Ryan & Cohen, 2004), but also sensory cortices where external and internal information is processed and held online (Ryan et al., 2008; Vaidya, Zhao, Desmond, & Gabrieli, 2002; Wheeler, Petersen, & Buckner, 2000), and prefrontal regions where search strategies are executed and monitored (Buckner, 2003; Korniat, 2000). During comparison, the functional role of the hippocampus may be to coordinate activity between different neural regions and allow for the exchange of information in a phase-locked manner via theta oscillations (Buzsaki, 2002; Duzel, Picton, et al., 2001; Duzel, Vargha-Khadem, et al., 2001; Rugg et al., 1996; M. E. Smith & Halgren, 1989). The current findings revealed that hippocampal oscillations occurred within the theta frequency band, consistent with other work that has observed hippocampal theta oscillations in animal (Huxter, Burgess, & O’Keefe, 2003; O’Keefe & Nadel, 1978; Wiebe & Staubli, 2001), human intracranial (Raghavachari et al., 2001; Rizzuto et al., 2003 Sederberg, Kahana, Howard, Donner, & Madsen, 2003) and imaging studies (Guderian & Duzel, 2005; Osipova et al., 2006; Tesche & Karhu, 2000).
An examination of the temporal dynamics revealed that hippocampal activity was evident as early as 120–130ms following stimulus onset (Breier et al., 1998; Gonsalves et al., 2005). This time frame is typically associated with perception of externally presented stimuli, independent of the hippocampus (Tsivilis et al., 2001), however, the current findings suggest that the hippocampus may be involved during early perceptual processing of old/new information. The functional role of the hippocampus during this stage may be to aid non-mnemonic visual discrimination of the externally presented stimuli (Barense, Gaffan, & Graham, 2007; Lee et al., 2005), or it may reflect part of a feed-forward sweep from visual cortices in order to prime other cortical regions for subsequent processing, such as recognition memory in the present study (Foxe & Simpson, 2002; Herdman et al., 2007). Alternatively, early onset of hippocampal activity may also suggest that processes related to memory recognition occur rapidly and perhaps in an obligatory fashion (Ryan, Hannula, et al., 2007; Ryan et al., 2008). However, since participants were instructed to perform a recognition task and were in a ‘retrieval’ mental set, the current results cannot address the issue of whether recognition memory is obligatory or not. At the very least, evidence of such an early onset of hippocampal activity suggests that processes related to recognition memory begin rapidly and operate in conjunction with, or parallel to, visual processing. Indeed, conscious identification of a visual stimulus may be aided by rapid access to stored memory representations (Bar, 2003, 2004; Bar, Kassam, et al., 2006; Ryan et al., 2008). Regardless of whether the early onset of hippocampal activity represents a contribution of mnemonic information to the building of perceptual representations (Ryan et al., 2008), perceptual processing in the absence of any memory component (Lee et al., 2005), or a preparatory response for subsequent processing (Herdman et al., 2007), the present findings demonstrate that hippocampal responses are evident at time when perception is thought to occur.

3.5.4 Concluding remarks and future considerations

The results of this study, together with previous literature, offer converging evidence in support of the feasibility of using MEG to record activity from the hippocampus. Unlike other neuroimaging techniques, MEG can outline the frequency range and temporal dynamics with good spatial resolution. This study highlights the importance of choosing an appropriate analysis method for the localization of deep sources. Specifically, it is critical to use localization algorithms that are not biased toward superficial sources, allow for the imaging of simultaneous sources, and use co-registration of MEG and structural MRI data. We observed that processing
of studied versus novel stimuli recruited the hippocampus at similar times and in a similar spectral frequency, suggesting that the hippocampus may be involved in general recognition memory processes. Specifically, the hippocampus may contribute to comparison achieved via theta oscillations (Buzsaki, 2002). Also, onset of hippocampal activity occurred rapidly after stimulus onset, during a time typically associated with visual perception. Future studies are needed in order to distinguish between mnemonic vs. non-mnemonic accounts of early hippocampal responses.

In addition to examining incidences of normal memory functioning, MEG can be applied to the study of memory impairments. It has long been noted that memory impairments are associated with aging and a number of disorders such as Alzheimer's disease, temporal lobe epilepsy, post-traumatic stress disorder, schizophrenia, among others (Eichenbaum & Cohen, 2001). While other neuroimaging techniques such as PET and fMRI show a relationship between decreases in memory performance and reduced hippocampal activity, MEG may reveal patterns of underlying spatiotemporal dynamics that are associated with distinct performance profiles, and are subsequently altered as a function of neurological impairment. Therefore, MEG has the potential to illuminate the nature of hippocampally-mediated memory disorders as well as the nature of normal.

3.6 Acknowledgments

The authors thank Guy Earle for programming and other technical assistance, and Christina Villate for her assistance with the stimuli. This work was supported by funding from the Natural Sciences and Engineering Research Council of Canada (JDR), the Canada Research Chairs Program (JDR), Michael Smith Foundation for Health Research (ATH), and a Canadian Graduate Scholarship from the Natural Sciences and Engineering Research Council of Canada (LR).
Chapter 5
Emotional Associations Alter Processing of Neutral Faces

4 Emotional associations alter processing of neutral faces

4.1 Abstract

A number of studies have shown that the processing of emotional as compared to neutral information is associated with different patterns in eye movement and neural activity. However, the ‘emotionality’ of a stimulus can be conveyed not only by the physical properties of the stimulus itself, but also by the context in which it appears and/or the information with which it is associated. We examined how association with emotional information may influence processing of otherwise neutral faces by using eye movement monitoring (EMM) and magnetoencephalography (MEG). Participants studied a series of faces, each with a neutral expression, paired subsequently with either a negative or a neutral sentence, and then the same face was presented again in isolation. The face and the sentence never appeared simultaneously on the screen. EMM revealed that viewing of isolated faces paired with negative versus neutral sentences was associated with increased viewing of the eye region. Source localization of MEG results were performed using event-related synthetic aperture magnetometry minimum-variance beamformer algorithm (ER-SAM) coupled with the partial least squares (PLS) multivariate statistical approach. This revealed that viewing of isolated faces paired with negative versus neutral sentences was associated with increased neural activity between 600-1500 ms after stimulus onset in emotion processing regions such as the cingulate, medial prefrontal cortex, and amygdala, as well as posterior regions such as the precuneus and occipital cortex. Viewing of isolated faces paired with neutral versus negative sentences was associated with increased activity in the parahippocampal gyrus during the same time window. The above results suggest that emotion may modulate associated, but otherwise neutral information, by altering visual processing and the type of representation that is formed.

4.2 Introduction

We are constantly involved in the interpretation of social and emotional cues from those around us. Such cues can be conveyed via facial expressions (e.g. Adolphs, 2003) and facial appearance (e.g. Bar, Neta, & Linz, 2006; Olson & Marshuetz, 2005; Willis & Todorov, 2006), as well as by biographical information (e.g. Carlston & Skowrons, 1994; Todorov & Uleman, 2002, 2003,
For example, imagine being at a party and being introduced to two different people who appear very neutral and non-threatening. However, right before you meet them, you are told that one person has just gotten out of jail for murder and the other person is working on a PhD. Research from social psychology suggests that from this minimal information, you will form a rapid, and perhaps automatic, and very different impression of the two people (e.g. Todorov & Uleman, 2002, 2003, 2004). As a consequence of forming such rapid impressions, this may then lead to differences in the way in which we perceive and remember otherwise neutral information (i.e. the person’s face).

A number of studies have shown that the processing of emotional versus neutral stimuli is characterized by different patterns of eye movement behaviour and neural activity. For example, compared with faces in a neutral expression, viewing to faces expressing threat is characterized by an overall increase in the number of fixations directed to the face, an increase in the number of regions sampled within the face (Bate et al., 2009), an increase in sampling of internal features of the face (Calder et al., 2000; Green, Williams, & Davidson, 2003b; M. L. Smith et al., 2005), and an increase in viewing the eye region of the face (e.g. Adolphs, Gosselin, et al., 2005; Gamer & Buchel, 2009; Itier & Batty, 2009). In addition to differences in eye movement behaviour, viewing of faces expressing emotion versus those in a neutral expression is accompanied by increased neural activity in regions of the brain, such as the amygdala, anterior insula and basal ganglia, which are associated with emotional processing (e.g. Adolphs, 2002; Adolphs, Tranel, & Damasio, 2003; Haxby, Hoffman, & Gobbini, 2002; Phelps, 2006). It is suggested that such differences in eye movement behaviour and neural activity may serve to aid in the recognition of different facial expressions and of the person’s identity (Bate et al., 2009; Haxby et al., 2002) and aid in the assessment of the person’s level of threat and their intentions (e.g. Haxby et al., 2002; Spezio, Huang, Castelli, & Adolphs, 2007).

However, the manner in which external information is processed is determined not only by the physical properties of the stimulus (i.e. facial expression), but also by the context in which the stimulus appears, as well as by prior knowledge (e.g. Althoff & Cohen, 1999; G. R. Loftus & Mackworth, 1978; Ryan, Hannula, et al., 2007). Aviezer and colleagues (Aviezer et al., 2008), demonstrated that identical facial expressions may be interpreted as different emotions depending on the context in which the facial expressions were presented. For example, viewing of a face expressing anger within a neutral context was associated with an increased number of
fixations to the upper region of the face (i.e. eyes and eye brows) and viewing of a face expressing disgust within a neutral context was associated with an equal number of fixations directed to the upper and lower region of the face (i.e. lower nose and mouth region). However, when the faces were placed into an emotional context, viewing patterns changed systematically. Specifically, when a face expressing anger was placed within a disgust context (i.e. on a body expressing disgust), participants directed an equal number of fixations to the upper and lower region of the face. Similarly, when a disgust face appeared within an angry context, participants directed significantly more fixations to the upper versus lower region of the face.

If perception of emotional expressions is malleable and depends in part on the context in which the expressions appear, then it is possible that the perception of neutral faces is also malleable and depends on the context in which they appear. One goal of the present study was to examine the extent to which association with emotional information may influence viewing of, and memory for, faces with neutral expression. After all, it is likely important to not only assess the level of threat and/or intentions of the ‘murderer’ as opposed to the ‘student’, but also to subsequently recognize him/her such that appropriate action may be taken (e.g. run away versus initiate a conversation). In support of this, prior research shows that emotions may enhance memory for both the emotional item (e.g. Christianson & Loftus, 1987 Cahill et al., 1996; Heuer & Reisberg, 1990; Phelps et al., 1997), as well as information associated with it (e.g. D'Argembeau & Van der Linden, 2004, 2005; MacKay et al., 2004).

In addition to examining whether association with emotional information may influence viewing of, and memory for, neutral faces, another goal of the present study was to examine precisely when emotion/context may exert its influence on associated information and how such processes may be supported in the brain. Aviezer and colleagues (Aviezer et al., 2008) found that the effects of context exerted their influence on eye movement behaviour early on during processing of different facial expressions, i.e. within the first 1000 ms after stimulus onset. This prompted the researchers to suggest that the context in which an item appears may actually alter perceptual processing. However, it is unclear exactly when during the first 1000 ms that context may be exerting its influence. Previous neuroimaging studies suggest that perceptual processing occurs largely within the first 250 ms after stimulus onset, as opposed to a later time window (e.g. 250-1500 ms) during which conceptual/semantic processes and/or the retrieval of associated information are largely purported to occur (e.g., Donaldson & Rugg, 1998, 1999; Itier et al.,
In light of this, the results from Aviezer’s study can be explained in one of two ways. First, as the authors suggest, the emotional context may have been invoked during the perceptual processing of the face, leading to differences in the actual visual percept that was constructed. Alternatively, the emotional context may not have influenced perceptual processing of the face per se; rather, it may have been invoked after perceptual processing of the face had occurred. In order to distinguish between these two possibilities, it is necessary to examine precisely when context may exert its influence on processing.

The present work had three goals, to examine the extent to which emotion modulates (1) viewing of associated neutral stimuli; (2) underlying neural activity invoked during viewing of associated neutral stimuli, and precisely when; and (3) subsequent memory for associated neutral stimuli. To address these goals, eye movement monitoring and magnetoencephalography (MEG) were used to characterize eye movement behaviour and neural activity, respectively. Eye movements have been shown to be sensitive to the effects of emotion and context (e.g. Aviezer et al., 2008; Bate et al., 2009; Green et al., 2003b; Riggs et al., 2010; Riggs et al., 2011). MEG is a non-invasive neuroimaging technique that measures the magnetic field differences produced by population of neurons (Hari et al., 2000; Hämäläinen et al., 1993), providing recording of neural activity with temporal resolution on the order of milliseconds and with spatial resolution comparable to that of functional magnetic resonance imaging (fMRI; Miller et al., 2007). Critically, through its precise timing information, MEG has been successfully utilized to study emotion processing (Cornwell et al., 2008; Furl et al., 2010; Garolera et al., 2007; Hung et al., 2010), as well as how knowledge and/or prior experience can influence the manner by which perceptual processing occurs (Riggs et al., 2009; Ryan et al., 2008).

In the present experiment, participants were presented with a neutral face (Face 1) followed by either a negative or a neutral sentence and, finally the neutral face was presented again in isolation (Face 2). During this study phase, eye movements and neural activity were recorded simultaneously. If association with emotional information affects processing of neutral stimuli, then differences in eye movement patterns and neural activity should occur during re-presentation of the face depending on whether the face had been previously paired with a negative or a neutral sentence. It was predicted that viewing of a face paired with a negative versus neutral sentence would elicit differences in viewing and underlying neural activity,
specifically, in enhanced activation of regions implicated in emotion processing such as the amygdala, cingulate and anterior insula (Adolphs, 2002; Adolphs et al., 2003; Chen et al., 2009; Garolera et al., 2007; Haxby et al., 2002; Hirata et al., 2007; Phelps, 2006), attention and facial processing such as the precuneus and fusiform gyrus (Cavanna & Trimble, 2006; Deffke et al., 2007; Fenker, Schott, Richardson-Klavehn, Heinze, & Duzel, 2005), memory and binding such as the prefrontal cortices and medial temporal lobe (Badgaiyan, Schacter, & Alpert, 2002; N. J. Cohen et al., 1999; Daselaar et al., 2001; Squire & Zola-Morgan, 1991; Yonelinas, Hopfinger, Buonocore, Kroll, & Baynes, 2001), and the processing of person identity and biographical information such as the superior temporal sulcus (Haxby et al., 2002; Todorov, Gobbini, Evans, & Haxby, 2007). Further, if associated information is invoked during the time of perceptual processing, then such eye movement and neural differences should manifest early during viewing (<200 ms after stimulus onset).

In order to examine whether association with emotional information has an effect on memory, during the test phase, participants were presented with a series of faces and were required to decide whether the presented face was novel, previously paired with a neutral sentence or previously paired with a negative sentence. If association with emotional information enhanced memory, then participants should be more accurate in identifying faces previously presented with a negative sentence than those previously presented with a neutral sentence.

To the best of our knowledge, no study has examined how association with emotion may influence the immediate processing of otherwise neutral stimuli. If differences in eye movement patterns and neural activity are found between processing neutral stimuli associated with emotional versus neutral information, this would suggest that emotion can influence the visual processing, and the mental representation, of associated neutral stimuli in a top-down manner that is independent of the neutral stimuli’s physical properties. Thus, we may not only form different impressions of the ‘murderer’ and ‘student’ (Todorov & Uleman, 2002, 2003, 2004), but we may also look at them differently, think about them differently and perhaps even remember them differently.
4.3 Methods

4.3.1 Participants

Twelve young adults (mean age = 21.6 years, 5 males) from the Rotman Research Volunteer Pool participated for $10 per hour. All participants had no history of neurological or clinical disorders, no history of head trauma and had normal or corrected-to-normal vision. All participants were either native English speakers or had at least twelve years of experience with English.

4.3.2 Stimuli and Design

The stimuli used consisted of 300 black and white, non-famous male faces with a neutral expression selected from a database of face images as outlined by Schmitz and colleagues (Schmitz, Cheng, & De Rosa, 2010). Briefly, the photographs showed front-view non-expressive faces. Faces were cropped and did not contain hair nor other nonfacial features. To prevent discrepancies in the spatial orientation and location of the face stimuli over trials, the eyes and philtrum of each image was aligned to a standard 3-point Cartesian space (for more details see: Schmitz et al., 2010). The faces were placed against a uniform black background – the resulting image was 300x300 pixels. Each face was randomly paired with a negative (e.g. “This person is a rapist”) and a corresponding neutral sentence (e.g. “This person is a linguist”). Each pair of sentences differed only by one critical word which was either negative or neutral, and was matched for the number of syllables (e.g. rapist versus linguist). All of the sentences were previously rated by 10 participants (mean age = 21.3, 4 males) on a scale of 1-5 for each of the following factors: familiarity (1 = not familiar at all, 5 = very familiar), tabooess (1 = not taboo at all, 5 = very taboo), arousal (1 = not arousing at all, 5 = very arousing), valence (1 = very negative, 3 = neutral, 5 = very positive) and coherence (1 = not coherent at all, 5 = very coherent). Negative and neutral sentences were matched for familiarity (p = .20) and coherence (p = .97). Critically, negative sentences were judged to be more taboo (p < .0001), negative (p < .0001), and arousing (p < .0001). The mean values can be found in Table 5.1.
Table 4.1 The mean and SEM of ratings for the negative and neutral sentences used in experiment

<table>
<thead>
<tr>
<th></th>
<th>Mean for Negative Sentences (SEM)</th>
<th>Mean for Neutral Sentences (SEM)</th>
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<tbody>
<tr>
<td>Familiarity</td>
<td>4.74 (.03)</td>
<td>4.79 (.03)</td>
</tr>
<tr>
<td>Coherence</td>
<td>4.84 (.02)</td>
<td>4.84 (.02)</td>
</tr>
<tr>
<td>Tabooiness</td>
<td>3.09 (.08)</td>
<td>1.06 (.02)</td>
</tr>
<tr>
<td>Valence</td>
<td>1.75 (.04)</td>
<td>3.20 (.04)</td>
</tr>
<tr>
<td>Arousal</td>
<td>2.68 (.06)</td>
<td>1.21 (.02)</td>
</tr>
</tbody>
</table>

During the study phase, participants were shown 200 unique faces across 5 study blocks (40 per block). Each face was paired with either a negative (100) or neutral (100) sentence. Faces were displayed in a pseudo random order such that no more than 3 negative or 3 neutral face-sentence-face pairings appeared in succession. Each study block contained 20 faces paired with a negative sentence, and 20 faces paired with a neutral sentence. In the test phase, participants were shown 300 faces in isolation (i.e., without sentences): 200 faces were previously viewed (100 old-negative, 100 old-neutral) and 100 faces were novel (new). Faces were presented in a pseudo random order such that no more than 3 faces of each type appeared in succession. Counterbalancing was complete such that each face appeared as studied with a neutral sentence, studied with a negative sentence, and as a novel face equally often across participants.

4.3.3 Procedure

Eye movements and neural activity were recorded simultaneously throughout the study phase. The test phase of the experiment took place outside of the imaging suite and only eye movements and explicit reports were recorded. During each trial of the study phase, a face was presented for 3000 ms (Face 1) followed by a sentence which was presented for 4000 ms. Subsequently, a blank screen was presented for 400 ms and then a fixation cross was presented for 100 ms in order to direct the participant’s eyes back to the centre of the screen. Following this, Face 1 was re-presented again, in isolation, for 3000 ms (Face 2; Figure 5.1). Participants were then asked to indicate via button press whether they would want to approach, avoid or stay neutral to the face. The purpose of the task was to encourage participants to process the meaning of the face-sentence pairings. Throughout the study phase, participants were instructed to freely view the faces and sentences presented. There was a 1500 ms inter-trial interval which consisted of a fixation cross in the center of a blank screen. Participants were instructed to fixate on the central
cross whenever it appeared. During a 30-minute delay (approximately) between the study and test phases, participants moved from the imaging suite to the eye tracking room and completed a background information form. During the test phase, 300 faces were presented (100 new, 100 old-negative, 100 old-neutral) in isolation, i.e., without any sentence pairings. Each face was presented for 5000 ms and participants were instructed to freely view each face, and indicate via a button press whether the face was previously viewed and paired with a negative sentence (old-negative), previously viewed and paired with a neutral sentence (old-neutral), or novel (new).

**Figure 4.1 Experimental procedure**

Participants freely viewed a face (Face 1) followed by a sentence that was either negative or neutral. The same face was presented again (Face 2) and participants were asked to judge whether they would want to approach, avoid or neither approach or avoid (remain “neutral” to) that person.

### 4.3.4 Data Acquisition

Eye movements were measured with either a SR Research Ltd. Eyelink 1000 remote eyetracker (during the study phase in the MEG suite) or a SR Research Ltd. Eyelink II eye tracker (during the test phase outside of the MEG suite). Each eyetracker recorded eye movements at a rate of
500 Hz and with a spatial resolution of 0.1 degrees. A 9-point calibration was performed at the start of each block followed by a 9-point calibration accuracy test. Calibration was repeated if the error at any point was more than 1 degree. Drift corrections were performed at the beginning of each trial if necessary.

MEG recordings were performed in a magnetically shielded room, using a 151-channel whole head first order gradiometer system (VSM-Med Tech Inc.) with detection coils uniformly spaced 31 mm apart on a helmet-shaped array. Participants sat in an upright position, and viewed the stimuli on a back projection screen that subtended approximately 31 degrees of visual angle when seated 30 inches from the screen. The MEG collection was synchronized with the onset of the stimulus by recording the luminance change of the screen. Participant’s head position within the MEG was determined at the start and end of each recording block using indicator coils placed on nasion and bilateral preauricular points. These three fiducial points established a head-based Cartesian coordinate system for representation of the MEG data.

In order to specify/constrain the sources of activation as measured by MEG and to co-register the brain activity with the individual anatomy, a structural MRI was also obtained for each participant using standard clinical procedures with a 3T MRI system (Siemens Magnetom Trio whole-body scanner) located at Baycrest.

4.3.5 Analysis for Study Phase

Eye Movement Analysis for the Critical Word. In order to provide evidence that the emotion manipulation had an effect on eye movement behaviour, we first examined differences in viewing the critical word when it was negative versus when it was neutral. Analysis of eye movements was performed with respect to the experimenter-drawn region of interest corresponding with the critical word within the sentence.

Eye Movement Analysis for Faces. Differences in the eye movement patterns made to faces that had been paired with negative versus neutral sentences were taken as evidence that the processing of faces may be changed via association with emotional information. Therefore, we compared eye movement behavior during viewing of Face 2 following a negative sentence (Face2–Negative) versus that of Face 2 following a neutral sentence (Face2–Neutral). As a control condition, we also compared eye movement during viewing of Face 1 that preceded a
negative (Face1–Negative) versus neutral sentence (Face1–Neutral). Since these faces had not yet been paired with either a negative or a neutral sentence, there should be no differences in measures of eye movement behaviour. Viewing to regions corresponding to the location of features within the face, i.e. eyes, nose, and mouth, were examined.

_Eye Movement Measures_: Eye movement analysis for both the critical word and face included measures of early viewing and measures of overall viewing (for more details see: Hannula et al., 2010). Measures of early viewing included: duration of first fixation, duration of first gaze, and number of fixations within first gaze. A fixation is defined as the absence of any saccade (e.g., the velocity of two successive eye movement samples exceeds 22 degrees per second over a distance of 0.1°), or blink (e.g., pupil is missing for 3 or more samples) activity. The first gaze designates the first time that the eyes enter a region of interest. Duration of first gaze is the total time spent within a particular region of interest on the first gaze before moving away from it. Number of fixations within first gaze is the total number of fixations directed to a particular region of interest during the first gaze before moving out of that region. Measures of overall viewing included: average duration of fixations, number of fixations and number of transitions into the region of interest, i.e. the number of times a particular region of interest is viewed.

_MEG Analysis for Faces_. Similar to the eye movement analysis for faces, spatiotemporal differences in neural activity underlying viewing of faces that had been paired with negative versus neutral sentences were taken as evidence that the processing of faces may be changed via association with emotional information. Further, differences in neural activity occurring within the first 200 ms were taken as evidence that association with emotion changes perceptual processing of neutral faces. We compared neural activity during viewing of Face 2 following a negative sentence (Face2–Negative) versus that of Face 2 following a neutral sentence (Face2–Neutral). A comparison of neural activity underlying viewing of Face 1 that preceded a negative (Face1–Negative) versus neutral sentence (Face1–Neutral) was also included as a control condition.

_MEG Analysis_. Source activity was estimated using the synthetic aperture magnetometry (SAM) minimum-variance beamformer (Robinson & Vrba, 1999; Van Veen et al., 1997) across the whole brain on a grid with regular spacing of 8 mm. The beamformer analysis, using the algorithm as implemented in the VSM software package, was based on individual multisphere
models, for which single spheres were locally approximated for each of the 151 MEG sensors to the shape of the cortical surface as extracted from the MRI. The MEG beamformer minimizes the sensitivity for interfering sources as identified by analysis of covariance in the multichannel magnetic field signal while maintaining constant sensitivity for the source location of interest. The covariances were calculated based on the entire trial duration (−1000 ms to 10,500 ms) with a low-pass filter at 30 Hz. Thereafter, the resultant SAM weights were applied to the MEG sensor data separately for epoch of interest based on an event-related spatial-filtering approach (ER-SAM; Cheyne et al., 2006; Robinson, 2004) as used in our previous studies (Fujioka, Zendel, & Ross, 2010; Moses, Brown, Ryan, & McIntosh, 2010). The MEG data were epoched from 100 ms prior to stimulus onset to 2800 ms after separately for each condition (i.e. Face2-Negative, Face2-Neutral). Using the MEG data of the entire segment of the trial to compute SAM separately from the epoch of interest is necessary to ensure that the resultant ER-SAM maps for each condition were due to differences in the MEG data and not due to differences in the spatial filter. Before applying the beamformer to each single epoch of magnetic field data, artifact rejection using a principal component analysis was performed such that field components larger than 1.5 pT at any time were subtracted from the data at each epoch. This procedure is effective in removing large artifacts caused by eye blinks (Kobayashi & Kuriki, 1999; Lagerlund, Sharbrough, & Busacker, 1997). Using the spatial filter, single-epoch source activity was first estimated as a pseudo-Z statistic for each participant and each condition. The time series of the source power within 1–30 Hz was then calculated for each single source waveform. Finally, the representation of the evoked response was obtained as a time series of the average power across trials normalized to the pooled variance across trials for each voxel and time point. These individual functional maps were then spatially transformed to the standard Talairach space using AFNI (National Institute of Mental Health, Bethesda, MD, USA), using the same transform applied to the anatomical MR image, and averaged across all participants. For each participant, functional data from the MEG was co-registered with their structural MRIs by using indicator coils placed on the nasion and bilateral periauricular points.

We hypothesized that differences in neural activity for faces following negative and neutral sentences (Face 2) may occur during early or later stages of the face processing in a distinct manner. Thus, we examined MEG data with sliding time windows of 600 ms, i.e. 0-600 ms, 300-900, 600-1200 ms, etc. (Staresina, Bauer, Deecke, & Walla, 2005; Walla et al., 2001), which
resulted in a total of 8 time windows. As a control condition, the same analyses were also applied to faces preceding negative and neutral sentences (Face 1). Spatiotemporal differences in the brain responses to viewing faces associated with negative versus neutral sentences were characterized using the partial least squares (PLS) multivariate approach (McIntosh, Bookstein, Haxby, & Grady, 1996; McIntosh & Lobaugh, 2004). The PLS approach has been successfully used for time-series neuroimaging data in multi-electrode event-related potential (Lobaugh, West, & McIntosh, 2001) and MEG (Fujioka et al., 2010; Moses et al., 2009). In order to accommodate computation demands, the Talairach-transformed individual functional maps for each participant were down-sampled to 78 Hz, which resulted in volumetric maps every 12.8 milliseconds, and used as input for a mean-centred PLS analysis. Mean centreing allowed values for the different conditions to be expressed relative to the overall mean. Using this type of analysis, activation patterns that are unique to a specific condition will be emphasized; whereas activations that are consistent across all conditions, such as primary visual activation, will be diminished.

The input of PLS is a cross-block covariance matrix, which is obtained by multiplying the design matrix (an orthonormal set of vectors defining the degrees of freedom in the experimental conditions), and the data matrix (time series of brain activity at each location as columns and subjects within each experimental condition as rows). The output of PLS is a set of latent variables (LVs), obtained by singular value decomposition applied to the input matrix. Similar to eigenvectors in PCA, LVs account for the covariance of the matrix in decreasing order of magnitude determined by singular values. Each LV explains a certain pattern of experimental conditions (design score) as expressed by a cohesive spatial–temporal pattern of brain activity (Fujioka et al., 2010). The significance of each LV was determined by a permutation test using 500 permuted data with conditions randomly reassigned for recomputation of PLS. This yielded the empirical probability for the permuted singular values exceeding the originally observed singular values. An LV was considered to be significant at \( p \leq 0.05 \). For each significant LV, the reliability of the corresponding eigen-image of brain activity was assessed by bootstrap estimation using 250 resampled data with subjects randomly replaced for recomputation of PLS, at each time point at each location. Sources with a bootstrap ration of ±3.5 were examined.
4.3.6 Analysis for Test Phase

In order to assess the extent to which association with emotion during the study phase influenced subsequent memory for the neutral faces, we examined recognition memory at two levels during the test phase. First, we examined the extent to which association with emotion influenced memory for the associated item (i.e. the face). If emotion enhanced memory for recognizing the neutral face, then participants should be more accurate in identifying previously presented faces paired with negative sentences as “old” (i.e. both “old-negative” and “old-neutral” responses were scored as correct) as compared to previously presented faces paired with neutral sentences. Second, we examined the extent to which emotion influenced memory for the relation between the neutral face and its associated sentence. If emotion enhanced memory for the relationship between the neutral face and the associated sentence, then participants should be more accurate in identifying previously presented faces paired with negative sentences as “old-negative”, as compared to previously presented faces paired with neutral sentences as “old-neutral”.

4.4 Results

4.4.1 Study Phase

4.4.1.1 Viewing of the Critical Word

The extent to which viewing of the critical word differed depending on whether it was negative or neutral was considered evidence for an emotion-modulated effect. Paired samples t-tests were conducted for the different eye movement measures.

Early differences in viewing. Eye movements distinguished between negative and neutral words with the very first fixation directed to the word. The duration of the first fixation was marginally longer for negative versus neutral words ($t(11) = 2.15, p = .06$). Other early measures of viewing did not reveal any significant differences (duration of first gaze: $t(11) = 1.72, p > .1$; number of fixations within first gaze: $t(11) = -1.26, p > .1$)

Overall differences in viewing. The average duration of all fixations made to the critical word was significantly longer when it was negative as compared to when it was neutral ($t(11) = 4.06, p < .01$). As a result of the longer average fixation durations, participants made fewer fixations ($t(11) = -2.42, p < .05$) and transitions ($t(11) = -2.19, p = .05$) to the negative versus neutral word
during the fixed viewing period. In other words, participants spent longer looking at the negative words, but explored the neutral words more. Mean values can be found in Table 5.2.

**Table 4.2 The mean and SEM for different eye movement measures of viewing to the critical word when it was negative and neutral.**

<table>
<thead>
<tr>
<th>Early Measures of Viewing:</th>
<th>Critical Word</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of First Fixation (ms)</td>
<td>Negative (SEM)</td>
</tr>
<tr>
<td></td>
<td>224.61 (11.66)</td>
</tr>
<tr>
<td>Duration of First Gaze (ms)</td>
<td>Neutral (SEM)</td>
</tr>
<tr>
<td></td>
<td>213.99 (8.58)</td>
</tr>
<tr>
<td>Number of Fixations within First Gaze</td>
<td>355.79 (29.46)</td>
</tr>
<tr>
<td></td>
<td>339.19 (24.92)</td>
</tr>
<tr>
<td>Overall Measures of Viewing:</td>
<td>1.53 (.06)</td>
</tr>
<tr>
<td>Average Duration of Fixations (ms)</td>
<td>267.58 (16.47)</td>
</tr>
<tr>
<td>Number of Fixations</td>
<td>247.63 (14.64)</td>
</tr>
<tr>
<td>Number of Transitions</td>
<td>4.16 (.14)</td>
</tr>
<tr>
<td></td>
<td>4.37 (.12)</td>
</tr>
<tr>
<td></td>
<td>2.67 (.08)</td>
</tr>
<tr>
<td></td>
<td>2.77 (.09)</td>
</tr>
</tbody>
</table>

**4.4.1.2 Viewing of Faces**

The extent to which viewing of faces paired with negative sentences differed from viewing of faces paired with neutral sentences was considered to provide evidence that, through association, emotional information can immediately modulate viewing of neutral information. Here, we focus on the significant results pertaining to emotion. Analyses of variance (ANOVA) were conducted on measures of viewing to Face 2 using emotion (negative, neutral) and face feature (eyes, mouth, nose) as within-subject factors. As a control, the same analyses were also conducted for viewing to Face 1 and no significant effects were found (all p’s > .1), therefore, for brevity, we only describe viewing to Face 2. Mean values can be found in Table 5.3.
Table 4.3 The mean and SEM for early (A) and overall (B) measures of viewing to different features within Face 1 and Face 2.

### A. Early Measures of Viewing:

<table>
<thead>
<tr>
<th>Duration of First Fixation (ms)</th>
<th>Face 1</th>
<th>Face 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyes</td>
<td>308.3 (37.5)</td>
<td>291.1 (24.0)</td>
</tr>
<tr>
<td>Nose</td>
<td>286.5 (24.1)</td>
<td>284.8 (22.5)</td>
</tr>
<tr>
<td>Mouth</td>
<td>264.4 (15.3)</td>
<td>294.0 (25.2)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Duration of First Gaze (ms)</th>
<th>Face 1</th>
<th>Face 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyes</td>
<td>1104.0 (133.5)</td>
<td>927.0 (86.9)</td>
</tr>
<tr>
<td>Nose</td>
<td>404.3 (55.5)</td>
<td>453.9 (74.9)</td>
</tr>
<tr>
<td>Mouth</td>
<td>275.6 (16.6)</td>
<td>323.7 (29.9)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Number of Fixations Within First Gaze</th>
<th>Face 1</th>
<th>Face 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyes</td>
<td>.41 (.04)</td>
<td>.39 (.04)</td>
</tr>
<tr>
<td>Nose</td>
<td>.17 (.02)</td>
<td>.19 (.03)</td>
</tr>
<tr>
<td>Mouth</td>
<td>.11 (.01)</td>
<td>.12 (.00)</td>
</tr>
</tbody>
</table>

### B. Overall Measures of Viewing:

<table>
<thead>
<tr>
<th>Average Duration of Fixations</th>
<th>Face 1</th>
<th>Face 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyes</td>
<td>332.07 (38.33)</td>
<td>316.45 (26.68)</td>
</tr>
<tr>
<td>Nose</td>
<td>300.76 (25.28)</td>
<td>316.06 (29.84)</td>
</tr>
<tr>
<td>Mouth</td>
<td>265.91 (14.90)</td>
<td>287.55 (21.39)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Number of Fixations</th>
<th>Face 1</th>
<th>Face 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyes</td>
<td>5.60 (.48)</td>
<td>5.53 (.49)</td>
</tr>
<tr>
<td>Nose</td>
<td>2.38 (.27)</td>
<td>2.33 (.30)</td>
</tr>
<tr>
<td>Mouth</td>
<td>.27 (.05)</td>
<td>.30 (.01)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Number of Transitions</th>
<th>Face 1</th>
<th>Face 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyes</td>
<td>1.82 (1.00)</td>
<td>1.93 (.09)</td>
</tr>
<tr>
<td>Nose</td>
<td>1.75 (.13)</td>
<td>1.63 (.14)</td>
</tr>
<tr>
<td>Mouth</td>
<td>.25 (.05)</td>
<td>.26 (.06)</td>
</tr>
</tbody>
</table>
Early differences in viewing. Participants spent significantly more time (F(1,11) = 4.76, p = .05, d = .30) and directed marginally more fixations (F(1,11) = 3.62, p = .08, d = .25) during the first gaze to the different features of faces paired with negative versus neutral sentences. There was also a marginal interaction between emotion and face feature for the duration of the first gaze (F(2,22) = 3.10, p = .07, d = .22) and the number of fixations within first gaze (F(1,11) = 2.92, p = .08, d = .21). Follow-up t-tests revealed that during the first gaze, participants spent significantly more time (t(11) = 2.31, p < .05) and directly marginally more fixations (t(11) = 1.93, p = .08) to the eye region of face, but not for other regions of the face (i.e. the nose and the mouth, p’s > .1). Participants first entered the eye region around 400 ms after face onset. There were no significant differences in the time at which participants entered the eye region of faces paired with negative versus neutral sentences (t(11) = 1.43, p > .1). Thus, emotion-modulated viewing differences found during the first gaze occurred approximately between 400-1400 ms (the duration of the first gaze was approximately 1000 ms, see Table 5.3).

Overall differences in viewing. In contrast to early measures of viewing which showed increased eye movement sampling of negative versus neutral faces, viewing across the entire trial revealed fewer fixations (F(1,11) = 4.34, p = .06, d = .28) and fewer transitions between face features (F(1,11) = 10.51, p < .01, d = .49) for faces paired with negative versus neutral sentences. A significant interaction for the number of transitions (F(2,22) = 5.40, p < .05, d = .33) revealed that participants made fewer transitions into the eye region of faces paired with negative versus neutral sentences (t(11) = -3.45, p < .01), whereas there was no difference in viewing of the other features (p’s > .1). No significant effects were found for the measure of average fixation duration (p’s > .1).

In summary, emotion led to early changes in viewing for both emotional stimuli (i.e. words) and neutral stimuli that were associated with emotion (i.e. faces). Specifically, association with negative versus neutral sentences initially led to an increase in viewing of the eye region of neutral faces, and perhaps as a consequence, decreased overall sampling (i.e. fewer fixations and transitions) across the remainder of the trial.
4.4.1.3 Neural Activity to Faces

As for the above analyses regarding eye movement behaviour, the extent to which neural activity observed during viewing of faces paired with negative sentences differed from neural activity observed during viewing of faces paired with neutral sentences, was considered to provide evidence that emotion modulates immediate processing of neutral information via association. PLS analysis did not reveal any differences between Face1-Negative and Face1-Neutral. For Face 2, PLS analysis yielded one significant design LV for the time window 600-1200 (p < .05; Figure 5.2) and 900-1500 ms (p = .05).

Figure 4.2 LV1 from PLS analysis

LV1 revealed that association with negative or neutral sentences yielded unique patterns of brain activation during 600-1200 ms after stimulus onset. The same pattern was observed for the time window 900-1500 ms.

LV1 revealed greater activation for faces paired with negative versus neutral sentences in emotion processing regions such as the left amygdala (950-976 ms), right cingulate (1027-1142 ms), and left medial frontal gyrus (1078-1104 ms), and in posterior regions such as the right precuneus (989-1053 ms), right inferior parietal lobule (1014-1040) and dorsolateral prefrontal cortex (1155-1245 ms; Figure 5.3).
Figure 4.3 Sources showing stronger activation for faces paired with negative as compared to neutral sentences.
A. PLS bootstrap ratio plots from LV1. B. Corresponding ER-SAM waveforms from LV1. Blue dots denote bootstrap ratios < -3, and red dots denote bootstrap ratios > 3.

Greater activation for faces paired with neutral versus negative sentences was found in the left parahippocampal gyrus (835-925 ms) and right superior frontal gyrus (733-810 ms; Figure 5.4). Interestingly, activation in fusiform gyrus and bilateral lingual gyrus initially showed a larger response for faces paired with neutral versus negative sentences, but ultimately showed a larger response for faces paired with negative versus neutral sentences (Figure 5.5).
Figure 4.4 Sources showing stronger activation for faces paired with neutral as compared to negative sentences

A. PLS bootstrap ratio plots from LV1. B. Corresponding ER-SAM waveforms from LV1. Blue dots denote bootstrap ratios < -3, and red dots denote bootstrap ratios > 3.
Figure 4.5 Sources initially showing stronger activation for faces paired with neutral as compared to negative sentences, then stronger activation for faces paired with negative as compared to neutral sentences.
4.4.2 Test Phase

Analyses of variance (ANOVA) were conducted on uncorrected hits using face type (novel, repeated-negative, repeated-neutral) as a within-subject factor. We first examined the extent to which emotion influenced memory for the associated item. No significant differences in accuracy emerged between the three face types (F(2, 22) = .15, p > .1). Corrected hit rates were around chance levels (chance = .44; old-negative: M = .41, SEM = .03; old-neutral = .46, SEM = .03). We also examined the extent to which emotion influenced memory for the relationship between the neutral face and the associated sentence. There was a significant effect of face type
such that accuracy for identifying novel faces was significantly higher than accuracy for identifying repeated faces that had been presented with a negative \( t(11) = 5.93, p < .001 \) or a neutral sentence \( t(11) = 6.56, p < .001 \). There were no differences in uncorrected \( t(11) = .63, p > .1 \) or corrected hits \( t(11) = -1.44, p > .1 \) between identifying repeated faces that had been presented with a negative and neutral sentence. Mean values can be found in Table 5.4. Of note, when hits were corrected by false alarms (i.e. for old-negative faces, responses of “old-negative” to new and old-neutral faces were scored as false alarms), accuracy fell below chance levels suggesting that participants were unable to differentiate between the face types. Taken together, the results suggest that the task was too difficult to observe any potential effects of emotion on memory.

### Table 4.4 Mean accuracy and SEM for identifying different face types during the test phase

<table>
<thead>
<tr>
<th>Response Type – Uncorrected</th>
<th>Face Type</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>“Novel”</td>
<td>New</td>
<td>.64 (.04)</td>
<td>.39 (.02)</td>
<td>.38 (.03)</td>
</tr>
<tr>
<td>“Old-Negative”</td>
<td></td>
<td>.20 (.03)</td>
<td>.34 (.03)</td>
<td>.30 (.02)</td>
</tr>
<tr>
<td>“Old-Neutral”</td>
<td></td>
<td>.16 (.02)</td>
<td>.27 (.02)</td>
<td>.32 (.02)</td>
</tr>
<tr>
<td>Chance</td>
<td>Old-Negative</td>
<td>-.17 (.04)</td>
<td></td>
<td>-.11 (.04)</td>
</tr>
</tbody>
</table>

#### 4.5 Discussion

Previous research showed that viewing of faces expressing emotion was associated with distinct viewing patterns, but that such viewing patterns can be altered by contextual information (Aviezer et al., 2008). However, previous research has not examined the influence of emotion on the processing of neutral information when that neutral information is presented in isolation during the study phase. In other words, it is not clear whether emotion may exert influence on the processing of neutral information via association, even when it is no longer present. In the current study, it was found that: (1) emotion led to increased early viewing of both the stimulus itself (i.e. the negative word) and the associated neutral stimulus (i.e. the neutral face); (2) emotion exerted its influence on neutral faces during later stages in processing, between 600-1500 ms after stimulus onset, as revealed by magnetoencephalography (MEG); and (3) observed differences in viewing and neural activity during the study phase was not related to subsequent memory effects. In the next sections, we discuss our results in light of prior findings regarding...
how association with emotional information may modulate processing of neutral information, and how the current work may inform theories regarding the influence of emotion on perception and memory.

4.5.1 Emotion-Modulated Viewing of Words

In the present experiment, it was found that eye movements differentiated between the critical negative and neutral word within the sentence within the first fixation. Further, it was also found that over the entire trial, the average duration of a fixation was longer for negative than neutral words. These results suggest that emotions modulate online processing and that this occurs very early. This is consistent with previous neuroimaging studies showing that compared to neutral stimuli, emotional stimuli elicit increased processing within the first 500 ms, with some reports as early as 120 ms, after stimulus onset (e.g. Kissler, Herbert, Winkler, & Junghofer, 2009; Vuilleumier & Pourtois, 2007; Peyk, Schupp, Elbert, & Junghofer, 2008). This may be an adaptive function allowing one to prioritize the detection and processing of potentially threatening and/or important information.

4.5.2 Emotion-Modulated Viewing of Neutral Faces

In addition to emotion-modulated differences in viewing words, association with negative versus neutral information also influenced viewing to neutral faces. Specifically, it was found that when faces were paired with negative versus neutral sentences, there was increased viewing to the eye region of faces during the first gaze, i.e. between 400-1400 ms. This finding could be interpreted in two possible ways. First, association with negative information may fundamentally change the way in which a neutral face is processed, i.e. it may change perceptual processing of neutral faces (Aviezer et al., 2008). Previous studies have shown that the viewing of threat-related versus non-threat-related facial expressions is also characterized by increased viewing to the eye region (e.g. Adolphs, Gosselin, et al., 2005; Gamer & Buchel, 2009; Itier & Batty, 2009). Within the current experiment, the neutral faces may have taken on emotional qualities and elicited viewing patterns similar to those reported for the viewing of faces that are actually expressing emotion. Further work is needed to directly compare viewing of faces expressing emotion and viewing of faces associated with emotion. Alternatively, emotion-modulated differences in viewing neutral faces associated with negative versus neutral information may not reflect differences in perceptual processing per se, but may rather indicate...
processing differences after perceptual processing has occurred. Specifically, after building a visual percept of the neutral face, participants may have then bound the associated information to the neutral face. Faces paired with negative versus neutral sentences may have invoked a greater need to reappraise the face, leading to increased viewing to regions of the face that are the most informative (i.e. the eyes). Consistent with the axiom that the eyes may be a “window to the soul”, previous research shows that viewing to the eye region is associated with the assessment of interest, threat, and intentions of other people (e.g. Haxby, Hoffman, and Gobbini, 2002; Spezio et al., 2007).

4.5.3 Emotion-Modulated Processing of Neutral Faces

In addition to examining emotion-modulated differences in viewing, we also examined the extent to which emotion may influence underlying neural activity associated with processing the associated neutral face, and precisely when emotion may exert its influence. This may shed light on how the processing of faces associated with emotion may differ from that of faces associated with neutral information. For example, if emotion modulated processing of neutral faces early, i.e. within the first 200 ms, then this may suggest that emotion changes perceptual processing of associated neutral faces. However, PLS analysis did not reveal any significant spatiotemporal differences in processing neutral faces paired with negative versus neutral sentences within the first 200 ms after stimulus onset. In fact, no such differences were observed until a later period, between 600-1500 ms. This time frame is consistent with eye movement monitoring results which revealed viewing differences between neutral faces paired with negative versus neutral sentences between 400-1400 ms (discussed above). Taken together, this suggests that emotion may not exert its influence on the perceptual processing of associated neutral faces, rather, it may modulate later stages of processing such as binding the sentence to the face and/or the process of reappraising the neutral face in light of the new information obtained.

Further, given that the differences in viewing to- and processing of (i.e. underlying neural activity) neutral faces paired with negative versus neutral information occurred in and around the same time window, it could be argued that there may be a reciprocal relationship between eye movements and neural activity. Specifically, eye movements entered the eye region at around 400 ms after face onset. However, since we did not observe differences in the duration of the first fixation between viewing of faces associated with negative versus neutral sentences, this
suggests that emotion-modulated differences in viewing culminated only after participants had some time to explore the region. In this way, the emotional information associated with the face may drive participants to direct more viewing to informative regions of the face such as the eyes. In doing so, this may then increase neural activity in regions implicated in emotion processing (Hannula et al., 2010), which may then result in the construction of a different type of internal representations as compared to faces paired with a neutral sentence.

In support of the notion that association with emotion may lead to the construction of different types of representations, processing neutral faces paired with negative versus neutral sentences elicited stronger activity in neural regions implicated in emotion processing such as the amygdala, cingulate and medial prefrontal cortex (e.g. Adolphs, Gosselin, et al., 2005; Anderson, Christoff, Panitz, De Rosa, & Gabrieli, 2003; Craig, 2002; Culham & Kanwisher, 2001; Kensinger & Corkin, 2003; Lane, Reiman, Ahern, Schwartz, & Davidson, 1997). Interestingly, the brain region to first differentiate between neutral faces paired with negative versus neutral sentences was the amygdala, and dorsolateral prefrontal cortex which has been associated with memory encoding and retrieval (e.g. Blumenfeld, Parks, Yonelinas, & Ranganath, 2011; Nyberg et al., 2003; Ranganath, Johnson, & D'Esposito, 2003). It is possible that increased activity in these regions then drove subsequent changes in the brain, leading to increased reappraisal of neutral faces paired with negative as compared to neutral sentences. Consistent with this notion, activation differences in the amygdala and dorsolateral prefrontal cortex were followed by differences in neural activity in the precuneus and inferior parietal lobule, which has been linked to the maintenance of attention and the processing of salient information (e.g. Culham & Kanwisher, 2001; Singh-Curry & Husain, 2009). Activation peaks in these two parietal regions were followed by peaks in neural regions in other emotion processing regions such as the cingulate and medial prefrontal cortex (e.g. Craig, 2002; Culham & Kanwisher, 2001; Kensinger & Corkin, 2003). This may reflect the retrieval and attachment of emotional information to a neutral face (e.g. Fenker et al., 2005; E. J. Maratos, Dolan, Morris, Henson, & Rugg, 2001; Medford et al., 2005; A. P. Smith, Henson, Dolan, & Rugg, 2004) and/or the reappraisal and assessment of the neutral face in light of the negative sentence.

Further, the analysis also revealed a number of regions, namely the fusiform gyrus, superior temporal sulcus (STS) and bilateral lingual gyrus, which were first more active for faces associated with neutral versus negative sentences, but became more active for faces associated
with negative versus neutral sentences. The STS has been shown to be involved in inferring the intentions and attributes of other people (e.g. Winston, Strange, O'Doherty, & Dolan, 2002) and the representation of biographical information (Haxby et al., 2002; Todorov et al., 2007). In this way, associated information may then modulate and change encoding processes, possibly via enhanced activation of visual processing regions in the occipital cortex and specific face processing modules in the fusiform gyrus (Halgren, Raji, Marinkovic, Jousmaki, & Hari, 2000; Prince, Dennis, & Cabeza, 2009). Critically, these processes may be more delayed for neutral faces paired with negative versus neutral sentences because emotional significance of the face and/or congruence between the physical properties of the face and associated biographical information must first be evaluated/considered. Taken together, results from MEG suggest that emotional information may influence the processing of neutral faces via a parietal-limbic-frontal network that may both drive and be modulated by eye movement behaviour.

Contrary to our original predictions, results from MEG did not reveal differences in neural activity in the anterior insula. This is likely because the anterior insula is predominantly involved in the processing of disgust (e.g. Anderson et al., 2003; Lane et al., 1997). In contrast, the negative information presented within the paradigm may have elicited different types of negative emotions including fear, anger and disgust, which may have decreased the power with which emotion-modulated differences could be observed. Another possibility for why spatiotemporal differences in the anterior insula were not observed between processing of faces associated with negative versus neutral sentences may be related to individual differences. Specially, some recent research has shown that the level of activation in the anterior insula varies across participants, and may depend on factors such personality (Mataix-Cols et al., 2008; Schafer, Leutgeb, Reishofer, Ebner, & Schienle, 2009) and sex (Aleman & Swart, 2008; Caseras, Mataix-Cols, et al., 2007). Thus, it is possible that we failed to observe any emotion-modulated differences in this region because not all of the participants showed increased activation during processing of faces paired with negative as compared to those paired with neutral sentences. This is especially relevant because the bootstrap method used in the present experiment is a measure of stability across participants for a particular brain voxel, i.e. a high bootstrap ratio value indicates that most, or all of the participants showed similar spatiotemporal differences between the experimental conditions, and a low bootstrap ratio value indicates that few or none of the participants showed similar spatiotemporal differences.
In addition to the above, another unexpected finding was that the processing of faces paired with neutral versus negative sentences elicited stronger activation within the medial temporal lobe, i.e. in the parahippocampal gyrus. Given that the current task required participants to process two stimuli arbitrarily paired together (i.e. face and sentence), we had initially expected activation of the hippocampus proper as this has been shown to be critical for the formation of relations/associations among items into a lasting representation (e.g. Chun & Phelps, 1999; N. J. Cohen et al., 1997; Ryan et al., 2000). The absence of activation differences in the hippocampus proper, and the presence of activation differences in the parahippocampal gyrus may suggest that the processing of faces paired with neutral versus negative sentences may rely more on a blended versus relational representation. For instance, Moses and Ryan (Moses & Ryan, 2006) argued that whereas the hippocampus mediates relational representations that are flexible; structures outside of the hippocampus such as the parahippocampal gyrus mediate blended representations that are not flexible, i.e. a change in any aspect would significantly disrupt subsequent processing and memory.

Another possibility why we did not observe activation differences in the hippocampus proper may be due to source localization concerns. Specifically, in a study using simulated MEG activity presented with real background brain activity, it was found that MEG was not able to differentiate between the hippocampus and parahippocampal gyrus when activity in these two regions overlapped in time (Stephen et al., 2005). Instead, the source was placed in either the hippocampus or the parahippocampal gyrus. In other words, it is possible that in the current task, both the hippocampus and the parahippocampal gyrus were active at the same time, but only activity in the parahippocampal gyrus was observed. In support of this, a number of fMRI studies examining associative learning/memory have reported increased activity in both the hippocampus proper and the parahippocampal gyrus (e.g. Bar, Aminoff, & Schacter, 2008; Duzel et al., 2003; Kirwan & Stark, 2004; Yonelinas et al., 2001). This suggests that the hippocampus does not operate in a vacuum but interacts with other brain regions in order to form and support different representations for the same information input (i.e. relational and blended). Future research is needed in order to determine whether association with neutral versus negative information lead to a greater reliance on blended representations mediated by the parahippocampal gyrus, or blended and relational representations mediated by the parahippocampal gyrus and hippocampus, respectively.
Irrespective of whether association with neutral versus negative information led to a greater reliance on blended and/or relational representations, the finding that processing of faces paired with neutral versus negative sentences elicited stronger activation within the parahippocampal gyrus may represent enhanced processing of associated neutral versus negative information and the blending/binding of that information to the neutral face. This was somewhat counterintuitive as it seemed that it would be more important and relevant to bind emotionally salient information to the neutral face rather than affectively neutral information. However, there has been some suggestion in the literature showing that while the processing and memory of associated neutral information is mediated by the medial temporal lobes, processing and memory of associated emotional information may be more dependent on emotion processing regions such as the amygdala and temporal poles (Phelps & Sharot, 2008). For example, Todorov and Olson (Todorov & Olson, 2008) presented participants with neutral faces paired with positive or negative sentences and later asked them to rate each face on scales of likeability, trustworthiness and competence, and to make a force-choice judgment of preference between a face that had been previously paired with positive versus negative behaviours. They found that while healthy controls and patients with hippocampal damage showed learning effects (i.e. preferring faces previously paired with positive versus negative behaviours), patients with damage to the amygdala and temporal poles did not. In light of this, it is possible that in the present experiment, participants built different types of representations for the face-sentence pairings depending on whether the sentence was negative or neutral. Specifically, participants may have built a parahippocampal-based representation of faces with neutral sentences, and an emotion system-based representation of faces with negative sentences. However, it is important to note that these differences in neural activity were relative rather than absolute. In this way, the evidence lends support to the notion that binding/blending of emotional versus neutral information may depend more on one system versus another, not that they rely only on one system versus another. Future work can examine what this may mean for the type of representation formed, for example, if associations between neutral stimuli are mediated predominantly by the parahippocampal gyrus, then are these representations more flexible, detailed and/or more stable than those between emotional stimuli (e.g. N. J. Cohen et al., 1997)?
4.5.4 Emotion-Modulated Memory for Neutral Faces

Given the above emotion-modulated differences in viewing and underlying neural activity during the study phase, we were surprised to find that emotion did not seem to modulate subsequent recognition memory. This is likely due to the fact that there were too many face-sentence pairings, leading to at-floor memory performance, thereby masking any potential mnemonic effects that emotion may have had. In the absence of any emotion-modulated effects in memory performance, this suggests that the differences observed in eye movement patterns and neural activity between faces paired with negative versus neutral sentences during the study phase were the result of emotion’s effects on processing associated information, independent (or at least in part) of its effects on subsequent memory. It is possible that such effects would be more robust, or different altogether, if we only examined neural activity underlying faces that were subsequently remembered. Unfortunately, due to signal-to-noise constraints and the current study’s low accuracy rates, such a comparison was not possible. Further, in the present experiment, memory was examined via conscious explicit report. However, prior studies have shown that even in the absence of conscious awareness, memory can be gleaned from other aspects of behaviour such as eye movement behaviour (Hannula et al., 2010; Ryan et al., 2000). Thus, it would be interesting for future research to examine how association with emotion may modulate memory as indexed by different measures.

4.5.5 Conclusions

In the current work, it was found that emotions can alter processing of otherwise neutral information by changing overt viewing patterns. This adds to the growing literature showing that visual processing is determined not only by bottom-up physical characteristics, but also by top-down influences such as prior knowledge, memory and context (Aviezer et al., 2008; Ryan et al., 2008). Further, it was also found that processing of faces paired with negative sentences relied more on a neural network mediated by regions involved in emotion, whereas processing of faces paired with neutral sentences relied more on regions involved in memory (i.e. the parahippocampal gyrus). This suggests that not only do emotions influence online processing of associated information, but it may also alter the type of representation that is formed.
4.6 Acknowledgements

The authors wish to thank Douglas A. McQuiggan, Helen Dykstra, Nathaniel So and Amy Oziel for their assistance in data collection. The authors also wish to thank Sandra Moses and Bernhard Ross for their advice and technical assistance. This work was funded by Natural Science and Engineering Research Council and Canada Research Chair grants awarded to JDR; and a research studentship from Ontario Mental Health Foundation to LR.
Chapter 6
Theoretical and Methodological Contributions, and Concluding Remarks
5 Theoretical and methodological contributions, and concluding remarks

In this thesis, I sought to examine how emotions may influence relational memory, or more precisely, how emotions may influence the viewing, perception and retrieval of, associated neutral information. This is in contrast to previous literature that has focused predominantly on how emotions may influence memory for the emotion-eliciting item. This research provides a more comprehensive understanding of ‘emotional memories’ as our memories for emotional events or scenes are rarely composed of just a single item, but are rather composed of multiple items and the relations between them.

In order to examine how emotions may modulate relational memory, I set out to address the following questions: (1) To what extent do emotions modulate relational memory via differences in the amount of attention allocated during encoding (Chapter 2; Riggs et al., 2011); (2) to what extent do emotions modulate relational memory via differences in the retrieval process (Chapter 3; Riggs et al., 2010); and (3) to what extent do emotions modulate relational memory via the manner in which associated information is perceived and how are such processes supported in the brain (Chapter 5)? In order to address these questions, I used a convergent methods approach that included eye movement monitoring and magnetoencephalography (MEG). The advantage of using these methods to examine cognitive processes comes from the fact that, unlike verbal reports, they have the power to illuminate aspects of processing online, such as precisely when a certain operation occurs and how it is supported within the brain. However, in order to use MEG to address some of the theoretical questions above, I had to first overcome the methodological issue regarding whether MEG could be successfully utilized to localize activity in deep sources within the brain, critically the hippocampus (Chapter 4; Riggs et al., 2009).

In this final chapter, I provide a summary of the theoretical and methodological contributions of this work, outline some of the limitations and provide future directions.
5.1 Theoretical Contributions

In integrating all of the results from the chapters together, there are several overarching themes that emerge with regards to how emotions may influence memory, and also the nature of memory itself. Each of these is discussed in turn below.

5.1.1 Emotions Modulate Visual Processing of Associated Information

Prior studies have shown that the viewing of emotional and neutral stimuli is associated with different viewing patterns. For example, compared with faces in a neutral expression, viewing to faces expressing threat is characterized by increased viewing of internal facial features, especially of the eyes (Adolphs, Gosselin, et al., 2005; Calder et al., 2000; Gamer & Buchel, 2009; Green et al., 2003b; Itier & Batty, 2009; M. L. Smith et al., 2005). However, such differences in viewing are driven not only by the affective significance of the faces, but also by differences in the physical features. Specifically, compared to faces in neutral expressions, faces expressing fear show enlarged eyes and faces expressing disgust show narrowed eyes. Studies within the current thesis were not vulnerable to these concerns because they examined how emotions influenced viewing of associated information that was otherwise neutral, e.g. pairing either a negative or a neutral sentence with a face in a neutral expression (Chapter 5). Critically, the physical properties of the neutral face were held constant and counterbalanced across conditions. In this way, differences in viewing could only be the result of the type of information that was associated with the face.

Results from this thesis show that not only do emotions modulate the amount of viewing that is directed to associated neutral stimuli (Chapter 2), but also the pattern of viewing, i.e. participants increased viewing to the eye region of neutral faces associated with negative versus neutral sentences (Chapter 5). This suggests that visual processing is influenced not only by bottom-up factors such as the physical properties of a stimulus, but also by top-down factors such as prior experience and affective meaning (e.g. Althoff & Cohen, 1999; Bar, Neta, et al., 2006; Hannula et al., 2010). In this way, emotions may modulate visual processing of associated information which may then in turn influence the type of representation that is formed, i.e. a representation mediated by emotion-processing regions such as the amygdala and cingulate versus a representation mediated by memory-processing regions such as the parahippocampal gyrus (Chapter 5). It would be important for future research to examine the cognitive consequences of
different representations (e.g. is one type of representation more flexible, stable and/or long lasting?) and how they may be affected in clinical disorders. For example, it is possible that compared to healthy controls, patients with post-traumatic stress disorder or anxiety may rely more on emotion-processing regions even for the processing of neutral information. In this way, they may form internal representations that are more emotional, less flexible and/or more difficult to extinguish.

5.1.2 Emotions-Modulated Relational Memory is not Mediated by Attention

Although it has often been suggested that emotions modulate memory for associated information via differences in the allocation of attention (e.g. Armony & Dolan, 2002; J. M. Brown, 2003; Easterbrook, 1959; Kensinger et al., 2005; E. F. Loftus et al., 1987; Wessel & Merckelbach, 1997), this has not been examined directly. I examined this issue directly within this thesis and found that emotion-modulated memory was not mediated by differences in attention allocation. Specifically, Chapter 2 showed that although the presence of an emotional scene led to decreased amounts of attention to the associated neutral items, these emotion-modulated changes in attention were not related to subsequent memory performance. Further, in Chapter 5, I found that although association with emotions led to differences in the manner in which participants viewed otherwise neutral faces, this did not result in differences in memory performance. Taken together, this suggests that the relationship between attention and memory is not perfectly correlated and that perhaps it is not about how much attention is directed to a certain item or feature within an item, but rather how deeply the item is processed (Craik, 2002). Further, this also suggests that emotions may influence memory via other mechanisms including differences in the retrieval process and possibly the post-stimulus elaboration process.

Post-stimulus elaboration refers to the process in which participants may continue to process and elaborate on a stimulus even after the stimulus is no longer externally present (Hulse, Allan, Memon, & Read, 2007; Kern, Libkuman, & Otani, 2002). For example, although Chapter 2 revealed that emotion-impaired memory for associated neutral information was not the result of differences in the amount of attention allocated during the encoding phase (the time during which the stimulus was presented on the screen), it is possible that in between trials, participants continued to elaborate on the emotional item at the cost of encoding associated items, thereby leading to the memory effects observed. In light of the above, it would be important for future
research to examine whether emotions may influence relational memory via post encoding processes.

5.1.3 Emotion Has Differential Effects on Memory

Another theme to emerge from my work is that emotion has differential effects on relational memory, i.e. emotion does not always impair or enhance memory for associated information (Riggs et al., 2010; Riggs et al., 2011). This is in contrast to the binding theory described by MacKay and colleagues in which they proposed that emotions act as the ‘glue’ that binds the emotional item to associated information, thereby enhancing memory for the emotional item and associated information (Hadley & Mackay, 2006; MacKay & Ahmetzanov, 2005; MacKay et al., 2004). The notion that emotion may have differential effects on explicit memory is supported by prior literature. As described in Chapter 1, previous studies examining emotion-modulated relational memory have shown emotion-enhanced relational memory (e.g. D'Argembeau & Van der Linden, 2004, 2005; Hadley & Mackay, 2006; MacKay & Ahmetzanov, 2005; MacKay et al., 2004) while others have shown emotion-impaired memory (e.g. Jurica & Shimamura, 1999; Kensinger et al., 2005; Kramer et al., 1990; Levine & Pizarro, 2004; Pickel, 1998). This then leads to the question of why emotion may have such differing effects on memory, or more precisely, under what circumstances do emotions enhance versus impair relational memory?

It has been suggested that such selective effects of emotions may depend on relevancy (Burke et al., 1992; Heuer & Reisberg, 1990; Reisberg & Heuer, 2004). Specifically, emotions may enhance information for the item and associated information perceived to be relevant to the item, and this may occur at a cost of impaired memory for associated information that is perceived to be irrelevant. Consistent with this perspective, the current work also found that when the associated neutral information was arbitrary and not relevant for the understanding of the emotion-eliciting item, memory was impaired (Riggs et al., 2010; Riggs et al., 2011). However, when the emotion-eliciting information was meaningfully associated with a neutral stimulus, memory was not impaired (Chapter 5).

In addition to relevance, another factor that may influence whether emotion enhances or impairs memory for associated information may be the amount of detail contained therein. In Chapter 3, I found that while association with emotion impaired the more evaluative aspects of memory
retrieval, as well as recognition memory accuracy for specific visual details in the periphery (i.e. when participants had to distinguish displays of objects that had been manipulated from those that were repeated or novel), it did not impair memory when such detailed memory representations were not required for the task (i.e. when participants had to identify displays that were repeated). This is consistent with the notion that while emotions may enhance memory for gist information (i.e. a general representation of the central elements of a scene), it may impair memory for specific details (e.g. Adolphs et al., 2001). Further, results from Chapter 3 also revealed that emotion did not impair how quickly/easily memory for associated neutral information could be retrieved. This suggests that emotions do no impair all aspects of memory for associated details and/or early access to stored memory representations occur in an obligatory fashion. In this way, stored memory representations with affective associations/meaning may direct attention to potentially relevant information even if the representation is not sufficiently detailed to influence subsequent stages of retrieval and/or conscious awareness.

From the studies conducted in this thesis, it is possible that both relevance and the amount of details contained therein may play a role in determining whether emotions may impair explicit memory for associated information or not. Future research could clarify how such factors may interact and contribute to memory as measured by explicit report and memory as indexed by eye movement monitoring (e.g. how do we determine what is relevant and what is not?), especially when they may lead to conflicting predictions. For example, the ‘relevance’ hypothesis predicts that emotions would enhance all aspects of memory for associated information, regardless of how specific the details may be, as long as it was relevant. In contrast, the ‘gist/detail’ hypothesis predicts that emotions would impair memory for specific details regardless of whether it was judged to be relevant or not. Further, if early indices of memory are truly obligatory, then they should not be influenced by factors such as relevance.

Another factor that may influence whether emotions enhance or impair relational memory may be the valence of the emotion. In the present work, all of the experiments conducted used stimuli that depicted negative emotions such as fear and disgust rather than positive emotions such as happiness. There may be important psychological distinctions between different emotions (e.g. Aviezer et al., 2008). For example, prior research suggests that there are different information-processing strategies associated with positive versus negative emotions. For example, several studies have shown that positive emotions (happiness) can lead to a greater reliance on general
knowledge or stereotypes and be more vulnerable to intrusion errors in memory (Bless et al., 1996; Park & Banaji, 2000). Further, it has also been shown that positive affect is associated with a broadening of attention whereby one seeks a wider range of information from general knowledge and the environment (Rowe et al., 2007). On the other hand, fear is associated with a narrowing of attention whereby one focuses on the source of threat and the means available to escape that threat (e.g. Easterbrook, 1959). In light of the above, it is possible that while negative emotions may lead to certain tradeoffs in attention and memory, positive emotions may actually be associated with a generalized enhancement of both attention and memory. In other words, emotional valence may have different consequences on cognition.

In contrast to the above, prior literature also supports the possibility that both negative and positive emotions may have the same effect on attention and memory. Specifically, emotion may exert its effects via arousal rather than via valence. Valence refers to how positive or negative a certain stimulus is, while arousal refers to a physiological and psychological state of intensity. Prior research has shown that while arousal modulates memory via the amygdalar-hippocampal network, valence modulates memory via the prefrontal-cortex-hippocampal network (e.g. Anders, Lotze, Erb, Grodd, & Birbaumer, 2004; Kensinger & Corkin, 2004a; Lewis, Critchley, Rotshtein, & Dolan, 2007). Given that all emotional stimuli fall somewhere along the two dimensions of valence and arousal, it is likely that both characteristics play a role in determining how emotions may modulate cognitive processes such as attention and memory. It would be interesting for future research to specify the effects of valence versus arousal and how they may interact with other factors such as relevance of associated information.

5.1.4 Encoding and Retrieval Occur in Stages

Another theme to emerge from the current work is that emotions may have differential effects on memory depending on that stage of memory that is being examined. In Chapter 3, I examined how association with emotion during the encoding stage may influence the subsequent retrieval process. I found that while emotions influenced the more evaluative stages of retrieval, it did not modulate how quickly participants were able to access memory regarding information associated with an emotional stimulus. Further, in Chapter 5, I examined how association with emotion may influence the manner by which participants view otherwise neutral faces and found that emotion exerted its influence predominantly in early measures of viewing. Taken together, this
suggests that emotions may have differential effects on different stages of encoding and retrieval. This also suggests that encoding and retrieval may not occur in an all-or-none fashion; rather, they may proceed in stages (e.g. Parker, 1978).

The notion that encoding and retrieval may proceed in stages has important implications for our understanding of memory and memory-related disorders. Specifically, certain disorders may affect a particular stage of encoding or retrieval first. For example, it is often quite difficult to distinguish between healthy older adults and those with mild cognitive impairment (MCI) as both groups report difficulties with memory (Irish, Lawlor, O'Mara, & Coen, 2010; Price et al., 2010; Schacter, Koutstaal, & Norman, 1997; Grady & Craik, 2000). However, it is possible that while healthy older adults’ difficulties are in part the result of impairments in the evaluative stages of retrieval, those with MCI may have greater impairments in the evaluative, as well as the early stages of memory, i.e. they may have difficulties accessing stored memory representations as well. By distinguishing between different stages and characterizing how different disorders may influence these stages, we may increase the sensitivity with which we can diagnose them and be better able to tailor specific rehabilitative program to target those stages.

5.1.5 Memory Exerts Early Influences on Processing

In addition to the above insights regarding the nature of encoding and retrieval, my work also sheds light on the relationship between memory and perception as well. In Chapter 4, I examined the latency of hippocampal responses during a recognition memory task and found that activity within the hippocampus peaked within the first 150 ms after stimulus onset, a time that is typically associated with perceptual processing (e.g. Ryan et al., 2008; Tsivilis et al., 2001). Further, in Chapter 3, I found that eye movements distinguished between changed and unchanged visual displays within the first fixation and this was not modulated by emotion. This suggests that memory exerts early influences on processing, perhaps even changing one’s perception, and that such processes may occur in an obligatory fashion (Ryan et al., 2008).

The idea that our prior experience may influence the way in which we subsequently process the same item/event/scene is not new. In 1890, William James wrote that “whilst part of what we perceive comes through our senses from the object before us; another part (and it may be the larger part) always comes… out of our own head.” (James, 1983). In support of this, a number
of fMRI studies have found that when a visual stimulus is paired with an auditory stimulus, subsequent presentation of either stimulus alone elicited neural activity in both the visual cortex and the auditory cortex (e.g. Nyberg, Habib, McIntosh, & Tulving, 2000; Wheeler et al., 2000). Going further, Ryan and colleagues found that such differences in sensory activity occurred within the first 200 ms after stimulus onset (Ryan et al., 2008). The authors concluded that our prior experience may actually change subsequent perception such that we never perceive the same item in exactly the same way.

The notion that prior experience may influence perceptual processing has important theoretical implications for our understanding of memory and perception. First, it suggests that memory retrieval may occur in a rapid and obligatory fashion (Riggs et al., 2010; Riggs et al., 2009; Ryan, Hannula, et al., 2007; Ryan et al., 2008). In this way, prior experience may shape current perception and behaviour in a way that is most efficient with minimal or no need for top-down control. Second, if retrieval occurs in an obligatory manner and influences perception, this suggests that perception and memory may not be as modular and independent as previously described. Rather, these two processes may be plastic, intimately tied together and continually shaping the other such that we never perceive or remember the same item twice.

The ability to empirically examine the relationship between perception and memory has only been made possible in recent years with the advancement of technological tools such as eye movement monitoring and MEG. My work sought to take full advantage of these tools in order to begin addressing questions regarding the nature of emotion-modulated memory, and indeed the nature of memory itself, that could not be answered by using verbal reports alone. In doing so, the current thesis makes not only the theoretical contributions outlined above, but also methodological contributions to the field of cognitive neuroscience via elucidation and promotion of convergent methods.

5.2 Methodological Contributions

The majority of research in the field of emotions and memory has assessed memory through recall or recognition paradigms, which as mentioned in Chapter 1 (Section 1.1), cannot shed light on how such differences in memory may occur. Further, verbal reports cannot tell us exactly when memory may exert its influence during online processing of stimuli and how such processes may be supported in the brain. In order to address some of these issues, I utilized eye
movement monitoring and MEG. Both technologies are relatively under-used in the fields of emotion and memory research, but my research shows that the application of these tools can yield unique insights that cannot be gleaned from other methods such as verbal reports and/or other neuroimaging techniques such as fMRI and EEG.

5.2.1 Magnetoencephalography

The current work used MEG to study how emotions may influence perception. As mentioned in Chapter 1, MEG has traditionally been used as a method to study neural activity from superficial sources such as primary sensory or motor responses. Although cognitive neuroscientists are now beginning to appreciate the potential and utility of MEG imaging to illuminate the underlying mechanisms of complex cognitive processes such as memory, there has been a considerable debate regarding whether it is feasible to apply MEG to the study of memory due to difficulties with imaging the hippocampus, a critical mnemonic structure.

In the current thesis, I showed that MEG can be successfully used to localize and characterize hippocampal activity (Chapter 4; Riggs et al., 2009). In other words, MEG can be used to study complex cognitive processes such as memory. Further, since unlike more traditional neuroimaging methods such as fMRI or PET, MEG has excellent temporal and spatial resolution that can characterize the precise dynamics underlying different cognitive operations (e.g. memory encoding, memory retrieval), this has the potential to lead to new reconceptualizations of cognition and brain functioning in general. For example, as discussed above (Section 6.1.4), evidence from my MEG work suggests that memory and perception may not be modular processes that are distinct from each other, rather, our prior experience may change subsequent perception in an obligatory fashion. Further, my work has also shown that MEG can characterize how the hippocampus functions, i.e. it oscillates in a theta rhythm. Thus, MEG has the potential to reveal not only where and how fast a mnemonic process may occur, it could also reveal how this process may occur.

In addition to examining how the hippocampus may function, it would be interesting for future research to outline how the hippocampus may communicate with other regions in the brain, and specifically, the amygdala in order to support emotion-modulated memory. Unfortunately, I did not find significant differences in the hippocampus for viewing faces paired with negative versus neutral sentences in Chapter 5. Further, the low accuracy results in Chapter 5 did not permit me
to conduct a subsequent memory analysis (i.e. examine the brain regions associated with stimuli that are subsequently recognised versus the brain regions associated with stimuli that are subsequently forgotten) in which responses from the hippocampus and amygdala may have been more robust, but studies using fMRI have shown that a predictor of emotion-enhanced memory is the level of functional connectivity between the amygdala and the hippocampus during the encoding phase (e.g. Murty, Ritchey, Adcock, & LaBar, 2010; Ritchey, Dolcos, & Cabeza, 2008; St Jacques, Dolcos, & Cabeza, 2010). However, it is not clear how such ‘functional connectivity’ is mediated.

In light of my work on the function of the hippocampus (Chapter 4; Riggs et al., 2009) and previous literature (e.g. Buzsaki, 2002; Duzel, Picton, et al., 2001; Rugg et al., 1996; M. E. Smith & Halgren, 1989), it is possible that the amygdala and hippocampus may oscillate in a phase-locked manner in the theta frequency range. There has been some evidence in support of this in the animal literature (e.g. Seidenbecher, Laxmi, Stork, & Pape, 2003). In the human literature, amygdala activity has predominantly been associated with gamma oscillations (e.g. Luo et al., 2007; Luo et al., 2010; Oya, Kawasaki, Howard, & Adolphs, 2002), but some studies show that the amygdala also oscillates in the theta range during viewing of coarse fearful versus neutral faces (F. A. Maratos, Mogg, Bradley, Rippon, & Senior, 2009) and during affective priming (Garolera et al., 2007). However, further studies are needed in order to clarify whether the amygdala and other emotion-processing regions such as the caudate and cingulate (Chapter 5) may modulate the hippocampus in a phase-locked manner in the theta frequency, and how this may be related to subsequent memory performance.

5.2.2 Eye Movement Monitoring and Magnetoencephalography

In addition to showing that MEG can be successfully used to characterize hippocampal activity, I also showed that MEG can be combined with eye movement monitoring in order to characterize eye movement behaviour and underlying neural activity simultaneously (Chapter 5). This was one of the first few attempts to combine both technologies (Herdman & Ryan, 2007; Hirvenkari et al., 2010) and the first to use it in order to examine how emotions may influence online processing of associated information.

The combination of eye movement monitoring with MEG represents a powerful converging methods approach with which to study cognitive processes. For example, my current work using
eye movement monitoring showed that eye movements distinguished between changed and unchanged visual displays within the first fixation and that such early eye movement based effects of memory were uninfluenced by emotion (Chapter 3). This is consistent with my MEG work which suggests that memory may exert its influence very early on during online processing and that this may occur in an obligatory fashion (Chapter 4, 5). Future work could take this further and link specific eye movement indices of memory retrieval to the underlying neural activity as measured by MEG. In this way, one can outline exactly which neural regions/systems are driving certain eye movement behaviours. Specifically, which neural regions/systems drive early versus later and more evaluative eye movement based effects of memory?

Further, results from Chapter 5 showed that differences in viewing to (as measured by eye movement monitoring), and processing (as measured by MEG) of neutral faces associated with negative versus neutral sentences emerged in and around the same window, i.e. 400-1400 ms after stimulus onset. This suggests that emotion-modulated differences in viewing and processing may interact in a positive feedback loop such that associated emotional information about the face may drive participants to direct more viewing to informative regions of the face such as the eyes, leading to increases in neural activity in emotion-processing regions, which may then result in further differences in eye movement behaviour. It would be interesting for future research to examine precisely how indices of eye movement behaviour are related to underlying changes in brain activity.

By demonstrating that such a convergent approach to study cognitive processes is feasible, this paves the way for future research to expand and build upon my work and begin to address new kinds of questions that could not be empirically examined with other methods such as fMRI. For example: which neural networks underlie early obligatory versus later evaluative aspects of memory retrieval; and how do specific indices of eye movement behaviour and underlying neural activity relate to each other? With an ever-increasing push for interdisciplinary research, it seems that there also needs to be an accompanying push whereby we begin to move beyond a modular view of cognition, which albeit useful, may not be an accurate reflection of the way in which the brain operates. As my work has shown, eye movement monitoring and MEG are both excellent tools for the study of how ‘different’ cognitive operations may interact and influence each other, and both have the potential to reveal aspects of cognition that cannot be gleaned by
other methods such as verbal report or fMRI that can shape our theoretical understanding of the brain.

5.3 Summary and Concluding Remarks

The current body of work went beyond simple verbal report measures of memory and used methodologies that enabled us to address questions that could not be gleaned by verbal reports alone such as how do emotions influence online processing of associated information, and do emotions influence all stages of the retrieval process? In doing so, I found that emotions influenced not only the amount of attention allocated to the associated information, but also the manner in which participants viewed it and the type of representation formed. Further, contrary to previous assumptions in the literature (e.g. Armony & Dolan, 2002; J. M. Brown, 2003; Easterbrook, 1959; Kensinger et al., 2005; E. F. Loftus et al., 1987; Wessel & Merckelbach, 1997), I also found emotion-modulated differences in the amount of attention allocated to the associated information was not related to subsequent memory performance. Rather, emotion was found to modulate memory via the evaluative stages of the retrieval process and perhaps other unspecified factors not examined in the current work such as post-stimulus elaboration. Interestingly, I also found that emotion did not modulate earlier stages of retrieval (likely related to one’s ability to access stored memory representations) which may suggest that the early stages of memory retrieval may occur in an obligatory fashion.

In exploring how emotions may modulate memory for associated information, I also showed that MEG can be successfully used to outline hippocampal activity and that it can be combined with eye movement monitoring as a convergent method for the study of cognitive processes. In the future, the use of these methods can be applied to the study of how different cognitive processes may interact and the study of healthy versus ‘impaired’ populations. For example, MEG can be used to outline neural differences underlying emotion-modulated processing between healthy controls and patients with clinical disorders such as post-traumatic stress disorder. Further, by combining MEG with eye movement monitoring, this could lead to a more comprehensive understanding of how certain overt behaviours (i.e. eye movements) are directly linked with underlying neural systems, and how such interactions may be disrupted in clinical disorders. This may lead to insights on the nature of certain disorders and possibly better diagnostic
criterion and rehabilitative directions (e.g. Adolphs, Gosselin, et al., 2005; DeGutis, Bentin, Robertson, & D'Esposito, 2007; Schmalzl, Palermo, Green, Brunsdon, & Coltheart, 2008).

In summary, the current work encourages a reconceptualization of emotion, memory and perception and how they relate to one and another. Specifically, rather than viewing them as independent modular processes, they may, in fact, be more widely distributed in the brain and interact more closely than previously described. This may be evolutionarily adaptive allowing us to quickly and efficiently form memories for emotional events/scenes that can later guide perception and behaviour.
References


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