Event typicality and memory: Investigating how prior knowledge and novelty modulate memory for complex events

by

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Abstract

A complex set of processes and brain regions work together in healthy adults, allowing them to create and recall memories of daily events. Additionally, the perception and recall of these events is shaped by factors such as novelty and congruence with prior knowledge (typicality). Despite a long history of research, studies on the neural underpinnings of the mnemonic effects of novelty and typicality rarely examine complex naturalistic event memories. Moreover, it is uncertain how these effects evolve over time, as memories are stabilized and transformed from acquisition to retention and retrieval. In this thesis I use naturalistic film clip stimuli, behavioural measures, and functional magnetic resonance imaging (fMRI) to explore the effects of both novelty and typicality on the neural substrates mediating memory, and examine how these effects evolve through encoding and retrieval over the course of a week. Behaviourally, I find that both typicality and novelty enhance memory for events, but that atypical events are recalled with more errors over time. With respect to the neural bases of memory, I demonstrate that the greatest differences based on event typicality are seen during encoding - when typicality is correlated with greater medial prefrontal cortex (mPFC) and parietal activation, while novelty is correlated with greater activation in the medial temporal lobes (MTLs) and posterior sensory cortices. During retrieval, however, such differences based on typicality are subtler, with
retrieval supported by the MTLs, irrespective of event typicality, at all time points. Notwithstanding these overall neural similarities in the retrieval of all events, typical clips are associated with attenuated MTL activation during remote retrieval, indicating that recall dynamics may be influenced by event typicality over time. Furthermore, I provide evidence for differential functional connectivity of both the mPFC and MTLs during encoding and retrieval, based on event typicality. These results, which demonstrate how the neural substrates mediating narrative episodic memories are modulated by event typicality, are consistent with two complementary theories - Trace Transformation Theory and Schema Theory. Furthermore, they suggest, through mPFC and MTL functional connectivity, potential mechanisms by which typical and novel events may be differentially encoded and retrieved.
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Chapter 1
Introduction

1.1 Introduction

Creating and recalling memories of events (episodic memories) are daily activities for healthy adults. Implementing this encoding and recall, however, depends on complex networks of brain regions to support a set of processes that transform incoming sensory information into coherent percepts, combining this bottom-up information with relevant contextual, semantic, temporal, and affective information into a holistic representation that is later retrieved (Conway, 2009; Eichenbaum, 2014; Horner, Bisby, Bush, Lin, & Burgess, 2015; Knierim, Neunuebel, & Deshmukh, 2014; McKenzie et al., 2014; Rugg & Vilberg, 2012; St Jacques, Kragel, & Rubin, 2011). As such, memories reflect not only a record of the sensory input processed during a given event, but also the influence of past experiences (Bartlett, 1932). Two prominent factors known to guide and distort memory – novelty and typicality, or congruence with prior knowledge – have been the focus of much research over the past century (for example: Bartlett, 1932; Rumelhart & Ortony, 1977; van Kesteren, Ruiter, Fernández & Henson, 2012; von Restorff, 1933). More recently, neuropsychological studies and advances in neuroimaging technology have supported the identification of key nodes in the memory network that are linked to the effects of typicality and novelty. The medial temporal lobes (MTLs), though commonly associated with episodic memory in general (Nadel & Moscovitch, 1997; Scoville & Milner, 1957; Squire, 1992), are thought to subserve the detection and processing of novel or unexpected information specifically (Knight, 1996; Kumaran & Maguire, 2009; Schacter et al., 1995; Tulving, Markowitsch, Kapur, Habib, & Houle, 1994; Vinogradova, 2001). On the other hand, growing evidence suggests that the medial prefrontal cortex (mPFC) is associated with the mnemonic influences of prior knowledge (Ghosh, Moscovitch, Melo Colella, & Gilboa, 2014; Maguire, Frith, & Morris, 1999; Preston & Eichenbaum, 2013; van Kesteren, Ruiter, Fernández, & Henson, 2012). Thus, though complex networks of brain regions cooperate to support episodic memory (Moscovitch, Cabeza, Winocur, & Nadel, 2016; Moscovitch, 1992; Rugg & Vilberg, 2012; St Jacques et al., 2011), mPFC-MTL interactions are of particular interest for encoding and retrieval with respect to typicality and novelty.
Despite a long history of research on both novelty and typicality in memory, investigations into the neural underpinnings of these effects have often depended on impoverished stimuli, while their interactions in naturalistic event memories remain understudied. Thus, the primary objective of this dissertation was to deepen our understanding of how these two, seemingly opposing, factors modulate neural activity and connectivity during the encoding and retrieval of complex narrative event memories, shortly after acquisition and at longer delays. Specifically, I used naturalistic film clip stimuli and followed the effects of typicality and atypicality (novelty) through encoding, immediate, and delayed retrieval in order to characterize how these effects evolve as memories naturally undergo stabilization and transformation over the week following encoding (Winocur, Moscovitch, & Bontempi, 2010; Winocur & Moscovitch, 2011). Behavioural and functional magnetic resonance imaging (fMRI) evidence is provided for the modulation of memory and of neural activation patterns based on event typicality. Furthermore, the functional connectivity of the mPFC and MTLs with each other and with the rest of the brain is explored in order to identify potential mechanisms by which typical and atypical events may be differentially encoded and retrieved.

1.1.1 Prior knowledge and memory

In his seminal work, Bartlett (1932) demonstrated that remembering is a constructive process, shaped by prior knowledge and experiences. Bartlett observed that when people are asked to repeatedly recall an unusual story, elements of it that are inconsistent with participants’ own cultural knowledge tend to be either forgotten or distorted to be more consistent. For the sake of this thesis, prior knowledge is defined as abstract or generalized memory for facts, concepts, schemas, and scripts that is not associated with a specific event memory or context (Craik, 1979; Tulving, 1983). This includes general semantic knowledge, as well as personal semantic information and cultural knowledge, which is all thought to be developed through the extraction of consistencies from across multiple related events, resulting in the retention of common features and the loss of event-specific details (Brady & Oliva, 2008; Conway, 2009; Posner & Keele, 1968; Richards et al., 2014; Tulving, 1972).

In the 1970s and ‘80s there was a proliferation of research on the mnemonic effects of prior knowledge, demonstrating how congruency with general knowledge enhances memory, an effect that was attributed to semantic elaboration (Craik & Tulving, 1975; Schulman, 1974; also see
Staresina, Gray, & Davachi, 2009). Expertise was also shown to enhance memory, such that people with more pre-experimental knowledge about a given topic are more accurately able to recall and recognize newly learnt information related to that field (Chiesi, Spilich, & Voss, 1979; Spilich, Vesonder, Chiesi, & Voss, 1979; for a review see Alba & Hasher, 1983). Similarly, comprehension and memory are enhanced when participants are provided with relevant background information about prose passages (Bransford & Johnson, 1972) or people (Anderson, 1981), and when objects are consistent with the ‘action schema’ of a scene, rather than inconsistent or irrelevant (Goodman, 1980).

Even if relevant information is not explicitly provided to participants, the organization of a scene so that it is consistent with prior knowledge allows information - such as spatial relations, but not specific details of object appearance - to be retained for up to four months (Mandler & Ritchey, 1977). Without this organization the information from scenes is forgotten in less than a week. Interestingly, no differences were observed at immediate testing in that study, suggesting that the mnemonic effects of prior knowledge may become more pronounced over time. Friedman (1979) further demonstrated that participants preferentially noticed changes to unexpected objects embedded in scenes, while remaining oblivious to changes in expected objects. These latter two sets of results indicate that specific visual details tend to not be noticed or encoded for items that are congruent with prior knowledge, and that if two items instantiate the same semantic representation they may not be distinguished. We will return to these ideas - that prior knowledge can both enhance and impair or distort memory - at a later point.

The research outlined above, on prior knowledge and episodic memory, often focuses on the concept of schemas, which was introduced by Head and Holmes (1911) and adapted to memory by Bartlett (1932) (see Alba & Hasher, 1983 for a review). Despite great interest in schemas, defining this type of semantic knowledge has proven difficult. Some describe schemas liberally as any framework of knowledge that either: a) guides the interpretation of new events and upon which new learning is built (Bartlett, 1932; Piaget, 1929), or b) affects processing of new information (van Kesteren et al., 2012), or c) specifically enhances memory of new congruent information, supporting generalization and novel inferences (Preston & Eichenbaum, 2013). There have also been attempts, however, to define schemas more precisely as associative network structures of information, which are abstracted on the basis of multiple episodes, lack unit detail, and are adaptable, as differentiated from other semantic knowledge such as
categories, which are defined by features and are not adaptable or flexibly associative (Ghosh & Gilboa, 2014). Additionally, it is not clear whether schemas include only abstract features common across events (van Kesteren et al., 2012), or whether they also contain detailed features specific to discrete events (Preston & Eichenbaum, 2013). Indeed, the nature of different schemas may vary depending on the nature of one’s experiences, which can result in both specification and generalization within schemas (Rumelhart & Ortony, 1977). Due to the variation in knowledge that is considered ‘schematic’ across the literature, we will continue to use the term ‘prior knowledge’, which may include both schematic information as well as other semantic knowledge, as defined above. However, since the term ‘schema’ is used so widely across the literature, I will continue to use the term when discussing articles that describe their own results with respect to schemas. Note that this thesis is concerned with investigating the interactions of prior knowledge with memory for narrative events, rather than defining schemas per se.

In general, prior knowledge is thought to guide behaviour, facilitate the encoding, retention and retrieval of new information, and enable inferential processing (Alba & Hasher, 1983; Ghosh & Gilboa, 2014; Piaget, 1929; Preston & Eichenbaum, 2013; Rumelhart & Ortony, 1977). In particular, the automatic emphasis of relevant information, through the top-down influences of prior knowledge, may guide attention, which promotes context appropriate behaviour and maximizes the efficiency of new learning (Carpenter & Grossberg, 1993; Sweller, 1988). Reconstruction based on prior knowledge may be particularly important in supporting recall when episodic memory is weak, incomplete, or error prone, although this will lead to systematic biases in recall towards the ‘average’, such that things are remembered as more congruent with prior knowledge (Hemmer & Steyvers, 2009; Konkle & Oliva, 2007; Steyvers & Hemmer, 2012). In all of these ways, depending on prior knowledge may reduce the resources needed by the cognitive system at both encoding and retrieval (Steyvers & Hemmer, 2012). Furthermore, the effects of prior knowledge are evident whether that knowledge is acquired intraexperimentally, or based on pre-experimental real-world knowledge (Poppenk, Köhler, & Moscovitch, 2010).
1.1.2 Neural correlates for the interaction of prior knowledge with episodic memory

Semantic memory is generally associated with a distributed network of areas across the temporal, parietal, and frontal lobes (Binder, Desai, Graves, & Conant, 2009; Patterson, Nestor, & Rogers, 2007). This thesis, however, is not focused on semantic memory in general, but instead on the interactions of prior knowledge with episodic memory. The behaviour of patients with lesions to the ventral mPFC suggests a neural basis for such prior knowledge effects, which may both enhance and distort memory, as described above. For example, in healthy participants, items imagined in congruent, as opposed to incongruent, contexts are associated with increased rates of recognition, as well as increased false alarms to similar lures, suggesting that generalized memory has been enhanced by congruency, at the cost of detailed information (Spalding, Jones, Duff, Tranel, & Warren, 2015). Notably, patients with ventral mPFC lesions, extending dorsally into the mid-mPFC (Figure 1), do not show this effect, suggesting that the mPFC may be critical for the interaction of such prior knowledge with episodic memory. Lesions to the ventral mPFC also attenuate schematic effects on memory in the Deese-Roediger-McDermott paradigm (Melo, Winocur, & Moscovitch, 1999; Warren, Jones, Duff, & Tranel, 2014) and affect schema-based processing even in non-mnemonic tasks (Ghosh et al., 2014).

Figure 1: Neuroanatomy of the ventral mPFC lesion group from Spalding et al., 2015. Lesion overlap was concentrated in the ventral mPFC. Hotter colors indicate more cases with overlapping lesions (maximum of 6). Copyright the authors 2015.
Similar links between prior knowledge and the mPFC are seen in rodents. Tse and colleagues (2007) used the term ‘schema’ to refer to task knowledge and learned flavour-place associations. In their paradigm, the mPFC is associated with both encoding and retrieval of schema-related paired associates (Tse et al., 2011). In other tasks, inactivation of the rodent mPFC results in an inability to apply a rule correctly to the relevant context, indicating a failure in the integration of prior knowledge with a current experience, or a failure in the suppression of contextually inappropriate information (Navawongse & Eichenbaum, 2013). Similarly, Morici and colleagues (2015) demonstrated that the mPFC in rodents is critical for context-specific object recognition. Such rodent research highlights the potential importance of the mPFC in both activating relevant contextual or schematic information, and in suppressing inappropriate information.

Recently, paired-associate paradigms adapted from the one used by Tse and colleagues have been developed for fMRI use with humans. This work demonstrates that people, like rodents, acquire new object-place associations faster on a board about which they learnt schema-like information, and that this effect is linked with mPFC and precuneal activation during both encoding (Sommer, 2016) and retrieval (van Buuren et al., 2014).

Neuroimaging has also been used to show that the enhancement of memory for stories that are either consistent with prior knowledge, or accompanied by relevant contextual information, is correlated with mPFC and parietal activation (Maguire et al., 1999), suggesting that these areas may play an important role in linking semantic and episodic information. Furthermore, activation in the mPFC during the encoding of two contextually related objects predicts false recognition of a third related object, highlighting a role for the mPFC in activation of contextual knowledge (Aminoff, Schacter, & Bar, 2008), while mPFC activity also increases with the amount of prior knowledge, as indexed by familiarity, that participants have with a person or place during imagination (Benoit, Szpunar, & Schacter, 2014). Similar increases in mPFC activity are found when retrieving events or word-fabric-pattern associations that are consistent, rather than inconsistent, with prior knowledge (Brod, Lindenberger, Werkle-Bergner, & Shing, 2015; van Kesteren, Rijpkema, Ruiter, & Fernandez, 2010a). Van Kesteren and colleagues (2010b) also show that manipulating prior knowledge by having participants watch the first half of a movie either in the correct or scrambled order results in greater mPFC inter-subject synchronization while watching the second half of the movie, only for those participants who viewed the movie in the correct order, and thus had consistent relevant prior knowledge.
Taken together, the neuropsychological, rodent, and human neuroimaging data outlined above are all consistent with the theory, proposed by van Kesteren and colleagues (2012), named Schema-Linked Interactions between Medial prefrontal and Medial temporal regions (SLIMM). SLIMM suggests that the mPFC detects congruence between prior knowledge and a current experience, which they term ‘resonance’ (van Kesteren et al., 2012). This resonance is associated with a shift from MTL- to mPFC- based memory processing, such that the mPFC activates contextually relevant, and suppresses irrelevant, information in order to facilitate and constrain mnemonic processing (van Kesteren et al., 2012). This shift between mPFC and MTL mediated memory processes will be discussed further, in the section on mPFC-MTL interactions (below).

The MTL-independence of such prior knowledge effects is further evidenced by the normal susceptibility to false recall and preserved congruency benefits seen in patients with MTL damage, at short delays (Kan, Alexander, & Verfaellie, 2009; Melo et al., 1999; Race, Palombo, Cadden, Burke, & Verfaellie, 2015; Schacter, Verfaellie, & Pradere, 1996). In fact, his research on this topic led Schacter (1996) to assert that MTL amnesics’ free recall may consist entirely of degraded ‘gist’ information, while healthy individuals’ recall consists of both gist and specific information. Although the ‘gist’ of an event, based only on a single experience, is different from semantic knowledge, it is possible that part of the reason amnesics’ memories are gist-like is that they are more dependent on semanticized knowledge during recall. Due to the paucity of specific event details retrievable by amnesics (St-Laurent, Moscovitch, Jadd, & Mcandrews, 2014; St-Laurent, Moscovitch, Levine, & McAndrews, 2009), memory reconstruction may be more dependent on general knowledge, including both schematic information and personal semantics (Rosenbaum et al., 2005). Prior knowledge may thus play a greater role when MTL function is impaired, or when episodic memory is otherwise degraded. This could relate to the evidence outlined previously that schema effects become more pronounced over time, as episodic memory tends to fade and decline in detail (Sekeres et al., 2016; Winocur, Moscovitch, & Bontempi, 2010; Winocur & Moscovitch, 2011).

1.1.3 Novelty, memory, and the medial temporal lobes

The novelty or atypicality of a stimulus is also known to enhance memory (von Restorff, 1933). This is sometimes described as a bizarreness effect, with the overall distinctiveness of a stimulus thought to determine subsequent mnemonic effects (McDaniel & Einstein, 1986). This beneficial
effect of novelty on memory is thought to be supported by the dopaminergic system through the enhancement of long-term potentiation (Frey, Schroeder, & Matthies, 1990; Li, Cullen, Anwyl, & Rowan, 2003; Lisman, Grace, & Street, 2005). The detection of such novelty, or mismatch between expectations and reality, is strongly linked with the MTLs, particularly the hippocampus (Carpenter & Grossberg, 1993; Kumaran & Maguire, 2009; Vinogradova, 2001; Tulving, et al., 1994).

Not only does the hippocampus respond most to partially rearranged sequences, which generate and then violate expectations (Kumaran & Maguire, 2006, 2007), but it also automatically tracks the total number of changes between studied items and similar lures, whether they are behaviourally relevant or not (Duncan, Ketz, Inati, & Davachi, 2012). Note, however, that the hippocampus is not the only MTL region linked with novelty, as parahippocampal activity is also correlated with novelty in scene stimuli, providing evidence for more general MTL novelty processing (Kohler, Crane, & Milner, 2002). Similarly, activity across MTL regions tracks novelty in the meaning of sentences, rather than in syntax, providing evidence for selective processing of this behaviourally relevant novelty in the MTLs (Poppenk et al., 2008).

Furthermore, patients with MTL lesions fail to show characteristic event related potential (ERP) effects and autonomic skin conductance responses to novelty (Knight, 1996), and show working memory impairments specifically when the information to be maintained in memory is novel (Rose, Olsen, Craik, & Rosenbaum, 2012). Recently, Garrido and colleagues (2015) proposed a role for mPFC-hippocampal interactions in novelty, suggesting that the mPFC may actually drive the hippocampal activity induced by mismatch computations. Although the mPFC is not the focus of much research on novelty, these data are consistent with a role for mPFC-MTL interactions in memory and cognition when stimuli are novel or atypical (discussed below).

Despite being linked with the processing of novelty, the MTLs are more prominently associated with episodic memory in general. This has been the case since the seminal studies of patient HM, whose amnesia was attributed to MTL lesions (Scoville & Milner, 1957). The MTLs are thought to support episodic memory through the rapid and obligatory encoding of the contextual, item, and relational information that makes up an event (Cohen, 2015; McClelland, McNaughton, & O’Reilly, 1995; Morris Moscovitch, 1992, 2008; O’Reilly, Bhattacharyya, Howard, & Ketz, 2014). Cells in the hippocampus have been shown to encode space (O’Keefe & Nadel, 1978; O’Keefe, 1976), time (Eichenbaum, 2014), objects (Komorowski, Manns, & Eichenbaum, 2009),
affective associations (Liu et al., 2012), and complex conjunctions of these various features (McKenzie et al., 2014). In particular, the MTLs are thought to process the contextual relations among items in an event or scene, whether spatial, temporal, or otherwise (Cohen, 2015; Howard & Eichenbaum, 2015; Rolls, 2015; Winocur & Moscovitch, 2011). Evidence for the link between relational processing, episodic memory, and the MTLs is provided by conducting principle components analysis on a battery of neuropsychological tasks - long term memory and relational memory tasks load together onto a single component, performance on which is correlated with hippocampal volume (Monti et al., 2015). Indeed, the MTLs are critical for relational encoding and memory even when learning occurs in the absence of conscious awareness (Chun & Phelps, 1999; Henke, 2010; Moscovitch, Cabeza, Winocur, & Nadel, 2016; Ryan, Althoff, Whitlow, & Cohen, 2000). The importance of the MTLs in the detection of novelty and the encoding of novel or atypical stimuli may be due to this rapid and obligatory encoding of even arbitrary relations (Rolls, 2007). Unlike the neocortex, which gradually integrates new information with pre-existing representations, the hippocampus is ideally set up to rapidly process and encode novel stimuli (McClelland et al., 1995; O’Reilly et al., 2014; Rolls, 2007, 2015).

1.1.4 mPFC-MTL connections and interactions

The mPFC’s anatomical connections make it a likely candidate for the role proposed above, namely that of integrating incoming experiential information with pre-existing knowledge representations in order to detect congruence, modulating behaviour, encoding, and retrieval. The human functional neuroimaging evidence outlined above suggests that the mPFC region of interest with respect to the interaction of prior knowledge with episodic memory is a mid-mPFC area, roughly the ventral medial aspects of BA10/32, with some effects found more ventrally (see Figure 2). This is the region that is considered with respect to the human and non-human primate evidence outlined below. Possible functional differences between mPFC sub-regions in both primates and rodents will be considered in the final discussion of Chapter 6.

Figure 2: Peaks from previous literature on prior knowledge and memory. The mPFC peaks from the following articles are included: Aminoff, Schacter, Bar, 2008; Bein et al., 2014; Benoit, Szpunar, Schacter, 2014; Brod et al., 2015; Liu et al., 2016; Maguire et al., 1999; Sommer, 2016; van Dongen, Takashima, Barth, Fernandez, 2011; van Kesteren et al., 2010a, 2010b, 2013, 2014.
A sphere with a radius of 3mm was created surrounding each mPFC peak reported in the previous studies on the mnemonic effects of prior knowledge (all coordinates either reported in MNI space, or converted to MNI space). These peaks are overlaid on a standard MNI template. Brighter colours indicate the center of a sphere, while darker reds indicate the periphery; these colours do not indicate level of activation.

In humans and non-human primates the mPFC receives MTL input in conjunction with input from the thalamus, the amygdala, and higher-order perceptual cortices such as parieto-occipital areas and auditory association cortex, making it well situated to integrate neocortical and limbic information (Barbas & Blatt, 1995; Jin & Maren, 2015; Mackey & Petrides, 2010; Yeterian, Pandya, Tomaiuolo, & Petrides, 2012). Furthermore, in rodents, the mPFC receives prominent projections from the hippocampus, and projects back via the thalamus, or perirhinal and entorhinal cortices (Hoover & Vertes, 2007; Jones & Witter, 2007; Vertes, 2002, 2004). The importance of the mPFC in memory is also demonstrated by its consistent emergence in memory-related brain networks (Cabeza & St Jacques, 2007; Maguire, 2001; St. Jacques, Kragel, & Rubin, 2011) and as a core hub whose activity correlates with the MTL subsystem of the default network (Andrews-Hanna, Reidler, Sepulcre, Poulin, & Buckner, 2010). Thus, various types of evidence provide support for the mPFC’s role in integration, and for mPFC-MTL interactions in memory.

Functionally, a direct pathway from the mPFC to the hippocampus in rodents has recently been shown to be capable of driving memory retrieval, suggesting a mechanism by which prefrontal input might directly modulate memory (Rajasethupathy et al., 2015). In humans, mPFC-MTL connectivity is predictive of subsequent memory, even in tasks that do not explicitly involve prior knowledge effects (Ranganath, Heller, Cohen, Brozinsky, & Rissman, 2005). When prior knowledge is taken into account, mPFC-MTL interactions are thought to support the integration
of new information into pre-existing knowledge structures, as well as inferential processing, and the abstraction of knowledge across different episodes (McClelland, 2013; Preston & Eichenbaum, 2013; van Kesteren et al., 2012). Consistent with this proposal, mPFC-MTL functional connectivity tracks the emergence of conceptual knowledge in a weather prediction task, and is correlated with performance on probe trials (Kumaran, Summerfield, Hassabis, & Maguire, 2009). However, despite much research into the effects of prior knowledge on mPFC-MTL functional connectivity, the field is full of conflicting results with respect to the nature of these interactions.

Van Kesteren and colleagues have explored the mPFC-MTL relationship extensively. They have shown that mPFC activity is positively correlated with increasing congruency between object-scene pairs, while the MTLs (the parahippocampus specifically) show the opposite pattern - increasing activation with decreasing congruency (van Kesteren et al., 2013). They have also demonstrated that mPFC-MTL functional connectivity is greater when watching a movie after seeing the first half scrambled, suggesting that the greater mPFC-MTL crosstalk may be necessary to compensate for the absence of relevant prior knowledge (van Kesteren et al., 2010b). Similarly, learning new facts that are unrelated to one’s major in university is correlated with greater mPFC-MTL functional connectivity, as compared with learning facts related to one’s own field of study, which is associated with enhanced memory and mPFC activity (van Kesteren, Rijpkema, Ruiter, Morris, & Fernández, 2014). In the case of word pairs, mPFC-MTL functional connectivity is only predictive of subsequent memory in semantically incongruent trials (Bein, Reggev, & Maril, 2014). As discussed above, Garrido and colleagues (2015) find a similar relationship between the mPFC and hippocampus, driven by novelty. The enhanced mPFC-MTL connectivity seen for stimuli unrelated to prior knowledge may be due to novel contexts or increased task demands requiring greater integration of relevant semantic with event-specific information, while schematic representations may be sufficient to guide behaviour and memory in familiar contexts (Binder & Desai, 2011). Indeed, the mPFC is proposed to inhibit MTL-dependent binding of event elements in situations that are congruent with prior knowledge, since dependence on direct cortical learning is thought to be metabolically more adaptive (van Kesteren et al., 2012).

Conversely, Liu and colleagues (2016) found greater mPFC-MTL functional connectivity for houses paired with famous, rather than non-famous, faces. Likewise, elevated mPFC-MTL
functional connectivity was measured during the encoding of object-place (Sommer, 2016) and object-face paired associates (Schlichting & Preston, 2015) when they were related, rather than unrelated, to prior learning.

Thus, congruence with prior knowledge seems to both enhance and attenuate mPFC-MTL functional connectivity, with the nature of the relationship dependent on the context. This thesis will attempt to clarify the relationship between the mPFC and MTLs during memory encoding and retrieval.

### 1.1.5 Consolidation and memory over time

The idea that memories are organized and stabilized over time dates back to Ribot (1882) who observed that recent memories seem to be more affected by brain damage than remote ones, with the term ‘consolidation’ adopted several years later to refer to this process of memory stabilization (Muller & Pilzecker, 1900). Ever since the MTLs, and the hippocampus specifically, have been linked with memory (Penfield & Milner, 1958; Scoville & Milner, 1957), the process of consolidation has been similarly linked with a transition from hippocampal-dependence to independence during this stabilization of memory over time (McClelland et al., 1995; Squire & Alvarez, 1995; for a review see Moscovitch, 2014). Despite years of research, however, the roles of the hippocampus and neocortex in this process remain the focus of conflicting theories.

The traditional view on consolidation is captured by Standard Consolidation Theory (SCT), which posits that the acquisition of all declarative memories is hippocampus-dependent but that, with time, memory is consolidated and maintained in extra-hippocampal neocortical structures (Squire & Alvarez, 1995; Squire & Wixted, 2011). This is thought to be due to the neural architectures of the hippocampus and neocortex; the former is a structure capable of rapid learning with sparse representation that reduces interference, while the latter is a slow-learning system capable of gradually integrating across episodes to extract commonalities and generalizations (McClelland, McNaughton, & O’Reilly, 1995; O’Reilly, Bhattacharyya, Howard, & Ketz, 2014). During consolidation, the reactivation of specific memory representations by the hippocampus is thought to support the gradual integration of new episodes into structured neocortical memory representations, with a shift from hippocampal-dependence to dependence on neocortical areas such as the mPFC during remote retrieval (Frankland & Bontempi, 2005,
2006; McClelland et al., 1995; Takehara, Kawahara, & Kirino, 2003; Takehara-Nishiuchi & McNaughton, 2008). This theory is supported by evidence that, in rodents, mPFC activity tends to increase or become critical for memory over time, as hippocampal activity tends to decrease and hippocampal lesions tend to become less disruptive to memory (Bontempi, Laurent-Demir, Destrade, & Jaffard, 1999; Maviel, Durkin, Menzaghi, & Bontempi, 2004; Takehara, Kawahara, & Kirino, 2003; Takehara-Nishiuchi, Maal-Bared, & Morrissey, 2011; Takehara-Nishiuchi & McNaughton, 2008; Winocur, 1990; but see Goshen et al., 2011). These consolidation dynamics are also seen in humans, where memory for landscape items is associated with decreased hippocampal and increased mPFC activity over the three months following encoding (Takashima et al., 2006).

Lesion evidence, however, does not consistently support such time-limited roles for either the mPFC or MTLs. Instead, lesions to the mPFC in humans do not result in a selective remote memory deficit, and sometimes result in confabulation which involves recent and remote memories equivalently (Gilboa et al., 2006; Moscovitch & Melo, 1997; Moscovitch, 1995; Nieuwenhuis & Takashima, 2011; but see O’Connor & Lafleche, 2004). Confabulation, known as ‘honest lying’, is the report of memories that are false in the context of retrieval, characterized by the patient’s genuine belief in their veracity (Gilboa & Moscovitch, 2002). Although confabulations tend to involve autobiographical memories, they are also observed during recall of common fairy-tales and bible stories (Gilboa et al., 2006) and historical events (Moscovitch & Melo, 1997), and as increased false alarm rates on recognition tasks (Nieuwenhuis & Takashima, 2011). The link between mPFC lesions and confabulation across all these domains suggests a role for this region in the monitoring of current experience with respect to prior knowledge, and the suppression of contextually or schematically irrelevant information (Hebscher, Barkan-Abramski, Goldsmith, Aharon-Peretz, & Gilboa, 2015; Schnider & Ptak, 1999), consistent with the SLIMM model outlined above.

Similarly, MTL lesions often result in flat temporal gradients, affecting episodic memories from across the lifespan (Nadel & Moscovitch, 1997; Winocur & Moscovitch, 2011). Whether or not a temporal gradient is found in amnesia after MTL lesions seems to be particularly dependent on the quality of memory being tested, with deficits across both recent and remote time-points evident when assessing memory with respect to event specific detail (Corkin, 2002; Rosenbaum et al., 2008; Winocur et al., 2010; but see Kirwan et al., 2008; Bayley, Hopkins, & Squire, 2006;
for a recent review see Moscovitch et al, 2016). In particular, both hippocampal and parahippocampal activation has been linked with the detail or vividness of a memory, rather than its age per se, while damage to the MTLs is associated with a decline in the perceptual richness of memories of all ages (Addis, Moscovitch, Crawley, & McAndrews, 2004; Gilboa, Winocur, Grady, Hevenor, & Moscovitch, 2004; Levine et al., 2004; St-Laurent, Moscovitch, Jadd, & Mcandrews, 2014; Svoboda, McKinnon, & Levine, 2006). Furthermore, functional neuroimaging studies suggest that both the MTLs and the mPFC support episodic memories of all ages, from minutes to years after encoding (Bonnici et al., 2012; Cabeza & St Jacques, 2007; Furman, Mendelsohn, & Dudai, 2012; Maguire, 2001; Piolino, Desgranges, & Eustache, 2009; Winocur et al., 2010; Winocur & Moscovitch, 2011).

The Trace Transformation Theory, which arose out of the Multiple Trace Theory, accounts for these results by proposing that the MTLs are critical for the encoding of episodic memories and remain critical for the retrieval of such memories as long as they retain their detailed, context bound form (Nadel & Moscovitch, 1997; Winocur et al., 2010). Any shift in neural representation from hippocampal to extra-hippocampal neocortical structures is thought to entail a transformation of memory to a more generalized representation retaining the gist of the episode (Moscovitch et al., 2016; Winocur, Moscovitch, & Sekeres, 2007; Winocur & Moscovitch, 2011). These detailed MTL-dependent and gist-like neocortical memory representations are thought to co-exist, and dynamically interact, with memory strength and task demands determining which trace is dominant at a particular time (Winocur, Moscovitch, Bontempi, 2010; Winocur & Moscovitch, 2011).

1.1.6 Consolidation and schemas

The complexity of consolidation dynamics may be partly due to both congruence with prior knowledge and repetition modulating the transformation of memory and the integration of information into existing semantic networks, with correlated modulation of MTL and mPFC activity (van Kesteren et al., 2012; Yassa & Reagh, 2013).

The most striking evidence for modulation of consolidation dynamics by prior knowledge was provided by Tse and colleagues (2007), who showed, in rodents, that although the learning of paired associates is dependent on the hippocampus whether or not they are related to prior knowledge, related pairs are additionally dependent on the mPFC during encoding and are
consolidated more rapidly than unrelated pairs (Tse et al., 2007, 2011). This rapid consolidation is presumably due to the incorporation of related information into pre-existing knowledge structures (McClelland, 2013; Tse et al., 2007; Wang & Morris, 2010). Recently, similarly accelerated consolidation for paired associates related to prior knowledge was found in humans (Sommer, 2016). Schemas are thought to support such rapid consolidation through the potentiation of direct connections between neocortical representations (van Kesteren et al., 2012), and through either the direct or hippocampus-dependent reactivation of information that is related to prior knowledge, which is thought to underlie the stabilization of memories during rest and sleep (Dudai, Karni, & Born, 2015; van Dongen, Takashima, Barth, & Fernández, 2011). Physiologically, integrating new information into a pre-existing schema or neocortical framework is thought to occur rapidly since it requires fewer new links between neurons and other biological modifications (Wang & Morris, 2010). Thus, the normal increase in mPFC activity seen during retrieval as memories become more remote may reflect either the semanticization of specific information, or the integration of new information into prior knowledge representations, a process that occurs more quickly when the new information is consistent with those pre-existing representations.

A related and compatible hypothesis is that the decline in MTL activity, often reported over time, may also be due to the decline in rich episodic detail that tends to occur as memories become more remote (McKelvey & Moscovitch, 2013; Sekeres et al., 2016), resulting in an increased dependence on schematic knowledge and correlated mPFC activation. Critically, a similar decline in detail is seen with repetition, independently of time. For instance, when increasing numbers of scene category exemplars are studied, memory becomes generalized, as evidenced by a decreased ability to discriminate studied scenes from novel scenes of the same category (Konkle, Brady, Alvarez, & Oliva, 2010). A decline in the specificity of memory is also seen when single items are repeatedly viewed, with more study thus paradoxically decreasing the accuracy of memory (Reagh & Yassa, 2014), an effect that is associated with attenuated MTL activity and a shift towards mPFC and parietal activation (Reagh et al., 2015). Similarly, activity in the mPFC increases as short film clips are repeated, and is correlated with decreased vividness during mental replay (St-Laurent, Abdi, & Buchsbaum, 2015). Interestingly, schema-congruent items, which are similarly associated with attenuated MTL activity and enhanced mPFC activity (van Kesteren et al., 2013), are also associated with poor processing of specific detail, even
during encoding and recent memory (Friedman, 1979; Spalding et al., 2015). The above results highlight how the behavioural and neural patterns traditionally associated with consolidation over time (decline in detail, decreased MTL and increased mPFC activity) are also seen with repetition and prior knowledge congruency. Thus, the nature of a memory, rather than time per se, seems to be linked with its neural basis.

Critically, this would account for the fact that richly detailed episodic memories remain MTL-dependent as long as they exist, while other memories – those that become increasingly integrated with prior knowledge or dependent on schematic information during recall – are associated with a greater shift in activation from the MTLs to the mPFC. The proposal that a shift from MTL to mPFC based processing is due to a greater dependence on prior knowledge allows for a parsimonious integration of the evidence for increased mPFC but decreased MTL activation over time (Bontempi et al., 1999), along with evidence of prior knowledge effects on memory (Tse et al., 2007), and mnemonic generalization with repetition (Reagh & Yass, 2014).

Thus, the decline in MTL activity and increase in mPFC activity often observed over time may reflect the natural loss of detail from memory, along with a corresponding increased dependence on schemas and other semantic knowledge during the reconstruction of episodes from memory (Bartlett, 1932; Conway, 2009; Irish & Piguet, 2013; Moscovitch et al., 2016; Schacter et al., 1998). Note that this dependence on schemas during reconstruction is not hypothesized to be an effortful or explicit process, but an automatic and implicit neural process whereby the brain integrates relevant episodic and semantic information during event recall. Critically, for episodes that are congruent with prior knowledge, this reconstruction should result in recall of accurate details, whether these details are activated through episodic retrieval, or through inference from prior knowledge. On the other hand, for episodes that are incongruent or atypical, schema-based reconstruction should result in memory distortions and errors. The possibility that mPFC activation/dependence on prior knowledge may be differentially related to memory errors based on the congruence or typicality of an event will be investigated in this thesis.

1.1.7 Alternative theories of mPFC function

Despite its prevalence in discussions on memory, there is also a vast literature linking the mPFC to various other cognitive processes such as prediction and evaluation (Rudebeck & Murray, 2014), decision making (Bechara, Damasio, & Damasio, 2000), computation of subjective value
(Kable & Glimcher, 2007), reward (Knutson, Fong, Bennett, Adams, & Hommer, 2003), confidence (Barron, Garvert, & Behrens, 2015), and self-referential processes (Craik et al., 1999; Kurczek et al., 2015). Although an evaluation of all these areas is beyond the scope of this thesis, the role the mPFC plays in memory may be similar to the role it plays in these various cognitive processes. Namely, the mPFC may be critical for the integration of current experiences with pre-existing knowledge representations, such that relevant prior knowledge is activated while irrelevant information is suppressed, in a domain agnostic manner.

1.2 Dissertation Objectives

1.2.1 Broad objectives

The evidence outlined above illustrates that prior knowledge can both enhance and distort memory, via mPFC activity and connectivity, while novelty modulates episodic memory via the MTLs. Although these neural and mnemonic effects of prior knowledge and novelty have been explored before, research has consistently depended on basic stimulus pairings such as word or picture paired associates, flavour-place task knowledge, and other simplified examples of schemas. Additionally, despite much research delineating the patterns of neural activation seen as memories are consolidated – stabilized or transformed over time – the typicality or novelty of the original events is not often considered with respect to consolidation dynamics. Determining the effects of typicality on episodic memory using ecologically relevant, narrative stimuli will deepen our understanding of the neural networks that support memory in real world settings, where we are constantly experiencing a variety of events that fall along a spectrum of consistency with our previous experiences. With respect to the mPFC and MTLs in particular, the evidence outlined above suggests that activation in these areas may be affected not only by typicality and novelty, but also by time since encoding, with mPFC activation generally thought to increase during consolidation as MTL activity declines. Untangling these interactions of typicality, novelty, and consolidation will be critical for understanding the roles of the mPFC and MTLs in memory and cognition more generally. In order to explore these issues, the following broad questions will be addressed in this thesis:

1) How do typicality and novelty modulate the brain areas engaged during the encoding and retrieval of narrative event memories?
2) Do the effects of typicality and novelty on brain activation change over time between encoding, immediate retrieval, and delayed (7-day) retrieval, as memories undergo consolidation?

3) Does event typicality modulate the functional connectivity of our regions of interest, the mPFC and MTLs, with each other and with the rest of the brain?

To address these broad questions I used film clips to model event memory, since they involve complex events, which are dynamic, continuous, and contain perceptual and affective narrative elements within a spatial-temporal context (Furman, Dorfman, Hasson, Davachi, & Dudai, 2007; Hasson, Furman, Clark, Dudai, & Davachi, 2008; St-Laurent, Moscovitch, Jadd, & Mcandrews, 2014). Critically, although they thus capture some of the complexity of real world events, they retain the reproducibility and controlled nature of more traditional laboratory stimuli (Furman et al., 2007; Mendelsohn, Furman, & Dudai, 2010; St-Laurent et al., 2014). With respect to these film clips, a typical story is defined as ‘similar to an event you would normally encounter in day to day life’, while an atypical story is ‘very unusual and/or dissimilar to anything you would encounter in day to day life’. For the purposes of typicality ratings ‘encountering’ includes not only experiences in one’s own life, but also events experienced through books, movies, television, or other media. I argue that this is an ecologically valid form of prior knowledge since participants are likely to have much more extensive and robust prior knowledge applicable to the typical clips whose stories resemble events that they might encounter in their daily lives. Conversely, participants will lack, or have much weaker, representations of the novel/unusual information found in the atypical clips.

1.2.2 Specific hypotheses

In order to determine how typicality and novelty modulate memory accuracy (Chapter 3), and the brain areas engaged during the encoding (Chapter 4) and retrieval (Chapter 5) of complex event memories, I conducted behavioural analyses as well as four types of fMRI analyses. Parametric analyses were conducted to find activation patterns that increased with either increasing story typicality or atypicality in the film clip stimuli. To further explore these effects, I performed direct contrasts of the activation for the most typical clips as a group, with activation for the most atypical clips. Seed-based functional connectivity analyses were conducted to determine how our regions of interest, the mPFC and MTLs, work with each other and with the
rest of the brain during the encoding and retrieval of typical and atypical events. Finally, Region of Interest (ROI) analyses were conducted to test specific hypotheses with respect to MTL and mPFC activation over time, between immediate and delayed retrieval. This set of analyses was designed in order to test the following specific predictions:

1) Both typicality (congruency with prior knowledge) and atypicality (novelty) will enhance overall memory for film clips, with neutral clips forgotten at the highest rate, presumably due to the fact that there is neither strong schematic (mPFC-mediated) nor strong episodic (MTL-mediated) encoding (van Kesteren et al., 2012).

2) Clips with atypical stories will be more susceptible to memory errors and distortions over time as memory becomes increasingly dependent on prior knowledge (Bartlett, 1932). This will not cause as many errors in typical clips due to congruence between clip details and prior knowledge.

3) Typical clips will be associated with greater mPFC activation during encoding, while atypical clips will be associated with greater MTL activation. These differences will not exist at retrieval (see Hypotheses 6 & 7).

4) During both encoding and retrieval, typical clips will be associated with greater mPFC-neocortical functional connectivity, while MTL-neocortical functional connectivity will be greater for atypical clips, as suggested by the SLIMM theory that the mPFC and MTLs each act as hubs for schematic or novel stimuli in memory, respectively (van Kesteren et al., 2012).

5) mPFC-MTL functional connectivity will differ based on typicality during encoding and retrieval, although there is evidence that this connectivity may either increase or decrease with increasing typicality.

6) Film clips with both typical and atypical stories will be associated with MTL activation during immediate and delayed retrieval (Winocur et al., 2010; Winocur & Moscovitch, 2011), although this MTL activation will show a greater decline over the week following encoding for typical clips, presumably due to rapid integration with, or more dependence on, pre-existing knowledge (Tse et al., 2007, Sommer, 2016).
7) Delayed retrieval of both typical and atypical clips will be associated with mPFC activation. This may be due to standard consolidation dynamics, and/or due to a decline in episodic detail over time (Winocur and Moscovitch, 2011; Sekeres et al., 2016) with correspondingly increased dependence on schematic knowledge during recall.

8) If activation in the mPFC at delayed retrieval reflects dependence on schematic knowledge (Hypothesis 7), it will be positively correlated with errors for atypical, but not typical, clips.
Chapter 2
Materials and Methods

2.1 Participants

Twenty healthy, right-handed participants (12 female) were recruited through the participant database at Baycrest Hospital, ranging in age from 21-31 years old (mean age = 24.1, SD = 2.8). Participants were fluent in English, and screened using a detailed health questionnaire to exclude psychiatric or neurological disorders, previous head injuries, or other health problems and/or medications that might affect cognitive function and brain activity, including strokes and cardiovascular disease. All procedures were approved by Baycrest’s Research Ethics Board, and conducted in accordance with the guidelines set by the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans. All participants gave written informed consent, and were reimbursed $100 for their participation in the study.

2.2 Stimuli

Forty film clips from St-Laurent et al. (2014) were used to test episodic memory. All clips were 23 seconds in duration, taken from foreign films with limited dialogue, and have been used in various other studies (Sekeres et al., 2016; St-Laurent et al., 2014). Each clip was analyzed for its content based on various feature categories: visual complexity (colour, background complexity, movement, number of frame transitions, number of background characters), story complexity (number of central characters, storyline complexity), and sound complexity (speech, music, background noise). Three scorers (M.S., K.M., M.S-L.) independently rated each clip on each criterion, and assigned a score between 1 (low) - 5 (high), or a yes/no rating. Mean correlations between the three scorers were $r = .79$ (K.M. and M.S.), $r = .83$ (M.S. and M.S-L.), and $r = .78$ (K.M. and M.S-L.). Composite scores for each category were averaged, and mean scores were transformed to z-scores. Each clip’s z-scores were used to divide the 40 clips into two evenly distributed series of 20 clips, balanced across the feature categories. For each participant, each of the two series was pseudo-randomly assigned to be tested at one of the delays – either immediately or seven days after encoding (7d retrieval).
Clips were also rated with respect to typicality by sixteen independent participants (10 female, mean age = 25.6, SD = 3.1). Participants watched each clip, and then rated the typicality of the story on a scale of 1 (very typical) - 5 (very atypical). Typicality ratings were generally consistent across participants, with ratings for a given clip associated with a mean standard deviation of 1.1 points. Typical stories were defined as ‘similar to an event you would normally encounter in day to day life’. Atypical stories were defined as ‘very unusual and/or dissimilar to anything you would encounter in day to day life’. The raters were instructed that ‘encountering’ could include not only experiences in one’s own life, but also events experienced through books, movies, television, or other media. For some analyses all forty clips were retained, each associated with its specific mean typicality rating, while for other analyses a group of the most typical clips was compared against a group of the most atypical clips. The ten clips with the lowest ratings were categorized as typical clips (for example ‘Couple Meeting at the Restaurant’), while the ten clips with the highest ratings were categorized as atypical clips (for example ‘Woman Squeezing Food’). Typical and atypical clips were equivalent with respect to the above-mentioned feature ratings – visual, story, and sound complexity (all p’s > .15). Behavioural data for neutral clips (the ten clips with ratings in the center of the scale) were analyzed in order to provide a benchmark against which to test the effects on memory of both prior knowledge and novelty. See Appendix A for a list of clips, organized by typicality.

2.3 fMRI data acquisition

Encoding and replay retrieval sessions took place in the functional magnetic resonance imaging (fMRI) scanner, while a free-recall retrieval session took place outside the scanner. Participants encoded all forty film clips on the first day, followed by an immediate retrieval session (for half the clips) and, seven days later, a delayed retrieval session (for the remaining half of the clips). Anatomical and functional images were acquired with a 3T Siemens MRI scanner and standard 32-channel array head coil at Baycrest Hospital. For the anatomical scans, a T1-weighted volumetric anatomical MRI (160 axial slices, TE = 2.63 ms, 1mm thick, FOV = 256 cm) was acquired for each participant. The functional scans included thirty-six axial slices (3.5mm thick, skip 0.5mm), using a T2*- weighted pulse sequence with an echoplanar imaging (EPI) readout (TR = 2200 ms, TE = 27 ms, FOV = 225 mm, 96 x 96 matrix). Slices were obtained from an axial-oblique orientation, parallel to the Sylvian fissure. Brain activation was measured based on the blood oxygenation level-dependent (BOLD) signal.
2.4 Experimental procedure

During encoding participants viewed forty film clips in the fMRI scanner, presented in randomized order. Each clip was given a title (e.g., “Boy, Girl and Balloon”) that served as a cue in the retrieval portions of the experiment. Participants were instructed that this was a memory experiment, and that they should pay attention to the title and content of each clip. They were also informed that they would be tested on their memory for half of the clips shortly after encoding, while their memory for the other half of the clips would be tested one week later. The title appeared centrally on the screen for 4000 ms immediately before and after the clip. Clips were centrally presented on a computer screen, with the image reflected into participants’ view by a mirror. Sound was delivered through a rimless Avotech headset. A fixation cross was presented for 4000 ms between each clip. Encoding was performed across four runs in the scanner, with 10 clips presented in each run. No behavioural responses were required during the encoding session.

For retrieval, the total number of clips was divided into two sets of 20 clips each. One set of 20 clips was retrieved in the scanner immediately after the encoding session, and the other, after a seven day (7d) delay. Sets were assigned pseudo-randomly to a retrieval session in a manner that was counterbalanced across participants. In each retrieval session there were two runs of 10 clips each. Each run contained 2-3 typical and 2-3 atypical clips (classification of typical/atypical clips described above). During retrieval, participants were presented with the title of a clip for 16 seconds, during which time they were instructed to visualize the clip in their mind from beginning to end. Next, they used a keypad to rate how well they had recalled the clip’s story content, on a scale of 1 (low) to 4 (high). Story content referred to the general plot of the story (“what happened”), and events central to the progression of the episode (Berntsen, 2002; Sekeres et al., 2016; St-Laurent et al., 2014). A rating of ‘1’ indicated there was no story content recalled, while a rating of ‘4’ indicated participants believed that their memory contained all of the story elements. Next, participants rated the vividness of their memory’s perceptual content during the retrieval period in a similar way. Perceptual content referred to visual (colors, textures, facial features, clothing, object positions, background details, weather, lighting conditions, etc.) and auditory details (talking, laughing, background music, street sounds). Again, a rating of ‘1’ indicated no perceptual content, while a rating of ‘4’ indicated a maximal level of perceptual vividness. Each clip’s retrieval was separated by a fixation cross, presented centrally on the screen for 4000 ms.
After the two retrieval runs at each time point (immediately and seven days after encoding), participants were removed from the scanner, and completed the post-scan retrieval session in another room. During the post-scan session participants were again presented with the title of each clip they had retrieved in the scanner and asked to verbally report the story details they had recalled while in the scanner (what happened, who did what, what was the situation). Participants were next asked to verbally report any perceptual (visual or auditory) details they had imagined in their mind’s eye while retrieving the clip in the scanner. They were given a maximum of 60 seconds for each of these verbal report sections. Recordings of verbal responses were transcribed and scored according to a system described below.

The presentation order of clips was randomized within each retrieval session. See Figure 3 for a schematic of the procedure. Participants completed both retrieval sessions – memory replay inside the scanner and free recall outside the scanner – twice, once immediately after encoding and once seven days after encoding, with twenty different clips tested each session.

Figure 3: a) General outline of experimental procedure. b) Outline of retrieval sessions. The scanner portion of this procedure was repeated for all 20 clips, followed by the post-scan portion of this procedure for all 20 clips, in each session.
2.5 Data Analysis

2.5.1 Scoring and behavioural analyses

As described above, two separate recordings of the verbal retrieval were obtained for each clip to encourage participants to report everything they recalled about a clip’s storyline and perceptual content. The recordings were manually transcribed and responses were coded and scored to categorize and count central and peripheral details. Central details were elements that could not be modified or omitted without changing the plotline of the clip (Berntsen, 2002). In order to score central details consistently, five to seven central story points were identified for each clip and recorded as a ‘central narrative’. These central story points were identified based on narratives used in a previous study (St-Laurent et al. 2014). See Appendix A for each clip’s central narrative. A participant was given a score of one central point for each detail they retrieved that corresponded to a point in the central narrative for that clip. Peripheral details were considered any additional descriptive information, including perceptual, emotional, and contextual details present in the film clip. One peripheral point was scored for each peripheral detail reported during the verbal retrieval session. For each clip, central and peripheral details were coded and tallied across both recordings within a retrieval session. This was done for each film clip at each delay, by a scorer (S.P.) blind to the delay or typicality rating of each clip. Each reported detail was classified as either central or peripheral. No additional points were assigned for repeated details, or for unrelated information (i.e. opinions or speculations). Errors in central and peripheral details were also scored and tallied. Errors were considered any recalled details that did not match the information presented in the film clip. Participants were not penalized for failing to recall a detail. Thus, all errors analyzed below are errors of commission, rather than errors of omission.

As outlined above, ratings of ‘1’ indicated retrieval of no story or perceptual content. Thus, clips were classified as forgotten when participants provided ratings of ‘1’ for both these aspects of memory. Clips were also classified as forgotten when participants recalled the story of a different clip (for example relating the plot to ‘Couple Taking a Photograph’ when asked to recall ‘Couple at the Beach’), however this happened very rarely (0.2% of trials at immediate retrieval and 1.3% of trials at 7d retrieval). It was possible for participants to provide a rating of ‘1’ for one measure (for ex. perceptual vividness) with a higher rating for the other (for ex. story content), but this was
not the norm. Instead, ratings of story and perceptual content were highly correlated (r = .79, p < .001 for immediate retrieval; r = .78, p < .001 for delayed retrieval).

For each participant, self-report ratings of story/perceptual content, and central/peripheral details and errors were averaged across clips for each delay condition. All analyses of behavioural data were conducted as repeated measures ANOVAs. Significant effects were investigated using planned comparisons t-tests when they were consistent with a priori hypotheses, and post-hoc Tukey Honest Significant Difference (HSD) tests otherwise, to control the family wise error rate (FWE) at p < .05. All behavioural analyses were conducted using R software. One participant’s free recall data from the 7d retrieval session was lost due to a software malfunction.

2.5.2 fMRI data preprocessing

All pre-processing and statistical analyses described below were carried out using FSL (FMRIB’s Software Library, www.fmrib.ox.ac.uk/fsl). The data were skull stripped using the Brain Extraction Tool (BET), high-pass filtered at 100 seconds, and motion corrected using MCFLIRT (Jenkinson, Bannister, Brady, Smith, 2002). The data were spatially smoothed with a 6.0 mm full-width-at-half-maximum (FWHM) Gaussian kernel. Registration was carried out using FLIRT (FMRIB’s Linear Registration Tool; Jenkinson 2001, 2002). Individual participants’ functional data were first registered to their anatomical data using normal linear search and Boundary Based Registration (BBR). These data were then registered to MNI standard space (MNI 152 template) with a 2 × 2 × 2 mm voxel size using normal non-linear search with 12 degrees of freedom in FNIRT (Andersson, Jenkinson, Smith, 2010).

2.5.3 fMRI data analyses: general

Three participants were excluded from fMRI analyses due to an insufficient number of clips recalled. In order to be included in analyses each participant must have recalled at least 50% of the typical and atypical clips in each scanner retrieval session (min recalled = 5/10, max recalled = 10/10), and must have retrieved at least one typical and one atypical clip in each retrieval run.

Across all the analyses described below, statistical processing was carried out in three steps, using FEAT (fMRI Expert Analysis Tool, version 6.0). First, a general linear model (GLM) was applied at the level of each individual run. The specific explanatory variables (EV), used in each GLM will be described below, along with their corresponding analyses. Each EV was convolved with a
double-gamma HRF, included a temporal derivative and had temporal filtering. The initial results for each individual run were then passed up to fixed effects analyses at the subject level (combining runs 1 through 8 across each participant). Finally, each participant’s results were passed up to a final mixed effects analysis at the group level (FMRIB’s Local Analysis of Mixed Effects; FLAME 1). Group level analyses were cluster corrected to maintain FWE at $p < .05$. This general procedure was carried out for four different types of analyses: parametric analyses using all forty clips, each clip associated with a specific typicality rating; direct contrast analyses comparing the ten most typical and ten most atypical clips; seed-based functional connectivity analyses; and ROI analyses focusing on the mPFC and MTLs.

Note that all analyses described below include only subsequently remembered film clips, with subsequently forgotten clips modelled as ‘null’ events in each case. Supplementary analyses were carried out for encoding runs to include all clips, whether subsequently remembered or not. These analyses produced qualitatively equivalent results, such that clip perception was associated with the same patterns of neural activation, differing based on typicality, irrespective of subsequent memory. Analysis of ‘forgotten’ clips could not be carried out at retrieval since participants had not recalled any relevant information during these time periods or engaged in any particular cognitive task.

Cluster tables are provided following their corresponding figures, listing the peak coordinates, z-score, cluster size, and anatomical label of each significant cluster from the analyses described below. Cluster labels were determined from peak coordinates using the Harvard-Oxford cortical and subcortical structural atlases (Desikan, et al., 2006; Frazier et al., 2005; Goldstein et al., 2007; Makris et al., 2006), with names confirmed using Neurosynth (http://neurosynth.org/locations/) when a peak was associated with multiple names of equal probability in the atlases.

2.5.4 fMRI data analyses: parametric analyses

Parametric analyses were first conducted to determine whether there were patterns of neural activation predicted by typicality ratings, such that activation increased with either increasing or decreasing story typicality within our film clip stimuli. In this GLM, all clips were given equal weight in the first EV, to model the mean activity associated with encoding/recall. All clips were also included in a second EV, but in this case each clip was associated with a rating between 1 (most typical) and 5 (most atypical) in order to model the activity correlated with
increasing/decreasing typicality. EV2 was orthogonalized with respect to EV1 to control for mean activation across all film clips, allowing us to determine activation related to typicality. Null events were included in a third EV. As described above, once analyses were conducted at the level of each individual run, the results were then passed up to second (within participant) and third (across participant) level analyses. The GLM for the second level included three EVs: encoding, immediate retrieval, and 7d retrieval. At the third level, the general linear model included a single EV modelling the group mean.

2.5.5 fMRI data analyses: direct contrasts

Although there were clear effects of increasing and decreasing typicality on activation during encoding, no significant effects emerged for the retrieval parametric analyses. Thus, in order to fully explore neural differences based on typicality, we conducted analyses contrasting brain activation during the encoding and retrieval of the ten most typical clips with that for the ten most atypical clips. The GLM for the first level analysis in this case included four EVs modelling the activity associated with typical clips, atypical clips, neutral clips (from the center of the typicality scale), and null events, respectively. The second level analyses in this case included three EVs: encoding, immediate retrieval, and 7d retrieval. The third level analysis included a single EV modelling the group mean. Note that although neutral clips were included as a separate EV, all of the contrasts discussed below were between our two conditions of interest - typical and atypical clips.

2.5.6 fMRI data analyses: functional connectivity

In order to investigate the connectivity of our two regions of interest (mPFC and MTL) with the rest of the brain during encoding and retrieval, we conducted functional connectivity analyses using the psychophysiological interaction (PPI) method implemented in FSL (see O’Reilly, Woolrich, Behrens, Smith, & Johansen-Berg, 2012). The mPFC and MTL peaks from the encoding parametric analyses were used to investigate functional connectivity during encoding (mPFC: [-2, 56, 6]; MTL: [24, -38, -14]). The MTL peak, which was in the right parahippocampal cortex but associated with activation that spread into the hippocampus, was identified as a local maximum from within the large cluster peaking in the lateral occipital cortex that emerged in the encoding parametric analyses. Due to the null results of parametric analyses at retrieval, the mPFC and MTL peaks from a contrast of [(typical + atypical) retrieval >
encoding] were used to investigate functional connectivity during retrieval (mPFC: [-14, 50, 2]; MTL immediate: [-34, -34, -8]; MTL 7d: [-26, -20, -12]). Note that a significant mPFC cluster only emerged during delayed retrieval, so this peak was used for both retrieval analyses. We chose to use the peaks specific to each period (encoding, immediate retrieval, 7d retrieval) since our primary goal was to uncover the connectivity of the regions that had emerged in the previous analyses, rather than to focus on a single peak for its own sake. The following general procedure was followed for each PPI analysis. a) A spherical seed was created with a radius of 6mm centered on either an mPFC or MTL peak (coordinates listed above). b) This generic seed was then transformed into each subject’s native space using the reverse transformation matrix from registration. c) The time course of activity within each seed was extracted for each of the relevant runs, for each participant. d) This time course was included in a GLM, as described below.

PPI analyses were conducted to mirror the univariate analyses previously conducted at each time point. Thus, at encoding all forty clips were included with their specific typicality ratings and parametric modulations of functional connectivity were investigated, while at retrieval, where the parametric analyses did not yield significant results, functional connectivity for the ten most typical and ten most atypical clips was contrasted. For encoding, the first level GLMs involved five EVs. The first EV included all film clips, each associated with their specific typicality rating, while the second EV consisted of the relevant peak’s time course. The third EV modelled the PPI, and was constructed from the interaction of EV1 and EV2 (zero centered and mean centered, respectively). The fourth EV included all clips (without typicality ratings) in order to model the mean activity associated with encoding, while the fifth EV modelled null events. In the case of retrieval analyses, where functional connectivity for the ten most typical clips was compared with the ten most atypical clips, the model involved six EVs. The first EV included all typical and atypical film clips, assigned weights of ‘1’ and ‘-1’ respectively, while the second EV consisted of the relevant peak’s activity time course. The third EV was again a PPI EV, constructed from the interaction of EV1 and EV2 (zero centered and mean centered, respectively). The fourth EV in this case included typical and atypical clips, all assigned weights of ‘1’ to model mean activation. The fifth EV modeled the activity of neutral clips, while the sixth modeled null events.
2.5.7 fMRI data analyses: region of interest (ROI) analyses

ROI analyses focused on the mPFC and MTLs. ROIs were created using FSL’s Harvard-Oxford cortical and subcortical structural atlases. The MTL ROI included hippocampal, parahippocampal, entorhinal, and perirhinal cortices on both the left and right side. The mPFC ROI was defined as all cortical tissue in the medial frontal lobes anterior and ventral to the genu of the cingulate gyrus (upper bound: z = 10, left and right boundaries: x = ±16). See Figure 4 for a visualization of both ROI masks.

Figure 4: mPFC and MTL masks used in region of interest (ROI) analyses. mPFC ROI is shown in red, MTL ROI is shown in green.

These ROIs were used to investigate three specific hypotheses. Firstly, it was hypothesized that mPFC-MTL functional connectivity would be modulated by typicality, although there is evidence that this functional connectivity may either increase or decrease with increasing congruency. Secondly, it was hypothesized that typical and atypical clips would show differential declines in retrieval-related MTL activation over time. Finally, it was hypothesized that the delayed retrieval of both typical and atypical clips would be associated with mPFC activation.

To investigate the first hypothesis, the MTL ROI was applied before thresholding in functional connectivity analyses, using an mPFC seed and the same connectivity GLMs outlined above. To investigate the second hypothesis, the MTL ROI was applied before thresholding at the final (third) level of analysis for the [typical > atypical] (and vice versa) contrasts at immediate and 7d retrieval, using the same general linear model as was described above for retrieval contrasts. To investigate the final hypothesis, the ROIs were applied before thresholding for the [typical
retrieval > typical encoding] and [atypical retrieval > atypical encoding] contrasts separately. Results were cluster corrected to maintain FWE at $p < .05$ across both masks, unless otherwise indicated. It is noted in each result/figure when a ROI was used - where this is not stated explicitly, whole brain analyses were conducted.

The ROI masks were used only to investigate these three hypotheses and determine which particular mPFC and MTL sub-regions are implicated in each case. For connectivity analyses (outlined above) and brain-behaviour correlations (outlined below) specific mPFC and MTL seeds are chosen, so as to assess activity in the relevant sub-regions of each ROI and not water-down the results by including activity across the whole expanse of these exploratory ROIs.

### 2.5.8 Analysis of brain-behaviour correlations

In order to investigate how mPFC activity might be related to behaviour, we assessed the correlation between activity in the mPFC and errors during free recall. We investigated errors since, as mentioned above, a prominent effect of schema based processing is to distort memories that are inconsistent with one’s prior knowledge, while supporting accurate recall of consistent memories. The same mPFC seed was used for this analysis as was used during functional connectivity analyses ([−14, 50, 2], 6mm radius). First, mean activation for typical and atypical clips, assessed separately during both immediate and 7d retrieval (retrieval > fixation), was extracted in this seed. The Pearson correlation coefficient was then calculated between the activity in this mPFC seed and the mean number of errors (central and peripheral) made during free recall of typical or atypical clips. We conducted a one-tailed significance test since we had a specific hypothesis that mPFC activity would be positively correlated with errors for atypical clips, but negatively correlated with errors for typical clips.

### 2.6 Organization of Results

The results of this thesis are organized into three chapters. Chapter 3 reports the results from all behavioural analyses. Chapter 4 reports the results from all analyses of encoding fMRI data, while Chapter 5 reports results from all analyses of retrieval fMRI data. Note that each fMRI chapter covers the array of analyses described above. First average activity across all forty film clips is reported, followed by parametric results for increasing typicality and atypicality. Next, the results of direct contrasts are reported (typical $>$ atypical and vice versa), followed by functional
connectivity results. ROI analyses are reported across Chapters 4 and 5 to test the three specific hypotheses outlined above (with respect to mPFC-MTL functional connectivity, declines in MTL activation over time, and mPFC activation at delayed retrieval). Finally, in the retrieval chapter only, analyses of brain-behaviour correlations are also included. Each results chapter includes an interim discussion specific to the data reported within that chapter.
Chapter 3
Behavioural Effects of Event Typicality

3.1 Results

Both typicality and atypicality enhance memory for film clips, although atypical stories are recalled with a greater number of errors over time.

These behavioural data have already been analyzed with respect to detail type (central vs. peripheral) and retrieval time (immediate vs. 7d) in a recent publication (Sekeres et al., 2016). The following analyses will focus on the specific effects of typicality, which are the focus of this thesis. Although all analyses include detail type as an independent variable, there were no significant interactions of detail type with typicality; therefore we collapse across detail type in all figures. See Sekeres et al. (2016) for a full discussion of memory for these film clips with respect to detail type and time.

In order to test the effects of both typicality and atypicality on memory for film clip events, we conducted a \( 3 \times 2 \) repeated measures ANOVA with typicality (typical, neutral, atypical) and time (immediate, 7d) as independent variables, and number of clips forgotten as the dependent variable. There was no main effect of typicality (\( F(2,38) = 2.20, p = .13 \)), but a significant main effect of time (\( F(1,19) = 66.40, p < .001 \)) such that more clips were forgotten at 7d retrieval. There was also a significant interaction of typicality with time (\( F(2,38) = 5.15, p = .01 \)). Planned comparison t-tests revealed that at 7d retrieval, neutral clips were forgotten at a significantly higher rate than typical clips (\( t(19) = 2.77, p = .01, \text{cohen’s } d = .68 \)) and marginally higher rate than atypical clips (\( t(19) = 1.93, p = .07, \text{cohen’s } d = .55 \)) (Figure 5). Rates of forgetting for typical and atypical clips were equivalent (\( t(19) = 0.40, p = .69 \)). No significant differences existed at immediate retrieval (all \( p’s > .11 \)). All subsequent analyses include only successfully remembered clips.
Next we investigated whether or not typicality would affect the number of details correctly recalled for each clip. We conducted a $3 \times 2 \times 2$ repeated measures ANOVA with typicality (typical, neutral, atypical), time (immediate, 7d), and detail type (central, peripheral) as independent variables and number of details recalled as the dependent variable. There was a significant main effect of time ($F(1,18) = 40.81, p < .001$) such that fewer details were recalled at 7d retrieval, and a significant main effect of detail type ($F(1,18) = 29.84, p < .001$) such that more peripheral details were reported than central details, as well as a significant interaction of time with detail type ($F(1,18) = 36.38, p < .001$). These effects were not of interest with respect to this thesis, and are discussed elsewhere (Sekeres et al., 2016). There was no significant main effect of typicality ($F(2,36) = 1.34, p = .27$), and no significant interactions involving typicality (all $p$’s > .12).

Our main hypothesis with respect to free recall focused on errors, since a prominent effect of prior knowledge is to distort memory for atypical information. The mean number of errors made by participants at immediate retrieval was 2.55 (min = 0.77, max = 6.75). The mean number of errors made by participants at delayed retrieval was 2.69 (min = 0, max = 6.20). To investigate errors we conducted a $3 \times 2 \times 2$ repeated measures ANOVA with typicality (typical, neutral, atypical), time (immediate, 7d), and error type (central, peripheral) as independent variables and number of errors as the dependent variable. This analysis revealed significant main effects of
error type (F(1,18) = 90.45, p < .001) with more peripheral errors than central errors, and
typicality (F(2,36) = 5.80, p = .007), but no significant main effect of time (F(1,18) = 0.52, p =
.48). There were marginal interactions of time with typicality (F(2,36) = 2.82, p = .07), and error
type with typicality (F(2,36) = 2.62, p = .09), but a non-significant interaction of time and error
type (F(1,18) = 0.09, p = .77), and an non-significant three-way interaction (F(2,36) = 1.15, p =
.33). Tukey HSD tests for the typicality main effect revealed that errors for atypical clips were
significantly higher than errors for neutral clips (padj = .01), and marginally higher than errors for
typical clips (padj = .10). Equivalent errors were made for typical and neutral clips (padj = .69).
Based on our a priori hypothesis with respect to the distortion of memory over time for atypical
stories, we also unpacked the marginal time × typicality interaction. This clarified that the
typicality main effect (more errors for atypical clips) was driven by differences at 7d retrieval,
where there were significantly more errors for atypical clips than for either neutral (t(18) = 2.89, p
= .01, cohen’s d = .46) or typical clips (t(18) = 2.55, p = .02, cohen’s d = .35). An equivalent
number of errors was made for typical and neutral clips at 7d retrieval (t(18) = 1.09, p = .29), and
equivalent numbers of errors were made for all clips at immediate retrieval (all p’s > .15) (Figure
6).

Figure 6: Mean number of errors made during free recall at immediate and 7 day retrieval
sessions, separated based on clip typicality. Error bars represent the standard error of the mean.
(*p < .05)

Last, we investigated whether or not typicality affected self-rated quality of memory (ratings
collected in the scanner). We conducted a 3 × 2 × 2 repeated measures ANOVA with typicality
(typical, neutral, atypical), time (immediate, 7d), and rating type (story content, perceptual vividness) as independent variables, and memory rating as the dependent variable. There was a significant main effect of time (F(1,18) = 55.87, p < .001) with ratings declining over the week following encoding, as well as a significant main effect of rating type (F(1,18) = 59.19, p < .001), with higher ratings for story content, and a marginal main effect of typicality (F(2,36) = 3.16, p = .06). There were no significant interactions (all p’s > .43). Unpacking the marginal main effect of typicality revealed that self-ratings of memory were significantly higher for atypical clips than for typical clips (padj = .05, cohen’s d = .25, small effect size), but equivalent to ratings for neutral clips (padj = .20). Ratings for neutral and typical clips were equivalent (padj = .72). The difference in ratings between typical and atypical clips should be interpreted cautiously, and won’t be discussed further, since the typicality main effect is marginal, and the magnitude of the difference is small (Figure 7).

Figure 7: Mean self-ratings of memory content for typical, neutral, and atypical film clips. Ratings are averaged across story and perceptual content, for each of the two retrieval sessions. Error bars represent the standard error of the mean. (*p < .05)

3.2 Interim Discussion

There were no behavioural responses required at encoding, so our first behavioural measures of memory were taken during immediate retrieval. At this point, all film clips were forgotten at an equivalent (low) rate. One week later, however, clear benefits of both typicality and novelty emerged with respect to overall memory for the film clips. At this time, neutral clips were
forgotten at the highest rate. These results are compatible with van Kesteren and colleagues’ (2012) theory that experiencing something that is neither very novel, nor strongly related to prior experience, will fail to strongly engage either the episodic (MTL-mediated) or schematic (mPFC-mediated) memory systems, leading to poor memory. As discussed in the introduction, novelty is thought to trigger dopamine release, which strengthens long-term potentiation and memory encoding/stabilization in the MTL system (Frey et al., 1990; Li et al., 2003; Lisman et al., 2005). Prior knowledge, on the other hand, may guide perception and enhance memory stabilization through the engagement of higher order semantic representations (Dudai et al., 2015; van Kesteren et al., 2012; Wang & Morris, 2010). Thus, these two, seemingly opposing effects, may have the convergent result of strengthening memory, through different mechanisms.

Interestingly, although both typicality and atypicality attenuated forgetting of the film clips generally, atypical clips were recalled with a higher number of errors at delayed retrieval. This finding is consistent with Bartlett’s (1932) historic demonstration that unusual stories are more susceptible to memory distortions over time. These results are also consistent with other behavioural demonstrations of prior knowledge effects emerging over time (for example Mandler & Ritchey, 1977).
Chapter 4
Neural Substrates mediating the encoding of typical and atypical events

4.1 Results

4.1.1 Average results

The encoding of film clip events is supported by a distributed network of brain regions.

In examining mean activation across all forty film clips we find evidence that the encoding of narrative events is supported by a network of areas distributed across the brain. Encoding of film clips in this study was supported by activation across the occipital, temporal and parietal cortices, as well as in the dorsomedial/dorsolateral prefrontal cortices. The peaks in the superior temporal gyrus and the fusiform cortex extend into the right and left MTLs, respectively (primarily in the parahippocampal cortex). See Figure 8 for a visualization of mean encoding activations and Table 1 for a list of cluster peaks.

Figure 8: Mean activation during the encoding of film clip events. Green indicates areas that were significantly more active during encoding than during fixation, averaged across all clips. Colour intensity corresponds to the z-value of each voxel’s activation.

Table 1: Cluster peaks from average encoding analyses. Names refer to brain regions that are significantly active during the encoding of film clip events (all clips encoding > fixation).
<table>
<thead>
<tr>
<th>Brain Region</th>
<th>X (mm)</th>
<th>Y (mm)</th>
<th>Z (mm)</th>
<th>z-score</th>
<th>Cluster size (voxels)</th>
</tr>
</thead>
<tbody>
<tr>
<td>R superior temporal gyrus, extends into MTLs</td>
<td>68</td>
<td>-34</td>
<td>18</td>
<td>6.9</td>
<td>26293</td>
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<td>L fusiform cortex, extends into MTLs</td>
<td>-28</td>
<td>-50</td>
<td>-10</td>
<td>6.2</td>
<td>13661</td>
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<td>Dorsomedial prefrontal cortex</td>
<td>4</td>
<td>66</td>
<td>28</td>
<td>4.6</td>
<td>772</td>
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<tr>
<td>L precentral gyrus</td>
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<td>0</td>
<td>50</td>
<td>3.8</td>
<td>623</td>
</tr>
<tr>
<td>L cerebellum (9)</td>
<td>-16</td>
<td>-44</td>
<td>-52</td>
<td>4.3</td>
<td>768</td>
</tr>
<tr>
<td>L cerebellum (7b)</td>
<td>-10</td>
<td>-76</td>
<td>-42</td>
<td>4.7</td>
<td>562</td>
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</tbody>
</table>

4.1.2 Parametric results

The neural substrates of event encoding are modulated by typicality, with greater mPFC activation for increasingly typical events and greater MTL activation for increasingly atypical events.

Parametric analyses were conducted to determine if the encoding of complex events was modulated by event typicality. These analyses included all forty film clip events, each clip associated with a specific typicality rating determined in a separate behavioural study (described in methods). The results of these analyses clearly demonstrate that encoding is modulated by event typicality. As events increased in typicality, activity increased across a network consisting of the mPFC, posterior cingulate cortex (PCC), bilateral superior temporal gyri, and the right angular gyrus (Table 2). Conversely, as events decreased in typicality (increased in atypicality) activity increased across the bilateral MTLs, along the ventral visual streams, throughout occipital/temporal cortices, and in the bilateral superior frontal gyri. Note that the peak of the posterior cluster is in the lateral occipital cortex (Table 2), but this large cluster of activation extends through occipital/temporal cortices and into the MTLs (Figure 9).

Figure 9: Activation during the encoding of film clip events that correlates either with increasing typicality or with increasing atypicality of those events. Warm colours indicate areas whose activity increased with increasing typicality, while cool colours indicate areas whose activity increased with decreasing typicality (increasing atypicality) of events. Colour intensity corresponds to the z-value of each voxel’s activation.
Table 2: Cluster peaks from parametric encoding analyses. Names refer to brain regions whose activation increased either with increasing typicality or increasing atypicality of film clip events.

<table>
<thead>
<tr>
<th>Brain Region</th>
<th>X (mm)</th>
<th>Y (mm)</th>
<th>Z (mm)</th>
<th>z-score</th>
<th>Cluster size (voxels)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Increasing Typicality</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mPFC</td>
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<td>56</td>
<td>6</td>
<td>3.9</td>
<td>3253</td>
</tr>
<tr>
<td>R precuneus/posterior cingulate cortex</td>
<td>18</td>
<td>-40</td>
<td>20</td>
<td>4.6</td>
<td>3057</td>
</tr>
<tr>
<td>L superior temporal gyrus</td>
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<td>-52</td>
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4.1.3 Direct contrast results

Analyses contrasting the encoding of the ten most typical clips with the encoding of the ten most atypical clips produced an equivalent set of results as the parametric analyses (Figure 10). There were only two differences between the direct contrast and the parametric analyses. a) An angular gyrus cluster increased in activity with increasing typicality but did not emerge in the [typical > atypical] contrast. b) Activation spread more medially through the occipital lobes for increasing atypicality, over what was seen in the [atypical > typical] contrast. Note that there were no areas...
significantly active in the direct contrasts that were not seen in the parametric results. This suggests that the slight differences between these two analyses were due to the increased power of the parametric analyses, which included forty clips rather than twenty, with the convergent results from two different types of analyses suggesting that our effects are strongly tied to the typicality of the events being encoded, both across the spectrum of clips and at the extremes.

Figure 10: Activation during the encoding of film clip events. a) Red indicate areas that increased in activation with increasing typicality, while green indicates areas that were significantly more active for typical > atypical clips. b) Blue indicates areas that increased in activation with increasing atypicality, while gold indicates areas that were significantly more active for atypical > typical clips. Colour intensity corresponds to the z-value of each voxel’s activation.

4.1.4 Functional connectivity results

The mPFC and MTLs each show differential encoding connectivity with the rest of the brain, depending on event typicality. Additionally, atypical events are associated with greater mPFC-MTL functional connectivity at encoding.

The mPFC peak from the previous parametric results was taken as a seed for PPI analyses to investigate functional connectivity during encoding. These analyses revealed that, as story typicality increased, the mPFC was increasingly functionally connected with a network of areas including the PCC, supramarginal gyrus, right insula, and dorsolateral prefrontal cortex. This same peak shows a very different pattern of connectivity correlated with decreasing typicality. In this case, when events are increasingly atypical or novel, the mPFC shows greater functional connectivity with the right anterior hippocampus and left insula.
As outlined in the methods, ROI analyses were planned to test three specific hypotheses. The first of these hypotheses was that mPFC-MTL functional connectivity would be modulated by event typicality. Thus, although whole brain analyses revealed a cluster in the right anterior hippocampus that was increasingly functionally connected with the mPFC for increasingly atypical clips, further analyses testing for functional connectivity from the mPFC seed to the MTL ROI were conducted, to fully interrogate any potential mPFC-MTL functional connectivity. These analyses revealed an additional cluster in the left anterior hippocampus that was increasingly functionally connected with the mPFC during the encoding of increasingly atypical events. ROI analyses, like the whole brain analyses, did not reveal any mPFC-MTL functional connectivity that increased with increasing typicality. See Figure 11 for a visualization of all mPFC functional connectivity and Table 3 for a full list of clusters that were functionally connected with the mPFC in either condition.

Figure 11: Functional connectivity from an mPFC seed (shown in yellow) during encoding. Warm colours indicate areas whose functional connectivity with the mPFC during encoding increased with increasing typicality. Note that there were no significant results for increasing typicality when this analysis was restricted to the MTL ROI. Cool colours indicate areas whose functional connectivity with the mPFC increased with decreasing typicality (increasing atypicality), while green areas represent that same analysis, restricted to the MTLs. Colour intensity corresponds to the z-value of each voxel’s activation.

A local MTL peak from the parametric analyses, in the right parahippocampal cortex, was used as a seed to investigate MTL functional connectivity during encoding. In this case, we found no significant functional connectivity for increasing typicality. However, increasing atypicality was
correlated with increasing functional connectivity from the MTL seed to areas throughout the ventral visual stream and occipital cortex (peak in the left occipital pole; see Figure 12 and Table 3). Thus, the perception and encoding of increasingly atypical events seems to be associated not only with increased activity in sensory areas (shown in parametric analyses above), but also with increased functional connectivity between these areas and the MTLs. As a confirmation of the mPFC-MTL functional connectivity analyses reported above, we tested for functional connectivity between the MTL seed and areas within the mPFC ROI. Consistent with functional connectivity analyses using an mPFC seed, we found no significant mPFC-MTL functional connectivity for increasing typicality in the film clips. Increasing atypicality, on the other hand, was once again associated with increased mPFC-MTL functional connectivity. The mPFC area that emerged in this analysis was a little more anterior, but still close to the mPFC area that emerged in parametric analyses and that was thus used as a seed in the previous functional connectivity analyses, providing converging evidence for functional connectivity between this mPFC sub-region and the MTLs during the encoding of atypical events.

Figure 12: Functional connectivity from an MTL seed (shown in yellow) during encoding. Blue indicates areas whose functional connectivity with the MTL increased with decreasing typicality (increasing atypicality), while green areas indicate that same analysis restricted to an mPFC ROI. Note that there were no significant results for increasing typicality. Colour intensity corresponds to the z-value of each voxel’s activation.
Table 3: Cluster peaks from functional connectivity analyses at encoding. Names refer to brain regions with functional connectivity to either the mPFC [-2, 56, 6] or right MTL [24, -38, -14] that increases for either increasing typicality or increasing atypicality.

<table>
<thead>
<tr>
<th>Brain Region</th>
<th>X (mm)</th>
<th>Y (mm)</th>
<th>Z (mm)</th>
<th>z-score</th>
<th>Cluster size (voxels)</th>
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</thead>
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4.2 Interim Discussion

4.2.1 The mPFC, MTLs, and the encoding of events

Across all the film clips used in this study we found that encoding was supported by activation throughout a network of areas distributed across all the lobes of the brain. It is clear that the encoding of events is dependent on a complex set of processes supported by many different areas, as has been established in many previous experiments (Burke et al., 2014; Kim, 2011; Ranganath et al., 2005; Wagner et al., 1998). Critically, we also found that encoding activity was modulated by event typicality. Namely, as events increased in typicality, activation increased in the mPFC and PCC. Since the mPFC was not significantly active during encoding when averaging across all clips, taking typicality into account identified a new area associated with encoding, specifically for those clips that are congruent with participants’ prior knowledge. Conversely, as events
decreased in typicality (increased in atypicality or novelty) activity increased across the bilateral MTLs, along the ventral visual stream, and throughout posterior occipital/parietal cortices. Since the typical and atypical clips are equivalent with respect to sensory (visual, auditory) input and story complexity, as reported in the methods, the differences we observe here are likely to be due to our factor of interest: the typicality of the various events.

These results are consistent with our hypotheses, as well as with suggestions that the mPFC detects congruency between a current experience and prior knowledge, engaging appropriate semantic and contextual information when such congruence is detected (Preston & Eichenbaum, 2013; van Kesteren et al., 2012). In particular, the activation of relevant prior knowledge through the mPFC is thought to facilitate comprehension (Maguire et al., 1999; Preston & Eichenbaum, 2013; van Kesteren et al., 2010b), and enhance the integration of new information during encoding (Schlichting, Mumford, & Preston, 2015; Sommer, 2016; Zeithamova, Dominick, & Preston, 2012). Thus, the mPFC activation that we observe may reflect the integration of novel episodic information encoded from these film clips with related semantic representations, and/or the biasing of current processing based on relevant contextual and semantic information.

On the other hand, when such congruence with prior knowledge is not detected, our data are consistent with the literature outlined above in suggesting that encoding is more dependent on the MTLs. This effect may result from the need to rapidly encode the novel relations between the items, actions, context, etc., within these atypical events (Cohen, 2015; O’Reilly & Rudy, 2001; Rolls, 2007). Although much of the literature covered in the introduction refers to the MTLs generally, or focuses on the hippocampus, the fact that the MTL peak associated with decreasing typicality is in the parahippocampal cortex is consistent with previous findings. Not only is the parahippocampal cortex anatomically part of the MTLs, functionally part of the MTL subsystem of the default mode network (Andrews-Hanna et al., 2010), and associated with episodic memory generally (Maguire, 2001), but, in some cases, it is also specifically associated with subsequent memory for film clip events, where the hippocampus is not (Hasson et al., 2008). Furthermore, when looking more closely at much of the research outlined in the introduction that refers to the MTLs generally, activation in the parahippocampal cortex specifically is often linked to incongruence with prior knowledge. For example, the parahippocampus is the MTL area that is active during the initial learning of a weather prediction task, when the information is novel and participants have not yet extracted commonalities from across the patterns in the task (Kumaran
et al., 2009). Similarly, the parahippocampal cortex is the MTL peak specifically correlated with decreasing congruency of object-scene pairs (van Kesteren et al., 2013), while the learning of novel information unrelated to your university major is associated with MTL activation that encompasses both the hippocampus and parahippocampus (van Kesteren et al., 2014). Thus, although many people focus on the hippocampus when they consider the MTLs, it is clear that the parahippocampus also plays a significant role in event encoding and in the processing of information that is incongruent with one’s prior knowledge.

Although the evidence outlined above clearly links the parahippocampus with atypicality and encoding, it is also prominently associated with processing physical space (Aguirre, Detre, Alsop, & D’Esposito, 1996; Maguire, Frith, Burgess, Donnett, & O’Keefe, 1998) and non-spatial context (Baumann & Mattingley, 2016; Diana, 2016). The fact that the peak of MTL activity during encoding is found in the parahippocampus may point to a greater need for context construction and/or representation when one cannot organize an episode in one’s mind around prior knowledge or schematic contextual information (Irish, Addis, Hodges, & Piguet, 2012; Irish & Piguet, 2013). Instead of depending on prior knowledge, for those atypical clips participants must encode the novel contextual and event details of the clips in a bottom-up fashion, which may be particularly dependent on parahippocampal processing.

4.2.2 Perceptual processing during event encoding

Increasing atypicality is not only associated with activity in the MTLs, but also with widespread activation through posterior temporal, occipital, and parietal cortices. Moreover, increasing event atypicality correlates with increasing functional connectivity between these posterior sensory areas and the MTLs, indicating that these patterns of neural activation are mnemonically relevant. Thus, while encoding may be more affected by the influences of prior knowledge (presumably through the mPFC) during the encoding of typical events, processing seems to be more dependent on bottom-up sensory information when events are novel or atypical. This may be evolutionarily adaptive. For example, when encountering an item with which one is familiar, such as an apple, it would be unnecessary (and a waste of neural resources) to process all of the incoming sensory information associated with its exact shape, size, colour, etc. Instead, one’s brain can depend on semantic knowledge to guide perception (Oliva & Torralba, 2007), facilitate recall, and regulate behaviour (Binder & Desai, 2011). On the other hand, when encountering a novel fruit one has
never seen before, it would be critical to process and encode those specific details of its appearance, in order to recall/recognize the fruit at a later date and potentially use it as a food source.

Behaviourally, when participants study complex scenes they tend only to notice changes to unexpected objects, remaining oblivious to changes in objects that are consistent with the context, despite the fact that all manipulated objects had been fixated originally (Friedman, 1979). Similarly, people preferentially notice changes that make objects appear less typical, as compared to modifications of the same magnitude that make an object appear more typical (Konkle & Oliva, 2007). Together, these results suggest that more visual processing and encoding of specific object details occurs for unexpected objects and atypical items. Indeed, such differential processing of scenes with respect to prior knowledge may be accomplished even without conscious awareness. Using continuous flash suppression, Mudrik and colleagues (2011) demonstrated that scenes which included incongruent objects escaped perceptual suppression faster than normal scenes did. This suggests that the likelihood of an object appearing in a given context was processed without participants’ awareness of even having seen a scene. Furthermore, these results suggest that incongruency with expectations may trigger greater perceptual processing both rapidly and subconsciously.

Our results, demonstrating activation and connectivity through the MTLs, ventral visual stream, and occipital lobes, provide evidence for the neural bases of such enhanced perceptual processing of stimuli that are incongruent with prior knowledge and/or expectations. This is not to say that people are not processing visual input along with semantic information during the encoding of all events. Instead, it is the balance between dependence on bottom-up sensory information and the influence of prior knowledge that seems to be affected by event typicality.

4.2.3 The posterior cingulate cortex and the encoding of typical events

Although we did see increasing mPFC activity with increasing typicality, as predicted, this was not the only area of the brain to show that pattern of activity. Activation in the PCC also showed a positive correlation with typicality, as did mPFC-PCC functional connectivity. The specific area of the PCC implicated was near the precuneus, rather than the retrosplenial cortex. As a region that is associated with the supramodal representation of concepts and semantic knowledge (Fairhall & Caramazza, 2013), it is logical that the PCC would be more engaged during the
encoding of events that are consistent with participants’ prior knowledge. The PCC has been proposed to act as an interface linking semantic retrieval and narrative elements during episodic encoding, with this role emerging both in episodic memory studies using film clips (Bird, Keidel, Ing, Horner, & Burgess, 2015) and in a meta-analysis of semantic processing (Binder et al., 2009). This proposal implies that the PCC may integrate the prior knowledge activated by the mPFC with episodic information, presumably mediated by the MTLs. Indeed, in their work examining the neural dynamics underlying the comprehension of an extended film episode, Chen and colleagues (2015) suggest that the mPFC, angular gyrus, and PCC – areas that are all activated with increasing typicality in our study – are all critical for the construction of ‘situation models’ through the integration of prior knowledge with contextual and event-specific information. However, since the PCC is activated along with the mPFC in this study, as well as in many others (Andrews-Hanna et al., 2010; Binder et al., 2009; Kumaran et al., 2009; Ranganath et al., 2005; Schlichting & Preston, 2015; van Buuren et al., 2014; Wagner et al., 2015), and since mPFC-PCC functional connectivity increases with increasing event typicality, the distinct processes performed by these two areas are difficult to characterize independently. It would be an interesting avenue of future research to untangle the specific roles of these two strongly related areas in event perception and memory.

4.2.4 mPFC-MTL functional connectivity

As discussed above, each of our regions of interest – the mPFC and MTLs – show differential functional connectivity with the rest of the brain based on event typicality (MTL-sensory cortices for atypical clips, and mPFC-PCC for typical clips). However, they also show differential functional connectivity with each other, with greater mPFC-MTL connectivity specifically for atypical event encoding. This result is consistent with some of the previous findings outlined above (Bein et al., 2014; Van Kesteren et al., 2014; van Kesteren et al., 2010a), but inconsistent with other evidence showing increased mPFC-MTL functional connectivity for stimuli with a greater relation to prior knowledge (Liu et al., 2016; Schlichting & Preston, 2015; Sommer, 2016). The factor underlying the variance in these results may be the level and/or type of prior knowledge involved. In our case, participants are presumably accessing rich pre-experimental knowledge, developed over the course of their lives, with respect to the types of events and narratives that are normally encountered. Similarly, in van Kesteren’s study (2014) the effects of rich pre-experimental knowledge are investigated by looking at differences between learning facts
related to your own major, about which you have studied for at least one year, and an unrelated topic. In Bein and colleagues’ work (2014), participants also depend on the real-world semantic relatedness of their stimuli. On the other hand, the three studies listed that find increased mPFC-MTL functional connectivity for stimuli that are related, rather than unrelated to prior learning, all involve pairs of stimuli (face-house, face-object, and object-place pairs respectively) whose associations are acquired intra-experimentally. In these latter studies, there is presumably no prior knowledge at all relevant to the unrelated pairs, thus it is not surprising that an absence of mPFC-MTL functional connectivity is found. However, in our study (and Bein et al., 2014; van Kesteren et al., 2014) the incongruent conditions still involve some relation to pre-experimental knowledge. The greater mPFC-MTL functional connectivity in these cases is proposed to underlie the integration of novel event-specific and incongruent details with prior knowledge. Although the complex pre-experimental knowledge accessed in our study (and Bein et al., 2014; Van Kesteren et al., 2014) may be related to the type of learning assessed in the paired-associate studies, they clearly differ with respect to the level and type of prior knowledge involved. These differences presumably underlie the greater mPFC-MTL functional connectivity seen for less congruent stimuli in the former cases, but the opposite finding in the latter studies.
Chapter 5  
Neural substrates mediating the retrieval of typical and atypical events

5.1 Results

5.1.1 Average results

Retrieval of both recent and remote event memories is associated with MTL activation.

Assessing mean activation during immediate retrieval of all remembered clips (> fixation) irrespective of typicality revealed a network of areas including the bilateral MTLs, the precuneus, lateral occipital cortex, and mid frontal gyrus (see Figure 13 and Table 4). One week later, over which time memory for the film clips has presumably been consolidated, only two areas emerged for the retrieval of film clip memories irrespective of typicality - the left hippocampus and the left angular gyrus (see Figure 13 and Table 4). No significant differences were evident when comparing immediate and 7d retrieval averaged across all clips, even when looking specifically at activity within a MTL ROI.

Figure 13: Average activation during the retrieval of film clip events (all clips retrieval > fixation). Green indicates areas that were significantly active during immediate retrieval. Red indicates areas that were significantly active during 7d retrieval. Colour intensity corresponds to the z-value of each voxel’s activation.
Table 4: Cluster peaks from average retrieval analyses. Names refer to brain regions that are significantly active during the retrieval of film clip events (all clips retrieval > fixation) during each time point (immediate retrieval and 7d retrieval).

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<thead>
<tr>
<th>Brain Region</th>
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<th>Y (mm)</th>
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<th>z-score</th>
<th>Cluster size (voxels)</th>
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<td>4.8</td>
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<tr>
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<td>4.4</td>
<td>605</td>
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</tbody>
</table>

5.1.2 Parametric results

Parametric analyses of increasing/decreasing typicality at retrieval did not yield any significant patterns at either time point, even when testing within mPFC and MTL ROIs and lowering the threshold to p < .005 uncorrected.

5.1.3 Direct contrast results

MTL activation declines more over time for typical (vs. atypical) events.

Since the parametric analyses failed to reveal significant patterns of activation with increasing or decreasing typicality, we conducted direct contrast analyses to compare the retrieval of the ten most typical clips with the retrieval of the ten most atypical clips. These analyses were conducted in order to explore whether differences might emerge when comparing the two ends of the spectrum, rather than looking for continuous change across the entire group of clips, which may not exist at retrieval or which may be masked by noise across the mid-range clips. We will consider possible reasons why parametric analyses revealed significant differences at encoding, but not retrieval, in the discussion.

Specifically, we conducted direct contrast analyses within a MTL ROI, to test our second planned ‘ROI’ hypothesis - that typical and atypical clips would show differential declines in MTL
activation over time. This hypothesis was inspired by evidence from rodent experiments (Tse et al., 2007), and recently from the human literature as well (Sommer, 2016), that, although learning and immediate retrieval is MTL-dependent for all paired-associates, those that are consistent with a previously learned schema become MTL-independent more quickly than schema-inconsistent pairs. This ‘accelerated consolidation’ observed for paired associates engenders the hypothesis that typical and atypical clips might be equally MTL-dependent during retrieval shortly after encoding, but that one week after encoding, atypical events might be associated with greater MTL activation than typical clips.

The results from our ROI analysis are consistent with this hypothesis. Although there were no significant MTL differences at immediate retrieval, based on typicality, by the 7d retrieval session bilateral MTL clusters emerged that were more active for the retrieval of atypical than typical film clip events (Figure 14). In particular, the recall of atypical events was associated with greater activity in the bilateral entorhinal cortices (anterior MTLs), as well as in a small right posterior hippocampal cluster (Table 5). These results should be interpreted cautiously since they were thresholded at p < 0.005 uncorrected. We report them here since they were strongly motivated by evidence from the rodent literature suggesting that, at remote time points, schema-consistent memories may be less dependent on the MTLs for retrieval than unrelated memories. To our knowledge, this is the first time that this effect has been shown for narrative event memories in humans. There were no MTL clusters that were more active during the retrieval of typical > atypical clips, and no differences at the whole brain level for either contrast, at either time point.

Figure 14: ROI analyses contrasting activation during the retrieval of atypical > typical clips at both immediate retrieval (cool colours; note that this did not yield any significant clusters) and 7d retrieval (warm colours). The opposite contrast, typical > atypical, did not yield significant results at either time point. Colour intensity corresponds to the z-value of each voxel’s activation, voxels thresholded at p < 0.005 uncorrected within the MTL ROI.
Table 5: Cluster peaks from direct contrasts between typical and atypical clips at 7d retrieval. MTL ROI applied before thresholding at p<0.005 uncorrected.

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<thead>
<tr>
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<tr>
<td><strong>Atypical &gt; Typical</strong></td>
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<tr>
<td>R hippocampus</td>
<td>32</td>
<td>-40</td>
<td>-4</td>
<td>2.7</td>
<td>6</td>
</tr>
</tbody>
</table>

Remote memory retrieval is associated with activation in the mPFC, for both typical and atypical events.

Behavioural studies suggest that all events may be remembered as more consistent with prior knowledge than they actually were (Hemmer & Steyvers, 2009; Konkle & Oliva, 2007; Steyvers & Hemmer, 2012), and that schema effects may emerge over time (Bartlett, 1932, Mandler & Ritchey, 1977), suggesting that all clips should be associated with mPFC activity during delayed retrieval. This was the third and final hypothesis that we had planned to test with ROI analyses, with both typical and atypical clips predicted to be associated with mPFC activation at delayed retrieval. First, we tested whether or not there were differences between typical and atypical clips within the mPFC ROI at retrieval. These typical vs. atypical contrasts revealed null results at both retrieval time points, indicating that, unlike at encoding, typical and atypical clips do not
significantly differ with respect to mPFC activation at retrieval. Based on this absence of
typicality-based differences at retrieval, we next sought to determine whether or not typical and
atypical clips were both independently associated with mPFC activation during retrieval.
Although the contrast of retrieval vs. fixation did not yield any significant patterns of activation,
at either time point, contrasting retrieval with encoding revealed strong mPFC activation for both
typical and atypical clips at delayed retrieval ([typical 7d retrieval > typical encoding] and
[atypical 7d retrieval > atypical encoding]; see Figure 15 and Table 6). The mPFC thus shows
greater activation at 7d retrieval, compared with encoding, for both types of clips, despite the fact
that typical clips are already associated with increased mPFC activation at encoding. This
indicates that mPFC activity increases between encoding and delayed retrieval, above and beyond
the increases already seen based on typicality. There were no significant differences between
typical and atypical clips in this analysis ([typical retrieval > typical encoding] > [atypical
retrieval > atypical encoding] and the converse contrast both yielded null results).

Figure 15: mPFC ROI analyses contrasting activation during 7d retrieval of typical and atypical
clips with encoding ([typical 7d retrieval > typical encoding] and [atypical 7d retrieval > atypical
encoding]). Colour intensity corresponds to the z-value of each voxel’s activation.

Table 6: Cluster peaks from [7d retrieval > encoding] contrasts for typical and atypical clips
separately. mPFC ROI applied before thresholding.
In order to find mPFC and MTL peaks to use as seeds in functional connectivity analyses for retrieval (results described below) we collapsed across typicality and contrasted retrieval with encoding [(typical + atypical) retrieval > encoding], within the mPFC and MTL ROIs. This was done to find peaks common to both types of clips, in order to minimize any bias towards finding significant connectivity for one type of clip over the other. For the same reason, the common mPFC peak found in this contrast was also used in the brain-behaviour correlation analyses.

5.1.4 Brain-behaviour correlation results

Activation in the mPFC during 7d retrieval is negatively correlated with errors for typical clips, but marginally positively correlated with errors for atypical clips.

In order to investigate the relationship between mPFC activity and behaviour for typical and atypical events, we assessed the correlation between activity in the common mPFC cluster found in the previous analyses, and errors during free recall. We investigated errors since, as discussed in the introduction, a prominent effect of prior-knowledge-based processing is to distort memories that are inconsistent with one’s prior knowledge, while supporting accurate recall of consistent memories. There were no significant correlations between mPFC activity and errors at immediate retrieval (all p’s > .13). However, at 7d retrieval, the number of central (story-line) errors demonstrated relationships with mPFC activity for both types of clips. These story-line errors are of particular interest since it was the typicality of the stories in the film clips that was taken into consideration in this thesis; this will be considered further in the discussion. In particular, mPFC activity during the retrieval of typical clips was negatively correlated with errors made during the recall of those clips (r = -.47, p = .03). Conversely, mPFC activity during the retrieval of atypical clips was marginally positively correlated with errors made during the recall of those clips (r =
.37, p = .07), see Figure 16. These correlations, one positive and one negative, are also significantly different from each other (p = .02).

Across these data there is one participant who may be an outlier, whose activity change is more than two standard deviations below the mean (mPFC activity change = -0.53%, see Figure 16). This participant’s activation, however, is not driving the correlation observed. Instead, if the participant’s data are removed, the positive correlation between mPFC activity during retrieval and errors for atypical clips actually increases (from r = .37 to r = .48), and becomes significant (p = .03), rather than marginal (p = .07). There were no significant correlations for peripheral errors (all p’s > .21), although they showed the same pattern as story-line errors.

Figure 16: Correlation between activity of mPFC peak and central (story-line) errors during free recall for typical and atypical clips at 7d retrieval. Each data point represents a single participant’s mPFC activity during the retrieval of either typical or atypical stories (retrieval > fixation), plotted against their mean number of story-line errors for that type of clip.

5.1.5 Functional connectivity results

The mPFC and MTL are both functionally connected to the angular gyrus and precuneus during 7d retrieval, but only show this connectivity for either typical or atypical clips, respectively.

We next conducted functional connectivity analyses using mPFC and MTL seeds to determine whether the connectivity of these regions of interest would differentiate between events based on
typicality, as was seen at encoding. Whole brain functional connectivity analyses at immediate retrieval failed to reveal any significant patterns of connectivity, for either seed. At 7d retrieval, however, clear functional connectivity differences were observed. At 7d retrieval, the mPFC seed is functionally connected to the precuneus, left angular gyrus, and lateral occipital cortex for typical clips, with no significant connectivity for atypical clips. Conversely, the MTL seed is functionally connected to the precuneus and right angular gyrus, but only for atypical clips in this case, with no significant connectivity for typical clips. See Figure 17 for a visualization of these connectivity results and Table 7 for a list of peak coordinates. These results suggest that the mPFC and MTL are both connected with a similar network of areas, with each showing this connectivity for either typical or atypical clips, respectively. This similar pattern of connectivity may indicate that these two areas are supporting similar processing associated with event retrieval, with the mPFC dominant when events are more strongly related to prior knowledge, and the MTLs dominant when events are more atypical or novel. Seed-to-ROI functional connectivity analyses did not reveal any significant mPFC-MTL connectivity differences based on event typicality at either retrieval session.

Figure 17: Functional connectivity from mPFC and MTL seeds during 7d retrieval. Warm colours indicate areas whose functional connectivity with the mPFC during retrieval was greater for typical (vs. atypical) clips. Cool colours indicate areas whose functional connectivity with the MTL seed during retrieval was greater for atypical (vs. typical) clips. Note that the converse contrasts did not yield any significant clusters. Colour intensity corresponds to the z-value of each voxel’s activation.
Table 7: Cluster peaks from functional connectivity analyses at 7d retrieval. Names refer to brain regions whose functional connectivity with the mPFC [-14, 50, 2] or left MTL [-26, -20, -12] was greater for either typical or atypical clips. Note that the single precuneal cluster functionally connected to the mPFC for typical clips extended through the parietal lobe, thus the local maxima are listed below the peak.

<table>
<thead>
<tr>
<th>Brain Region</th>
<th>X (mm)</th>
<th>Y (mm)</th>
<th>Z (mm)</th>
<th>z-score</th>
<th>Cluster size (voxels)</th>
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<tr>
<td>Typical &gt; Atypical</td>
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<tr>
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<td>-60</td>
<td>50</td>
<td></td>
<td></td>
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<tr>
<td>L lateral occipital cortex</td>
<td>-38</td>
<td>-64</td>
<td>52</td>
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<tr>
<td>MTL seed</td>
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<td>Atypical &gt; Typical</td>
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<tr>
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<td>32</td>
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<tr>
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<td>3.1</td>
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5.2 Interim Discussion

5.2.1 MTL activation and theories of consolidation

MTL activation is seen at both immediate and 7d retrieval, with no significant differences evident between the two time-points, when all clips are averaged together. It is possible that we looked at memory over too short of a time-span compared to the longer intervals, sometimes extending over years, mentioned in the literature. An often-cited study of standard consolidation dynamics in humans, however, reported the largest hippocampal decrease between retrieval on the first and second days following encoding (Takashima et al., 2006). Thus, our time-frame of one week should not be too short to find significant declines in MTL activity.

It is also possible, however, that we lacked enough power to find a significant decline in MTL activity. An alternate set of analyses was conducted on these same data by a colleague (Sekeres et al., in preparation), using the multivariate Partial Least Squares (PLS) method of analysis. Sekeres and colleagues examined average activity for these film clips, as well as activity patterns with respect to participants' self-rated vividness of recall, rather than considering typicality of the film clip events. Sekeres and colleagues also found significant MTL activity at both immediate
and 7d retrieval, but our results differ in that their PLS analyses revealed a significant decline in MTL activity over time. These differential findings are presumably due to the high power of PLS analyses, where it is unnecessary to correct for multiple comparisons. Indeed, if we conduct uncorrected analyses we do find a general decline in MTL activity between immediate and 7d retrieval. We chose to conduct univariate analyses using FSL, despite the inherent loss of power, since it allowed us to conduct specific theory-driven contrasts and to conduct parametric analyses taking typicality into account. PLS, on the other hand, is a data-driven analysis technique that assesses co-varying activity across voxels in the entire brain without a priori contrasts (McIntosh, Bookstein, Haxby, & Grady, 1996). Although it is possible to test hypotheses using non-rotated PLS, FSL allowed for more control over the exact contrasts conducted at the different levels of analysis. Notwithstanding these reasons for depending on FSL for our analyses, we conducted supplementary analyses using PLS. PLS analyses at encoding and 7d retrieval revealed patterns of activity similar to those found with FSL (see Appendix B). Like FSL, PLS also failed to find significant differences based on typicality at immediate retrieval.

Despite finding a general decline in MTL activity over time, the results from Sekeres and colleagues’ work do not suggest that this decline is equivalent across all clips. When taking vividness of recall into consideration, they see a significant decline in MTL activity during 7d retrieval only for those film clips that are given low vividness ratings. For those events that are recalled with high vividness there is no significant decline in MTL activity. Thus, like us, they fail to find an indiscriminate decline in MTL activity over time. Instead, our two sets of results are consistent with Trace Transformation Theory, which suggests that the nature of a memory, rather than time per se, determines the neural substrates mediating its maintenance and retrieval (Winocur & Moscovitch, 2011; Winocur et al., 2010). Note that the (marginal) differences in self-rated vividness between typical and atypical clips are numerically larger at immediate retrieval, with smaller differences at delayed retrieval, while we only find differences in MTL activation between typical and atypical clips at delayed retrieval. Thus, the findings of Sekeres and colleagues with respect to vividness and MTL activation do not account for our findings with respect to typicality and MTL activation over time. The two sets of analyses provide independent but complementary results illustrating how different factors may influence neural activation during retrieval. Furthermore, their findings of decreased MTL activity over time, which we see when conducting uncorrected analyses, are also compatible with our hypotheses. Our hypotheses
are not meant to suggest that the neural substrates mediating memory do not tend to shift as memories are stabilized and transformed over time. Instead, our analyses and results highlight the ways in which these consolidation dynamics are modulated by the nature of the events being encoded and retrieved. In particular, we focus on how the typicality of an event may affect the neural substrates of memory.

With respect to immediate retrieval, the null results of atypical vs. typical comparisons – across all parametric, direct contrast, and functional connectivity analyses – suggest that a similar network, centered on the bilateral MTLs, supports recall of both typical and atypical memories, equivalently at this time. This dependence on the MTLs during the successful retrieval of both schema-congruent and incongruent events, shortly after they were encoded, was also found by Brod and colleagues (2015), and is consistent with evidence from the rodent literature suggesting hippocampal dependence for recent memories irrespective of prior knowledge (Bethus, Tse, & Morris, 2010; Tse et al., 2007). Thus, even though the encoding of events was strongly modulated by typicality, the MTLs mediate memory retrieval shortly after encoding for both typical and novel events. This absence of differential neural activity during immediate recall is also interesting since it is consistent with behavioural evidence that schema effects during retrieval emerge over time (Mandler & Ritchey, 1977), as well as with the behavioural results of our study – no differences based on typicality are seen at immediate retrieval. Instead, the forgetting of neutral clips and the increased numbers of errors for atypical clips are all differences that are evident at delayed retrieval only.

Alternatively, it is possible that our study was underpowered to find differences at immediate retrieval. Each retrieval session contained half as many clips as the encoding session. Perhaps if more film clips were used, or more participants recruited, differences would be found. Unfortunately, our scanning time during the first session (encoding/immediate retrieval) was already very long, which limited the number of film clips we could include. Despite the possibility that our study was underpowered, significant effects were found at delayed retrieval, in direct contrast and functional connectivity analyses. The fact that there were fewer trials at 7d retrieval, due to the number of film clips that were forgotten over the week following encoding, indicates that we should have been able to find differences at immediate retrieval if they existed and were at least as strong as the differences at 7d retrieval. It seems likely that the null results at
immediate retrieval are due, instead, to the more uniform dependence on reactivation of event
details by the MTLs shortly after encoding, irrespective of event typicality.

5.2.2 Declines in MTL activation and event typicality

Notwithstanding the overall neural similarities in the retrieval of both typical and atypical events,
some differences were evident. As mentioned above, typical clips were associated with attenuated
MTL activation during remote retrieval, indicating that consolidation dynamics may be
modulated by event typicality. The decreased MTL activation seen during the retrieval of typical
events, as compared with atypical events and only at a remote time-point, is consistent with
rodent (Tse et al., 2007) and human (Sommer 2016) investigations using paired associates,
suggesting that memories become less dependent on the MTLs for retrieval when they are
congruent with prior knowledge. This is known as accelerated consolidation, and may be due to
the potentiation of direct connections between neocortical representations (van Kesteren et al.,
2012), the schema-based enhancement of direct or hippocampus-dependent reactivation during
rest or sleep for information that is related to prior knowledge (Dudai et al., 2015; van Dongen et
al., 2011), and/or due to the decreased number of new connections and biological modifications
necessary to integrate a new event into a relevant pre-existing cortical framework (Wang &
Morris, 2010). Here we show for the first time that such mechanisms may also apply to the
consolidation of narrative event memories, despite the fact that such events generally demonstrate
much more dependence on MTL-based encoding and retrieval.

The decline in MTL activation for typical events specifically – or for schema-congruent stimuli
more generally, in other studies – is compatible with SLIMM theory, which proposes differential
neural substrates for typical and novel stimuli (van Kesteren et al., 2012). As discussed above, it
is also compatible with Trace Transformation Theory, which suggests that the nature of a
memory, and not its age, is the critical determinant of MTL-dependence and its neural
representation in general (Winocur et al., 2010; Winocur & Moscovitch, 2011; Moscovitch et al.,
2016). Finally, this result is consistent with a modified version of the complementary learning
systems theory, which takes the possibility of rapid neocortical learning into account and
demonstrates that it may occur without catastrophic interference (McClelland, 2013). However,
this result is inconsistent with the classic Standard Consolidation Theory proposal that all
memories become equivalently independent of the MTLs over time (Squire & Alvarez, 1995; Squire & Wixted, 2011).

The MTL sub-region that shows the greatest difference between typical and atypical events at 7d retrieval is the entorhinal cortex. This association between the entorhinal cortex and remote memory for atypical events is consistent with evidence that people with MTL damage extending into the rhinal cortices display retrograde amnesia that extends further back in time than patients with damage restricted to the hippocampus, linking the rhinal cortices with older memories (Bayley, Hopkins, & Squire, 2006). Indeed, Insel & Takehara-Nishiuchi’s recent review (2013), based largely on rodent work, suggests that the entorhinal cortex is particularly important for remote memory. It is possible that the general importance of the entorhinal cortex for remote memory may be partly driven by a role in the retrieval or recombination of event-specific details. This process would be particularly critical for those atypical memories, to compensate for less support from prior knowledge during event reconstruction, consistent with the localization of MTL differences based on event typicality to this specific sub-region.

5.2.3 mPFC activation and theories of consolidation

The mPFC activation found when contrasting 7d retrieval with encoding for both typical and atypical event memories is consistent with both prominent consolidation models outlined in the introduction. Specifically, both Trace Transformation Theory and Standard Consolidation theory are consistent with a role for the mPFC in delayed retrieval, though they interpret this role in different ways. Trace Transformation Theory suggests that any shift in representation from hippocampal to extra-hippocampal neocortical structures entails a transformation of memory from its initial detailed form to a more generalized, gist-like representation (Moscovitch et al., 2016; Winocur, Moscovitch, & Bontempi, 2010; Winocur, Moscovitch, & Sekeres, 2007). This transformation of memory may reflect either a greater dependence on prior knowledge, such that events are remembered as more schema-consistent than they actually were, and/or an abstraction of event details forming a more generalized representation. Standard Consolidation Theory, on the other hand, suggests that remote memories mediated by neocortical areas retain the features of the original hippocampally-mediated representations, with the mPFC’s role in remote memory similar to the binding role ascribed to the hippocampus in recent memory (Frankland &
Bontempi, 2006; Squire & Wixted, 2011; Takehara et al., 2003; Takehara-Nishiuchi & McNaughton, 2008).

Some evidence differentiating between these two theories is provided by looking at brain-behaviour correlations. Specifically, although mPFC activity is evident at delayed retrieval for both typical and atypical clips, the degree of mPFC activity is negatively correlated with errors for typical clips, but positively correlated with errors for atypical clips (marginal when outlier is included). This suggests that the prominence of mPFC activity at 7d retrieval may reflect dependence on prior knowledge during the re-construction of event memories, or the integration of event information with such semantic representations. If the mPFC were taking over as a linking structure for remote memory there is no clear reason to hypothesize a differential relationship between activation and memory errors based on event typicality.

5.2.4 mPFC activation, prior knowledge, and memory errors

The interpretation of the differential relationship between mPFC activity and memory errors based on event typicality, outlined above, is dependent on an understanding of memory as a constructive process. In Bartlett’s (1932) original study of cultural influences on memory for narratives, he characterized memory in this way – describing it as a construction based on the commonalities abstracted from across our past experiences along with a few event specific details. Since Bartlett’s time there has been growing interest in and evidence for this ‘constructive’ viewpoint (Bransford, Barclay, & Franks, 1972; Oldfield, 1954; Piolino et al., 2009; Rumelhart & Ortony, 1977; Schacter et al., 1998; Schacter et al., 2012). Semantic knowledge is thought to act as scaffolds for such reconstruction, and to fill in event details (Binder et al., 2009; Irish et al., 2012; Irish & Piguet, 2013; Schacter, Guerin, & St Jacques, 2011), with this filling in of details becoming more critical as episodic memory tends to fade over time, in some cases providing a significant contribution to recall (Steyvers & Hemmer, 2012). Critically, these influences of prior knowledge may either enhance or distort memory, depending on the congruency or typicality of the event being recalled (Alba & Hasher, 1983; Steyvers & Hemmer, 2012).

Note that this ‘use’ of prior knowledge as a scaffold for re-construction and to fill-in details during recall is not proposed to be effortful or explicit in any way. Reconstruction is proposed to occur automatically and sub-consciously, with the brain integrating both semantic and episodic
information during event recall. It is not proposed to be the case that a person, aware their memory is lacking in detail, explicitly attempts to activate relevant schemas and infer what must have occurred. For example, if I am recalling a birthday party from a year ago, my memory is likely to have faded over time. Thus, I may be implicitly dependent on schematic birthday party information during recall of this event, which would lead me to report details such as ‘there was cake at the party’. Whether or not this general ‘cake detail’ is based on true re-instantiation of a cake that I encoded a year ago, or part of my re-constructed memory due to my birthday party schema, is almost impossible to know without objective evidence from the event. If this particular party was a typical party, schematic influences would have enhanced my memory. However, if there was in fact no cake at this particular party, reliance on prior knowledge would have distorted my memory (see discussion in Moscovitch, 2007). The array of evidence outlined in the introduction suggests that mPFC activity reflects the activation of such prior knowledge. If one accepts this evidence, then the finding that the degree of mPFC activity at delayed retrieval is negatively correlated with errors for typical clips, but positively correlated with errors for atypical clips, is consistent with the proposal that semantic influences become more prominent over time – enhancing memory for events that are congruent with prior knowledge, while distorting memory for atypical events.

It is notable that story errors in particular showed this relationship with mPFC activity for typical and atypical clips. These story errors are of special interest since they are more relevant to the typical and atypical aspects of our clips, which were originally classified according to ratings of story typicality specifically. Thus, it was only these relevant elements that were affected, rather than the unrelated peripheral elements. Despite the fact that these story errors were of the greatest interest, the low number of such errors that people generally made limited our analysis. Consequently, although this correlation between neural activation and memory accuracy is intriguing, further investigation is necessary to determine whether or not this relationship is dependable and found in other contexts. A more comprehensive investigation into the relationship between mPFC/schema activation and memory errors might include a greater number of clips and follow them over a longer period of time. Including more clips would increase power, which would presumably clarify the nature of such a brain-behaviour correlation. Following the clips over a longer period of time would be interesting, since dependence on prior knowledge might increase as more time passes between encoding and retrieval.
5.2.5 mPFC and MTL activation during retrieval

Activity in the mPFC cluster, which was correlated with memory errors, also increased between encoding and delayed retrieval for both typical and atypical clips, independently. Unlike at encoding, when increasing mPFC activation was correlated with increasing typicality, at delayed retrieval there was no longer a significant difference between mPFC activation for typical and atypical events. Similarly, although atypical clips were associated with greater MTL activation at delayed retrieval, all clips were generally associated with MTL activity during recall. Thus, neural differences based on typicality seem to be less pronounced during retrieval.

These results are inconsistent with SLIMM’s proposal of an inhibitory relationship between the mPFC and MTLs (van Kesteren et al., 2012). Although we observed a negative relationship between mPFC and MTL activation at encoding, activity is evident in both the MTLs and mPFC at retrieval and we don’t find evidence for inhibition. The absence of an inhibitory relationship may be due to the complex narrative nature of our stimuli. Indeed, memory retrieval mediated solely by neocortical traces, without any MTL involvement, seems less probable for naturalistic events like those investigated in our study. Instead, retrieval is likely to depend on a mix of both semantic and episodic information as narrative events are reconstructed during recall (see Levine, Svoboda, Hay, Winocur, & Moscovitch, 2002).

5.2.6 Functional connectivity of the mPFC and MTLs

Both the mPFC and MTLs are functionally connected with the angular gyrus and precuneus during 7d retrieval. The notable aspect of this finding is that the mPFC shows this pattern of connectivity only during the retrieval of typical events, while the MTLs conversely show this pattern of connectivity only during the retrieval of atypical events. These results may indicate that our two regions of interest support similar neural processes associated with event retrieval, with dominance shifting between the mPFC and MTLs depending on the nature of the event being retrieved. Specifically, the mPFC may play a greater role within this network when events are more strongly related to prior knowledge, due to dependence on semantic information during retrieval (Alba & Hasher, 1983; Ghosh & Gilboa, 2014; Piaget, 1929; Preston & Eichenbaum, 2013; Rumelhart & Ortony, 1977). Conversely, the MTLs may be the central hub in this network when events are more atypical or novel, due to a greater dependence on reactivation of the arbitrary associations and relations bound by the MTLs during the encoding of those events.
Generally, the inferior parietal lobes, which consist of the angular and supramarginal gyri, are associated with recollection and the bottom up capture of attention in memory – including the capture of attention by memory cues or retrieved information – which is contrasted with top-down explicit/effortful direction of attention (Cabeza, Ciaramelli, & Moscovitch, 2012; Cabeza, Ciaramelli, Olson, & Moscovitch, 2008). Thus, the functional connectivity that we observe during retrieval may reflect the capture and subsequent implicit direction of attention by mnemonic information reinstated predominantly through either the mPFC (for typical clips) or the MTLs (for atypical clips). Although the mPFC and MTLs are connected with the left and right angular gyri, respectively, the overarching process occurring bilaterally is thought to be the same, differing only in the material processed based on that differential connectivity (Cabeza, Ciaramelli, Moscovitch, 2012; Cabeza et al., 2008). Interestingly, a recent study by Bellana and colleagues (2015) also found that, during episodic retrieval, the mPFC was preferentially connected to the left angular gyrus, while the bilateral MTLs were functionally connected to the right angular gyrus specifically. These convergent results suggest that the lateralization observed in this study may be systematic rather than task-specific.

The mPFC-angular gyrus interactions illustrate a possible neural mechanism for one of the major roles ascribed to prior knowledge: the facilitation and guidance of memory retrieval. The activation of schematic information in the mPFC could capture attention during retrieval, through communication with the angular gyrus, which would subsequently support the reinstatement of congruent event information. Similarly, in scene perception, contextual information is thought to focus attention on the most relevant areas of a scene through mPFC-inferior parietal lobe interactions (Oliva & Torralba, 2007), while in a paired associates task mPFC interactions with the angular gyrus are only seen in the schema-congruent condition, and are thought to underlie the schematic guidance of memory search (van Buuren et al., 2014). Note that this schematic ‘guidance’ of memory retrieval is proposed to be due to the automatic activation of schematic information, which captures attentional mechanisms during retrieval in a bottom-up implicit manner, rather than being an explicit method of targeting attention engaged by participants, in line with the inferior (rather than superior) parietal lobe activity observed in our data (Cabeza, Ciaramelli, Moscovitch, 2012; Cabeza et al., 2008). The MTL-angular gyrus interactions may
similarly reflect the MTL-dependent activation of episodic information during retrieval that captures attention during the reconstruction of atypical events.

An alternative possibility is that the angular gyrus’s functional connectivity with both the mPFC and MTLs is due to the re-combination of episodic and semantic information during retrieval. This possibility is suggested by a recent study from Wagner and colleagues (2015) who had participants acquire and retrieve rule-based schemas over two consecutive days. Although schema retrieval was associated with activation through midline areas, including the mPFC, PCC, and MTLs, multi-voxel pattern analysis indicated that the convergence of schema components occurred in the angular gyrus (Wagner et al., 2015). Critically, this convergence in the angular gyrus was only seen after 24 hours, during retrieval, suggesting that the angular gyrus was recombining consolidated schema components into a coherent representation (Wagner et al., 2015). It is possible that the angular gyrus is fulfilling a similar role during the retrieval of events in this study, acting as a convergence zone for semantic and episodic information. However, it is also possible that the reactivation of schema components observed in the angular gyrus in Wagner and colleagues’ study reflects the activation of schematic information capturing attention in a bottom-up fashion. This interpretation could also account for the convergence of schema components in the angular gyrus, as the recurrently activated information accumulates in the service of guiding memory retrieval and behaviour.

During 7d retrieval, the mPFC and MTLs both also show significant functional connectivity across the medial parietal cortex, with activation peaking in the precuneus but extending into the PCC. For typical clips, this functional connectivity is consistent with the enhanced mPFC-PCC/precuneus connectivity reported during the retrieval of schema-congruent associations by van Buuren and colleagues (2014). The interactions of both the mPFC and MTL with this area are also consistent with the overlap of retrieval networks in the PCC seen by St Jacques and colleagues (2011), suggesting that this heteromodal association cortex is particularly critical for the integration of semantic and episodic information. As discussed in Chapter 4 on encoding, the PCC is thought to be necessary for linking narrative information with semantic information during encoding and recall (Binder et al., 2009; Bird et al., 2015). The PCC is likely playing a similar role during retrieval as it was playing during encoding, namely, integrating semantic, contextual, and event-specific information.
Chapter 6
Discussion

6.1 Summary

The primary objective of this thesis was to deepen our understanding of the neural networks that support event memory in real world settings, where our experiences fall along a spectrum of novelty and congruence with prior knowledge and expectations. With respect to the mPFC and MTLs in particular, the evidence motivating this study suggested that activation in these areas is affected by typicality and novelty, as well as by consolidation dynamics, as events are stabilized and transformed over time. Thus, our second objective was to characterize the neural bases of typical and atypical memories over time, untangling the interactions of typicality, novelty, and memory consolidation. I achieved these objectives through the use of naturalistic film clip stimuli, which capture the dynamic narrative structure of real-world events, within a spatial-temporal context, while retaining the reproducibility and controlled nature of more traditional laboratory stimuli. Using these film clips, I examined behavioural measures of memory, as well as the patterns of neural activity and connectivity underlying memory as people encoded, retained, and retrieved event memories over the course of a week.

Behaviourally, I demonstrated that both typicality and novelty enhance memory for events, but that atypical events are recalled with more errors over time. With respect to the neural bases of memory, it was during encoding that I found the greatest differences based on event typicality. Specifically, increasing typicality was correlated with greater mPFC and PCC activation, as well as increasing functional connectivity between these two areas. On the other hand, increasing atypicality, or novelty within the film clips, was correlated with greater activation in the MTLs, ventral visual stream, and posterior sensory cortices, as well as increasing functional connectivity from the MTL to these posterior sensory areas and enhanced mPFC-MTL functional connectivity.

Retrieval of all film clip events was associated with MTL activation, irrespective of typicality or time since encoding. Similarly, both typical and atypical events were associated with mPFC activation during delayed retrieval, when contrasted with encoding.
Notwithstanding these overall neural similarities in the retrieval of both typical and atypical events, when contrasting the recall of very typical and very novel film clips, some differences were evident. Namely, typical clips were associated with attenuated MTL activation during remote retrieval, at which time the mPFC and MTLs also showed differential functional connectivity based on event typicality. Both of these regions of interest were functionally connected to the angular gyrus and precuneus/posterior cingulate cortex during remote retrieval, but the mPFC demonstrated this pattern of connectivity only for typical clips, while the MTLs showed this pattern of connectivity only during the retrieval of atypical events.

6.2 Final Discussion

This thesis addressed three broad questions, which will be answered in the three following sections.

1) How do typicality and novelty modulate the brain areas engaged during the encoding and retrieval of narrative event memories?

The results described in this thesis clearly demonstrate that the neural substrates mediating narrative episodic memories are modulated by event typicality, both at encoding and retrieval (see the activation and functional connectivity differences outlined directly above). However, these differences are much stronger at encoding, an effect that will be discussed below. Furthermore, the findings are consistent with two complementary theories - Trace Transformation Theory and SLIMM Theory.

Trace Transformation Theory posits that the neural substrates mediating memory are determined by the nature of the representation, with detailed episodic memories mediated by the MTLs and generalized memories supported by extra-hippocampal neocortical regions. Critically, Trace Transformation Theory does not propose that there is an indiscriminate decline in MTL-dependence for memories after encoding. Instead, any shift in the neural representation of a memory is thought to be accompanied by a transformation in the nature of the representation, either over time or with experience. Our findings of equivalent MTL activation during immediate and delayed retrieval sessions, when averaging across all clips, are consistent with this lack of an indiscriminate decline in MTL activation. Indeed, MTL differences are only seen when taking
event typicality into consideration, consistent with the hypothesis that the neural substrate of a memory is reflective of the nature of the representation, rather than reflective of its age per se.

SLIMM theory, as described in the introduction, suggests that the mPFC detects the congruence between one’s prior knowledge and one’s current experience, which is associated with activation of relevant semantic information and a shift from MTL to mPFC based processing (van Kesteren et al., 2012). Consistent with this theory, at encoding we find that increasing typicality is correlated with increasing activity in the mPFC, while increasing atypicality is associated with increasing activity in the MTLs. Our findings illustrate patterns of neural activity that have been shown before with paired associates (van Kesteren et al., 2013) and fact learning (van Kesteren et al., 2014), but not yet in events that have a narrative structure. Thus, we provide evidence for the applicability of these results to naturalistic event memories. Despite confirming these aspects of SLIMM, we do not find evidence for an inhibitory relationship between the mPFC and MTLs. Although we do see a negative correlation between mPFC and MTL activity at encoding when taking typicality into account, at retrieval all clips are associated with both MTL and mPFC activity. As discussed above, this may be due to the complex narrative nature of our stimuli. The retrieval of these naturalistic event memories is likely to depend on a mix of both semantic and episodic information as narrative events are reconstructed during recall (see Levine, Svoboda, Hay, Winocur, & Moscovitch, 2002), supported by cooperation among medial temporal and neocortical areas.

2) **Do the effects of typicality and novelty on brain activation change over time between encoding, immediate retrieval, and delayed retrieval, as memories undergo consolidation?**

Although the SLIMM theory predicts that mPFC activity increases while MTL activity decreases, with increasing congruency, across both encoding and retrieval (van Kesteren et al., 2012), we do not find evidence for such homogeneous effects. Instead, we observed the greatest differences based on typicality at encoding, with the neural substrates mediating typical and atypical event memory more similar at retrieval. The stronger effects of typicality and novelty during the perception and encoding of events makes sense, since that is the time when the stimuli are actually being experienced, along with all of the contextual and episodic story details that constitute their ‘typicality’ or ‘novelty’. At this time there is a direct interplay between the typical stimuli triggering the engagement of relevant semantic and contextual information, which then
guides perceptual processing (Oliva & Torralba, 2007; Preston & Eichenbaum, 2013; van Kesteren et al., 2012). Similarly, during encoding the novelty of the stimulus is presumably having a direct effect – triggering MTL engagement and the release of dopamine to influence mnemonic and cognitive processing (Lisman et al., 2005; Kumaran & Maguire, 2006, 2007; Duncan et al., 2012). Once encoding is over, participants are left with their own internal representations of the events, which are more likely to depend on a mix of prior knowledge and event-specific information. This dependence on both semantic and episodic information during recall, which was proposed to underlie the lack of an inhibitory relationship between the mPFC and MTLs, may be more evident in our study, which uses narrative events, since the integration of both types of information may be more critical during the reconstruction of these complex events than during the recall of simple stimuli or paired associates, like those that have been the primary basis of schematic memory retrieval research in the past.

3) Does event typicality modulate the functional connectivity of our regions of interest – the mPFC and MTLs – with each other and with the rest of the brain?

At both encoding and retrieval, event typicality modulated the functional connectivity of both the mPFC and MTLs. Firstly, our functional connectivity findings illustrated potential mechanisms by which typical and novel events may be differentially encoded. Specifically, the greater functional connectivity between the mPFC and PCC during the encoding of increasingly typical events, and increasing functional connectivity between the MTLs and sensory cortices for increasingly novel events, might represent a neural basis for the greater influence of prior knowledge on perception in congruent contexts and the greater dependence on bottom-up sensory information during encoding in incongruent contexts. For congruent events, this dependence on prior knowledge may reduce the resources needed by the cognitive system at encoding (Steyvers & Hemmer, 2012). While for atypical events, these connectivity differences may underlie the enhanced processing of specific visual details that presumably supports the greater ability of participants to differentiate targets from similar lures and notice changes to items, when items are embedded in incongruent contexts (Friedman, 1979; Konkle & Oliva, 2007; Mandler & Ritchey, 1977; Spalding et al., 2015). The additional enhancement of mPFC-MTL functional connectivity during the encoding of atypical events may represent a mechanism underlying the greater integration necessary for novel information, in the absence of relevant prior knowledge to guide encoding.
At retrieval, the functional connectivity of the mPFC and MTLs with the angular gyrus and the precuneus/PCC may illustrate the similar roles that these two regions of interest are playing within a retrieval network, with dominance shifting between them based on event typicality. In particular, the connectivity with the angular gyrus is proposed to reflect attentional capture by reactivated mnemonic information, which supports re-construction of event memories. For typical clips, on the one hand, reactivated semantic information may be the more prevalent source of this information. For atypical clips, on the other hand, MTL-dependent reactivation of episodic information may be predominantly capturing and guiding attention. In both situations, the precuneus/PCC connectivity is proposed to reflect the integration of contextual, semantic, and episodic information in the service of event reconstruction.

**mPFC sub-regions**

Although it was not a focus of this thesis, a discussion of variation across mPFC sub-regions is warranted. In considering the role of the mPFC in the introduction, confabulation was discussed, since it is the primary symptom of ventral mPFC lesions in humans. In humans, unlike in rodents, mPFC lesions do not tend to result in selective remote memory impairments, with deficits pervasive across time, and even across episodic and semantic memory (Gilboa et al., 2006; Melo & Moscovitch, 1997; Nieuwenhuis & Takashima, 2011). This is inconsistent with the proposal that the mPFC takes over from the MTLs as a linking structure for remote memory, but consistent with a role for the mPFC in the monitoring of current experience, and/or the activation of relevant and suppression of irrelevant prior knowledge. The area of the mPFC that tends to be damaged in cases of confabulation is the sub-genual mPFC (Ghosh et al., 2014; Gilboa & Moscovitch, 2002; Schnider & Ptak, 1999; Schnider, 2003; Turner, Cipolotti, Yousry, & Shallice, 2008). This sub-genual area is more ventral than the mPFC area found in this thesis and in many other studies of prior knowledge and episodic memory, which tend to report mPFC activation anterior to the genu of the corpus callosum (van Kesteren et al., 2014; Sommer, 2016; van Kesteren et al., 2010a; van Kesteren et al., 2013; see Figure 2). This area is neither very ventral, nor dorsal, and might be more appropriately referred to as the ‘mid-mPFC’. Although ventral mPFC damage resulting in confabulation often extends dorsally, allowing for the possibility that the sub-region activated in schematic processing is also implicated in confabulation, it may be useful to consider different functions mediated by different sub-regions of the mPFC.
In rodents, inactivation of the infralimbic and prelimbic regions of the mPFC can have opposite effects on memory, with the infralimbic region linked to context-sensitive learning and/or the suppression of a contextually inappropriate memory, while the prelimbic region is linked with memory activation, as evidenced by the expression of fear after contextual conditioning (Sierra-Mercado, Padilla-Coreano, & Quirk, 2011). With respect to studies on prior knowledge and memory in rodents, it is the prelimbic region that is implicated in schema activation (Tse et al., 2007, 2011). As discussed above, in humans, activity in the mid-mPFC is often linked with the activation of prior knowledge, while damage to the sub-genual mPFC is linked with confabulation. There is also evidence that the sub-genual mPFC is specifically involved in monitoring processes (Hebscher et al., 2015). Although it is difficult to determine how the mPFC sub-regions in rodents correspond to those in humans, these results suggest that the infralimbic region in rodents, which is involved in the suppression of contextually inappropriate memories, may correspond to the sub-genual or ventral mPFC in humans, which is linked with corresponding deficits in monitoring and/or suppression of contextually inappropriate memory traces, as seen in confabulation (Gilboa et al., 2006; Hebscher et al., 2015; Nieuwenhuis & Takashima, 2011; Schneider, 2003; Sierra-Mercado, Padilla-Coreano, & Quirk, 2011). The rodent prelimbic cortex, on the other hand, which is linked with memory activation and the influences of prior knowledge on new learning, may correspond to the mid-mPFC region often observed in human studies on prior knowledge and memory. Thus, these ventral and middle regions of the mPFC may work together to guide behaviour and facilitate memory, but with the former playing an inhibitory role to suppress contextually irrelevant information, and the latter playing an excitatory role to activate relevant information.

6.3 Conclusion

The concept of memory as a constructive process runs through our findings, from encoding to retrieval, and across time. The constructive nature of encoding is evidenced by the modulation of activity in primary sensory areas by the congruency of events with prior knowledge. During retrieval there seems to be a dependence on both MTL-mediated episodic information, and mPFC-mediated prior knowledge during the re-construction of events – which benefits memory in some cases and distorts it in others. From the nearly century’s worth of evidence surveyed in this thesis, these results call to mind Bartlett’s (1932) original characterization of memory – not a direct record of any single event, but a construction based on the entirety of past experiences,
combined with event-specific details, and modulated by our expectations. These constructions may not always be accurate, but they are well suited to guiding behaviour, promoting inferential thinking, and supporting problem solving across the wide array of contexts and situations we experience throughout our lives.

6.4 Future Directions

1) Due to the coincident activity often seen across the mPFC and PCC, in both this thesis as well as across the literature, it is difficult to disentangle their distinct roles. We characterize the mPFC as critical for detecting congruence between prior knowledge and current experiences, while the PCC is thought to integrate semantic and episodic information in the construction of a narrative. Many other people have similarly outlined divergent roles for these two structures, despite observing similar patterns of activation across them, leaving uncertainty as to these conclusions. Future research may try to delineate the differential contributions that these two highly related areas make to memory and cognition.

2) Although mPFC and MTL activity at encoding is generally modulated by event typicality when looking across a group of participants, it would be interesting to investigate individual variation across complex event stimuli such as ours. In particular, the accuracy of memory during later retrieval may vary with respect to patterns of neural activity at encoding. For example, although a certain clip may be generally perceived as atypical and associated with greater MTL activation, it is possible that some participants were dependent on (inappropriate) prior knowledge-based processing during the encoding of that clip. This might be reflected by greater mPFC activity during encoding for that clip, and a correlated increase in errors during retrieval. An exploration of such individual differences in patterns of neural activity and behaviour would deepen our understanding of the precise links between brain activity and the nature of mnemonic representations.

3) Across the literature, many different types of prior knowledge have been referred to as ‘schemas’. Although this thesis attempted to define schemas – based on the work of many others – and settled instead on the more neutral term of ‘prior knowledge’, there remains a paucity of neural evidence for the differentiation of schematic information from other related semantic representations. In order to fully understand the neural mechanisms underlying schema activation and use in cognition and memory, it will be critical to define exactly what types of prior
knowledge we consider to be ‘schematic’ and to characterize the neural substrates of such schemas, as contrasted with the neural substrates mediating other types of semantic knowledge.

4) Although we outlined a proposal for distinguishing between different functions mediated by different sub-regions of the mPFC, this proposal was purely speculative. We suggested that the ventral mPFC may play an inhibitory role while the ‘mid-mPFC’ (anterior to the genu of the corpus callosum) may play an excitatory role. Further experimentation in both rodents and humans would be necessary to test our proposal and to delineate the precise functions that the different mPFC sub-regions play in memory and cognition. Future studies on the effects of prior knowledge should take this possible sub-regional variation into account, and be precise in reporting which specific areas of the mPFC are implicated in their results.
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Appendices

Appendix A: List of all film clips used in study, with narratives. Clips are organized from most typical to most atypical, based on ratings of story content by an independent participant group, as described in methods.

Couple in the Kitchen
- Man standing in kitchen
- Woman cooking/preparing food/washing dishes (point given for any of these actions)
- Man approaches her
- Man hugs woman
- Woman stops working

Couple Meeting at the restaurant
- Man waiting for a woman in a restaurant
- Woman enters restaurant
- Woman sits down
- Man offers her his glass
- Woman takes a sip

Men Toasting
- Man #1 enters the living room
- Man #1 turns a light on
- Man #2 is waiting on the couch
- Man #1 sits down beside Man #2
- Man #1 pours two drinks
- The men toast

Boys Watching Soccer
- Two boys watching soccer on TV
- Soccer player scores
- Boys cheer
- Boy rewinds video
- Boys rewatch the goal
- Boys cheer just as loudly as the first time

Boys Playing at the park
- One boy sitting on a swing
- One boy spinning in circles
- Boy jumps on rocking park toy
- Boy runs over to friend on swings
- One boy turns upside down on the swing

Parents fighting
- Couple is fighting
- Girl is playing the piano
- The piano is being played violently/very loudly
- Parents stop arguing
- Man stops the girl’s piano playing

Cyclist Waiting for Her
- Man waiting with his bicycle
- Woman walks right past him
- They greet each other
- Man chases her
- Man must return for his bicycle
- Couple walks and talks

Snowy Car
- Man finds car covered in snow
- Man cleans car (maximum of 2 points for listing different parts of cleaning car)
- Man tries to unlock car
- Car in front is unlocked instead
- Man realizes he has been cleaning wrong car

Meeting at the mosque
- Young man waiting outside
- Girl comes out from mosque
- Both happy to see each other
- Father comes out
- Boy looks upset/sad/downfallen

Family Dessert
- Mother, father, son sit down at dining room table
- Boy eats all his fruit
- Boy doesn’t eat rest of dessert
- Parents look at each other, upset/confused
- Mother scolds son

Couple Taking a Photograph
- Man sets up camera timer
- Man goes back to his wife
- Wife tries to hold his arm
- Man shakes the woman off
- Car drives between camera and couple
- Camera takes a picture of the car
- Couple laughs

Picking up Mangos
- Boy is picking up mangos
- Mangos get dropped down from tree
- Boy leaves tree with full basket
- Boy puts basket down
- Boy pockets some mangos
• Boy grabs a new empty basket

Family painting a cottage
• 2 women painting a house
• Man walks up
• Man puts a bucket down
• Man takes over from one of the women
• That woman walks to front of house

Boy and his jersey
• Boy is colouring a shirt
• Boy puts shirt on
• Boy looks at self in mirror
• Boy is excited/happy
• Boy pulls shirt over his face (like soccer player)

Picking up a Hitchhiker
• Man is driving down desert road
• Driver sees female hitchhiker
• Hitchhiker has a sign
• Driver stops the car
• Hitchhiker runs up to the car window

Leaving Home
• Parents and son standing in front of house
• Son gets last box to put in his car
• Son sits in driver’s seat of car
• Son and parents say goodbye
• Son drives off
• Unattached trailer is left behind

Thief
• Girl is walking around (record) store
• Girl puts record in her folder/bag
• Girl tries to leave store
• Clerk stops her, asking for folder/bag
• Girl passes clerk her folder/bag

Policeman Flirting
• Policeman sees a woman with her daughter
• Policeman blows whistle to stop traffic
• Policeman crosses the road
• Policeman and woman talk
• Policeman helps woman across the road

Sleeping Boy
• Boy #1 is pulling a cart down a road
Boy #1 sees Boy #2 sleeping
Boy #1 pours water from a bottle into its cap
Boy #1 pours water on Boy #2
Boy #2 wakes up

Couple Fighting in the Car
Couple arguing in a car
Heavy rain outside
Man stops the car
Woman gets out
Car drives off
Woman walks off in the rain

Lone Man at the theater
Theater in the middle of nowhere
Man buys ticket
Man sits down in theater
Man is the only one in the theater
Projectionist yells
Movie starts

Teenagers teasing
Boy shows a note to his friend
Friend teases him
Friend begins to walk away
Friend steals fruit on his way
Fruit vendor is angry
Friend throws fruit back to boy with note
Boy returns the fruit to the vendor

Woman Buying Lettuce
Woman picks up head of lettuce
Woman looks to the vendor
Vendor shakes his head ‘no’
Woman picks up another head of lettuce
The vendor approves/shakes his head ‘yes’
Woman takes two heads of lettuce
Woman leaves some money

Waitress and the Pianist
Waitress knocks on the door
Pianist doesn’t stop playing piano
Waitress lets herself into the room
Waitress places tray down on a table
Pianist hears the noise from the tray
Pianist stops playing the piano
Meeting the flute player
• A man is playing a flute
• A woman hears the flute
• The woman goes towards the man
• He tries to find her
• She surprises him
• She grabs his flute

Crashing the Bicycle
• Man and boy on bicycle
• Going down a hill
• Man discovers brakes don’t work
• Man tries to slow down
• They crash into tree
• They fall off of bike

Grandfather babysitting
• Grandfather squeezes squeaky toy
• Grandfather lights cigarette
• Grandfather sits down by baby carriage
• Grandfather speaks to baby
• Baby starts crying
• Grandfather swears/is upset/is angry

Penalty Kick
• Group of people are playing soccer
• One player places a soccer ball (for a penalty kick)
• Referee blows the whistle
• Player kicks the ball
• Ball flies way over the net
• Ball hits something in the background

Boys Faking a Car Accident
• Group of boys walking down street
• Boy stomps on bumper of car (stopped at a light)
• Front driver thinks he has been rear-ended
• Front driver gets out of car
• Front driver yells at driver behind him
• Rear driver gets out of his car
• Boys laugh

Man, Bird, and Window
• A man is opening/closing a window
• He notices that the window is focusing/directing light on neighbour’s wall
• Neighbour bird is singing
• The man moves the window/bar of light back and forth
• The man closes the window
Girl Chasing her Shoe
• A girl loses her shoe in the gutter
• Shoe is carried away by the water
• Girl chases her shoe down the street
• Shoe gets caught
• Girl is sad/upset

Husband Smokes
• Husband and wife are standing on their stoop/in their backyard/on their porch
• Husband gets out a cigarette
• Wife goes inside house
• Wife returns outside with lighter
• Husband lights his cigarette
• Wife returns inside

Mom putting boy into car
• Boy gets into car
• Mother hands him briefcase/bag
• Car drives away
• Mother follows behind car for a short while
• Mother is wiping car (with a rag) the whole time it is driving away/she is following
• Mother waves goodbye (with rag)

Chasing the red balloon
• Boy walking alone with balloon
• Group of kids chase him
• Boy runs up stairs
• Second group of kids runs towards him
• Boy loses his balloon
• Boy catches balloon
• Boy runs off safely

Boy, Girl, and Balloons
• Boy and girl each have large balloons
• Boy walks away
• Girl’s balloon floats towards boy
• Boy catches girl’s balloon
• Girl retrieves her balloon from the boy
• Children walk in opposite directions

Man Against Door
• Man knocks on closed door
• Two men are waiting on the other side of the door
• Man tries to force the door open (shoulder checks door)
• The men on the other side unbar the door
• The door opens the next time the man throws his body against it
• The man falls to the floor
• They all shake hands

Couple at the beach
• Couple standing by the shore
• Boy taking picture of girl
• Little wave splashes girl
• Boy offers tissue
• They both get splashed by giant wave
• Their clothes are ripped off/soaking wet

Woman Dropping a Shell
• Woman enters a museum
• Woman picks up a shell
• Woman drops the shell so it breaks
• The noise wakes up a security guard
• Woman replaces the shell with a piece of pasta
• Woman writes a note
• Woman leaves the museum

Woman Squeezing Food
• Woman in grocery store
• Woman is squeezing a peach
• Woman squeezes so hard juice squirts out
• Cashier is angry/surprised
• Woman runs away
• Cashier follows her
• Woman squeezes a round of cheese

Gunman at the window
• Gunman retrieves gun
• Gunman opens up window
• Gunman aims outside
• Gunman shoots toy dog
• Woman (owner of toy dog) looks up at the gunman
Appendix B: Partial Least Squares (PLS) methods and results.

**PLS Specific Methods**

We performed supplementary analyses using the mean-centered Partial Least Squares approach, with a blocked design (PLS; McIntosh, Bookstein, Haxby, & Grady, 1996). PLS is a multivariate, data-driven analysis technique that assesses covarying activity across voxels in the entire brain with no *a priori* contrasts. This technique detects whole-brain patterns of activity that covary across or between experimental conditions, without requiring the contrast analyses typical of univariate methods.

In this analysis the correlations between activities in each set of voxels at each timepoint are computed across subjects within each condition, and then contrasted across conditions. Singular value decomposition is performed on the correlation matrix, which produces a set of latent variables (LVs). The LVs produced by this analysis describe patterns of activity that covary together over time, and are orthogonal to one another. Each LV is associated with a linear contrast between experimental conditions, with each pattern showing a network of brain regions associated with one (or more) of the conditions. The contribution of each voxel to the LV is indicated by its bootstrap ratio (BSR), which represents the salience of each voxel divided by its standard error. The sign of the BSR indicates which regions are coactive (same sign), or differentially active (opposing signs). The sign itself is arbitrary – negative BSR values do not represent deactivations, but rather a set of covarying regions with an activation pattern that differs from the activation pattern seen in regions with positive BSRs.

The statistical significance of results was determined using permutation testing (1000 permutations were carried out), using the sums of squares of the dot product images, which measures the amount of covariance accounted for by the contrast (McIntosh & Lobaugh, 2004). The reliability of each voxel’s salience was determined with bootstrap estimation of standard errors, which was carried out 1000 times. Clusters of 5 or more voxels across the whole brain in which BSRs were greater than ±3 were considered significant. The threshold of ±3 corresponds to *p* = 0.0027, and is commonly used in PLS studies (Addis, Knapp, Roberts, & Schacter, 2012; Sheldon & Levine, 2013; Spreng & Grady, 2010). No correction for multiple comparisons is necessary, since PLS performs all calculations in a single computational step, preventing inflation of the family-wise error rate. We conducted three independent PLS analyses, one for encoding, one for immediate retrieval, and one for 7d retrieval, each including typical, neutral, and atypical clips.

**PLS results – Encoding**

When the encoding trials of typical, neutral, and atypical clips are all included in a PLS analysis, the first, and only, significant LV (*p* = 0.007) explains 64.6% of the variance. This LV shows a pattern of covariance for typical clips that is orthogonal to the pattern observed for atypical clips, with neutral clips showing neither pattern, see Supplementary Figure 1. The pattern for typical clips includes a single significant cluster in the mPFC. Atypical clips are associated with a more distributed pattern of covarying regions, notably including a right MTL cluster that extends through the parahippocampal cortex (PHC) and fusiform area. The bilateral inferior parietal lobules, right temporoparietal junction, occipital areas, and bilateral inferior frontal gyri are also seen for atypical clips; see Supplementary Table 1 for a full list of significant clusters.
Supplementary Figure 1: Patterns of covariance for typical and atypical clips at encoding (LV1). Warm colours indicate areas that covaried for typical clips; cool colours indicate areas that covaried for atypical clips. Colour-intensity represents the robustness of each voxel’s contribution to this pattern.

Supplementary Table 1: Brain regions showing significant covariation associated with encoding of typical (positive BSR) and atypical (negative BSR) clips. Coordinates represent the peak of each cluster.

<table>
<thead>
<tr>
<th>Brain Region</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>BSR</th>
<th>Cluster size (voxels)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Typical Clips</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L mPFC</td>
<td>-12</td>
<td>32</td>
<td>-8</td>
<td>3.47</td>
<td>13</td>
</tr>
<tr>
<td><strong>Atypical Clips</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R parahippocampus/fusiform</td>
<td>32</td>
<td>-33</td>
<td>-14</td>
<td>-5.51</td>
<td>37</td>
</tr>
<tr>
<td>R inferior parietal lobe</td>
<td>20</td>
<td>-48</td>
<td>52</td>
<td>-6.05</td>
<td>125</td>
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<tr>
<td>L inferior parietal lobe</td>
<td>-36</td>
<td>-40</td>
<td>44</td>
<td>-5.84</td>
<td>166</td>
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<tr>
<td>R posterior temporal gyrus</td>
<td>44</td>
<td>-60</td>
<td>8</td>
<td>-5.27</td>
<td>46</td>
</tr>
<tr>
<td>L mid temporal gyrus</td>
<td>-48</td>
<td>-56</td>
<td>20</td>
<td>-4.32</td>
<td>28</td>
</tr>
<tr>
<td>R supramarginal gyrus</td>
<td>60</td>
<td>-16</td>
<td>28</td>
<td>-5.71</td>
<td>34</td>
</tr>
<tr>
<td>R inferior frontal gyrus</td>
<td>52</td>
<td>36</td>
<td>12</td>
<td>-4.51</td>
<td>11</td>
</tr>
<tr>
<td>L inferior frontal gyrus</td>
<td>-48</td>
<td>36</td>
<td>8</td>
<td>-4.48</td>
<td>12</td>
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<tr>
<td>L precentral gyrus</td>
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<td>4</td>
<td>48</td>
<td>-4.44</td>
<td>19</td>
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<tr>
<td>L cerebellum (area 6)</td>
<td>-28</td>
<td>-56</td>
<td>-16</td>
<td>-7.49</td>
<td>889</td>
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<tr>
<td>L cerebellum (area 7b)</td>
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<td>-72</td>
<td>-48</td>
<td>-4.92</td>
<td>12</td>
</tr>
</tbody>
</table>

**PLS results – Retrieval**

When typical, neutral, and atypical clips are all included in a PLS analysis for immediate retrieval no significant LVs emerge (LV1 p = 0.51). This is consistent with the null results based on typicality found at immediate retrieval in FSL analyses.
When typical, neutral, and atypical clips are included in a PLS analysis for delayed retrieval the first LV is significant (p = 0.01), explains 65.3% of variance, and includes a pattern of covariance that is common across typical and atypical clips. This pattern includes the right mPFC and the posterior tip of the right HPC, see Supplementary Figure 2. Other areas that significantly covaried include the right mid frontal gyrus, right temporal pole, and two left cerebellar areas. See Supplementary Table 2 for a full list of significant clusters. No clusters reached significance for neutral clips.

Supplementary Figure 2: Common pattern of covariance for typical and atypical clips at 7d retrieval (LV1). Warm colours indicate areas that covaried for typical and atypical clips. Colour-intensity represents the robustness of each voxel’s contribution to this pattern.

Supplementary Table 2: Brain regions showing significant covariation associated with 7d retrieval of typical and atypical clips (negative BSR). No clusters reached significance for neutral clips (positive BSR).

<table>
<thead>
<tr>
<th>Brain Region</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>BSR</th>
<th>Cluster size (voxels)</th>
</tr>
</thead>
<tbody>
<tr>
<td>L mPFC</td>
<td>-16</td>
<td>44</td>
<td>-8</td>
<td>-3.76</td>
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<td>L HPC</td>
<td>-20</td>
<td>-32</td>
<td>8</td>
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<td>R mid frontal gyrus</td>
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<td>40</td>
<td>24</td>
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<td>53</td>
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<tr>
<td>R mid frontal gyrus</td>
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<td>24</td>
<td>40</td>
<td>-5.09</td>
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<tr>
<td>L anterior cingulate cortex</td>
<td>-4</td>
<td>40</td>
<td>12</td>
<td>-4.96</td>
<td>21</td>
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<tr>
<td>L superior frontal gyrus</td>
<td>-4</td>
<td>56</td>
<td>12</td>
<td>-3.72</td>
<td>11</td>
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<tr>
<td>R insular cortex</td>
<td>48</td>
<td>8</td>
<td>-4</td>
<td>-4.38</td>
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<tr>
<td>R supramarginal cortex</td>
<td>52</td>
<td>-40</td>
<td>40</td>
<td>-4.35</td>
<td>33</td>
</tr>
<tr>
<td>R superior temporal pole</td>
<td>48</td>
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<td>-12</td>
<td>-4.73</td>
<td>27</td>
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<tr>
<td>R mid cingulum</td>
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<td>-4.27</td>
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<tr>
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<tr>
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<td>-68</td>
<td>-24</td>
<td>-4.32</td>
<td>18</td>
</tr>
<tr>
<td>L cerebellum (area 8)</td>
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<td>-68</td>
<td>-52</td>
<td>-3.84</td>
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</table>