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Neurobiology of specific and general prior knowledge

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Declaration

The current thesis conforms to a 'paper style format' in which Chapters 2, 3, 5 and 6 are written in format appropriate for publication in peer-reviewed journals in the field. Chapter 4 closely follows information presented in Chapter 3 and to reduce repetition is written in a style highlighting the rationale and effects specific to the experimental task. The thesis starts with a general introduction describing briefly some of the previous work done on the topic and providing rationale for the experiments reported in the following chapters. The final chapter provides some discussion on the research undertaken and the field.

Chapter 3 has been published in Cognitive neuropsychology as:

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Author contributions are: Petar Raykov was responsible for the initial study design, for the collection and analysis of the data and writing and editing of the manuscript. James Keidel and Jane Oakhill were involved in providing comments on the study design. Chris Bird has provided feedback on the manuscript.

Chapter 2 has been posted on http://biorxiv.org/ as

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Author contributions are: Petar Raykov was responsible for study design, for the collection and analysis of data and for writing and editing the manuscript. James Keidel provided feedback on the design and ran the FIR analyses used in supplementary materials. Jane Oakhill provided feedback on the design. Chris Bird provided feedback on the manuscript.

I hereby declare that this thesis has not been and will not be submitted in whole or in part to another University for the award of any other degree.

Signature: ………………………………………….

Dedicated to my mother and my late dad

Acknowledgements

Summary

To understand the world around us we largely rely on our prior knowledge, which can help us structure newly incoming information. My research implemented naturalistic fMRI studies to investigate how previously acquired information affects the encoding and retrieval of new, but related, events. It is important to note that our stored knowledge can be either more general (schematic) knowledge – such as what typically happens at restaurants – or can be referring to a specific event – such as when we start listening to a lecture to which we have missed the beginning. In my first experiment I focused on examining effects of more specific prior knowledge. I presented participants with the first and second halves of clips. The speech in some of the first half videos was made unintelligible. The second half clips were identical for everyone. This design allowed me to investigate how we integrate prior (topic specific) information with newly incoming information. I observed better memory for the clips for which prior information was provided. Interestingly I also observed higher brain activity synchronization across participants sharing the same prior knowledge in a subset of brain regions. This result suggested that these brain regions play a role in the integration of new and prior information. In a separate experiment I examined the effects of more generic prior knowledge. I familiarised participants over the course of a week with one of two shows. Inside the scanner participants performed a picture and a video clip task. In the picture task participants watched pictures of characters that were either from the trained or the untrained show. I found higher activations in ventromedial prefrontal cortex, hippocampus and retrosplenial cortex when participants were viewing pictures from the trained show versus the untrained show. In the video task I asked participants to watch and recall previously unseen clips from both the trained and untrained shows. I observed higher pattern similarity between trained clips when compared to the untrained clips, in frontal regions suggesting that they are involved in maintaining schema knowledge during encoding of new information. Apart from schema knowledge effects, I ran a project where I examined which brain regions might be particularly important for representing knowledge about social categories. I

have also examined event cognition in individuals with mild cognitive impairment.

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Chapter 1: General Introduction

Where am I? Who are all these people around me and what do they want? What time is it? What will I do now? What did I do yesterday? These are all questions one can often answer relatively easy, however by no means are they easy questions. One must perceive, maintain and integrate information from multiple modalities and time-scales in order to make sense of his or her situation. Our prior knowledge can play an important role on how we comprehend and remember our surroundings. For instance, if we go to a library, we expect that people would be studying rather than dancing. In order to structure, comprehend, remember and predict what would happen in the near future, we often rely on our prior knowledge. Knowledge could be general (schematic), such as what typically happens at restaurants or how people typically act, or refer to a specific event, such as when we start listening to a lecture to which we have missed the beginning. In the current thesis I investigated the effects of different types of prior knowledge on event cognition, by using naturalistic stimuli presented in a functional magnetic resonance scanner (fMRI). In this introduction I first provide an overview of the some of the core psychological concepts and theories that lie at the heart of this thesis. I will then introduce the specific research questions that were addressed in the experimental chapters.

Before continuing it is important to introduce the concept of an event model, and I do this with the aid of an example. In a typical day, one might have breakfast, commute to work, interact with colleagues, have dinner with friends, brush their teeth and go to sleep. Although these might be mundane activities, each of these events consists of multiple features (location, people involved, semantic themes etc.) and represents information unfolding in time. Indeed, in our waking lives we are continuously exposed to rapidly changing sensory input, yet we perceive the world around us as a coherent sequence of meaningful events. It is thought that we achieve this by building mental representations of the slowly changing features (e.g. location, people, goals)

relevant to specific situations. These mental representations are often termed event (or situation) models and are thought to represent the spatio-temporal and causal relationships between entities present in a particular context (Johnson-Laird, 1983; Ranganath & Ritchey, 2012; Zwaan & Radvansky, 1998). More colloquially, they represent the what, where, who, when and why of a situation. In order to comprehend incoming information and build coherent event models we often rely on our previous experience with similar situations.

Seminal behavioural studies in psychology have demonstrated that our prior experiences and schematic representations of the world can have large influence on our comprehension and memory of particular events (Anderson, 1984; Bartlett, 1932; Bransford & Johnson, 1972; Carmichael et al., 1932; Dooling & Lachman, 1971; Posner & Keele, 1968). One of the most famous examples is a study by Bransford and Johnson (1972). They presented participants with difficult to comprehend narratives. Each sentence was grammatically correct and comprehensible on its own. However, participants could not link the sentences and understand the subject of the narrative, unless they were provided with key information beforehand. Presenting participants with a picture representing the situation being described by the paragraph greatly improved their comprehension and later recall of the passages. Importantly, the comprehension and memory benefits were present only if the participants were provided with knowledge about the context before reading the paragraphs (see also Bransford & Johnson, 1979; Dooling & Lachman, 1971). The provision of prior knowledge allowed participants to link and organise the new information coming from the individual sentences and to build an event model of the situation being described.

The concept of a "schema" is associated with event models (Alba & Hasher, 1983; Ghosh & Gilboa, 2014; Zacks et al., 2007). However, it can be differentiated on the premise that schemas are thought to be mental scripts of stereotypical situations, whereas event, or situational, models refer to specific events (Zwaan & Radvansky, 1998). Individuals might have a schema about the typical actions that take place in restaurants. For example, we might expect to be handed a menu on arrival rather than a bazooka. On the other hand, an event model would refer to a particular visit to a restaurant (e.g. Tuesday 16th

May dinner with Ben). The implication of these definitions is that schema representations can lay the ground work for the construction of event models (see also Van Dijk & Kintsch, 1983; Zacks et al., 2007; Zwaan & Radvansky, 1998).

It still unclear how different types of prior knowledge affect event cognition. Furthermore, little is known on which brain systems are involved in the building of event models and the integration of prior knowledge with incoming information. Previous studies have often relied on highly controlled but simple, often unimodal, stimuli (such as words or pictures) to examine cognition (Liu et al., 2016; Polyn et al., 2005; Richter et al., 2016; Staresina et al., 2013). They have been incredibly informative and indeed have also provided some initial evidence on which brain systems might be supporting processing of complex events (Ranganath & Ritchey, 2012). However, recent developments in fMRI have allowed experimenters to implement more complex stimuli to examine cognition. Naturalistic stimuli, such as videos, narratives and audio stories are particularly well suited for examining event cognition, since they represent complex situations evolving over time, which are commonly interpreted with reference to prior knowledge (Bartlett, 1932; Bower et al., 1979; Bransford & Johnson 1972; Brewer & Treyens 1981). The presence of inherent temporal information in such stimuli can also elucidate when during an event (onset, throughout, offset) cognitive processes occur (Ben-Yakov et al., 2012; Ben-Yakov et al., 2014). Naturalistic stimuli can provide a more ecologically valid way to examine everyday processing. Furthermore, apart from their clear importance in examining event cognition, they have also been shown to elicit more reliable neural responses compared to simpler stimuli and may be more engaging for the participants (Hasson et al., 2010). For instance, face-processing networks have been shown to be more consistently activated by natural dynamic faces rather than static or rigid pictures (for review Adolphs et al., 2016; Fox et al., 2009; Schultz et al., 2012).

Box 1. Brain Regions and Event Cognition
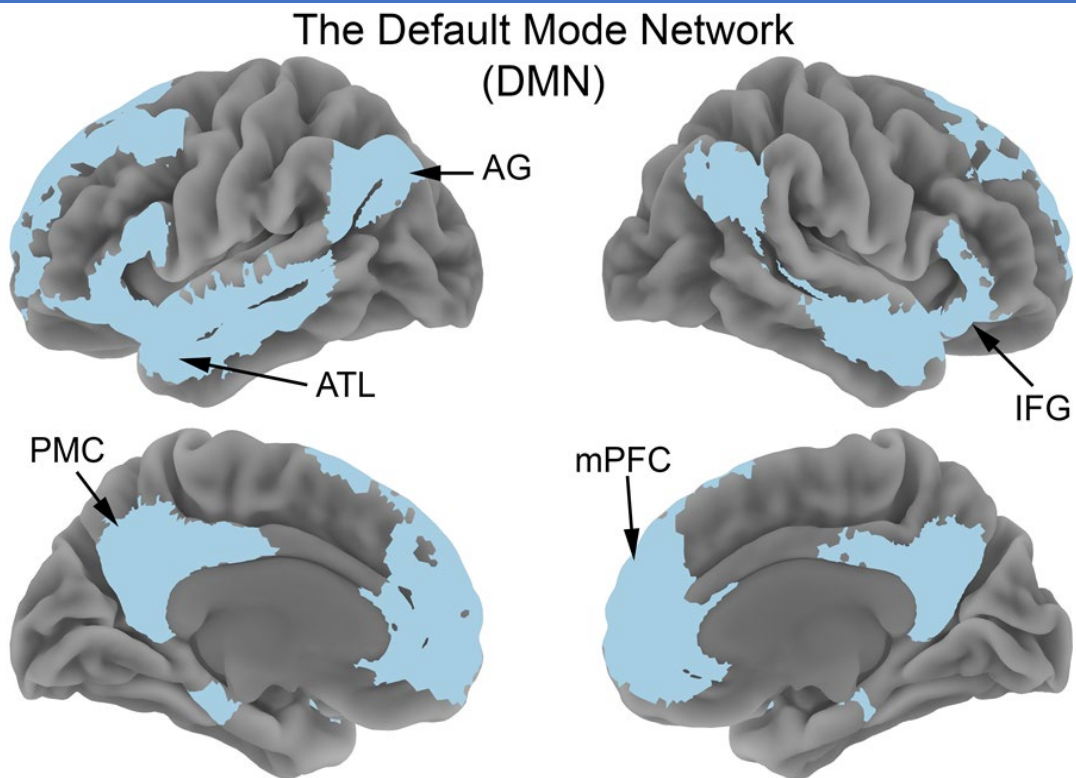
Figure 1-1 *Default Mode Network*. The map shows a network of brain regions, which often show high resting-state functional connectivity. Figure was created using functional network atlas created by Yeo et al. (2011). PMC – Posterior medial cortex; mPFC – medial prefrontal cortex; AG – angular gyrus; IFG – inferior frontal gyrus; ATL – anterior temporal lobe.

A network of regions often exhibits increased connectivity during resting-state tasks and has been termed default mode network (DMN) (Buckner et al., 2008; Raichle et al., 2001; Yeo et al., 2011). The brain regions that are often associated with this network include medial prefrontal cortex (mPFC), posterior medial cortex (PMC), retrosplenial cortex, medial temporal lobes and angular gyrus (AG). We note this set of regions have been associated with various cognitive functions such as episodic and semantic memory, the construction of imaginary scenarios, the integration of information over long time-scales, and discourse comprehension (Binder et al., 2009; Hasson et al., 2015; Mar, 2011; Spreng et al., 2009; Svoboda et al., 2006). Indeed, there is overlap between the DMN and other brain networks such as the core retrieval network (King et al., 2015; Rugg & Vilberg, 2013), long-timescale processing network (Hasson et al., 2015), semantic network (Binder et al., 2009) and PMAT network (Ranganath & Ritchey, 2012), but see Bellana et al. (2017). It has been proposed that these brain areas are particularly important for event models (Ranganath & Ritchey, 2012).

Recent naturalistic fMRI designs have benefited from newly developed methods of analysis, which have been particularly helpful for the investigation of event cognition. Hasson and colleagues (2004) found that the BOLD time-courses in sensory and default mode network regions (DMN; see Box 1) were similar across participants watching the same movie. They used inter-subject correlation (ISC) analysis to examine the shared BOLD signal across participants. ISCs have proven very useful for naturalistic fMRI studies. Traditional fMRI analysis methods (e.g. general linear model - GLM) rely on pre-defined model of the expected BOLD activity and often involve averaging over events or time. However, in naturalistic settings the prior context of a stimuli can affect its interpretation. For instance, the BOLD response to the word dog might differ depending on the words preceding it ('The kid petted the dog' vs 'The woman ran from the dog'). As such averaging over all instances of the stimuli might lead to loss of information (Ben-Yakov et al., 2012). Therefore, GLM analysis may not always be well suited for naturalistic stimuli that involve rapidly changing information evolving over time. ISC does not rely on a pre-defined model of the timing of the stimuli or expected neural response. ISC utilises the data of other participants experiencing the same stimuli and is sensitive to the stimulus-locked shared signal across participants (Nastase et al., 2019; Pajula et al., 2012). If participants are watching or listening to the same story, they will show high similarity (high ISC) in brain areas that are showing similar processing. However, areas that are processing the stimuli idiosyncratically across participants will show lower ISCs.

ISCs have been a very useful tool in the investigation of event cognition. For instance, Regev and colleagues (2013) dissociated modality-specific responses in sensory cortices from responses to the underlying meaning in DMN regions. In their study participants either listened or read a story. Using ISCs, they showed that early sensory cortices (visual or auditory) showed modality specific responses to the story. On the other hand, higher order regions overlapping with the DMN: medial prefrontal cortex (mPFC), precuneus, angular gyrus (AG), inferior frontal gyrus (IFG) and superior temporal sulcus (STS) showed reliable responses across participants regardless of the presentation modality. Similar effects were also shown across participants

listening to the same story presented in different languages (Honey et al., 2012b). These studies have been helpful to elucidate that frontal and parietal areas involved in the processing of the content of narratives regardless of the method of presentation. Indeed, they imply that these areas are important for the representations of event (situation) models. More recent studies have also found that participants experiencing the same events showed shared patterns of activity (Bird et al., 2015; Chen et al., 2017; Oedekoven et al., 2017; St-Laurent et al., 2015). Zadbood et al. (2017), for instance, showed shared patterns of BOLD activity across participants watching, remembering or listening to descriptions of the same events.

Further evidence that DMN regions are important for event models comes from research showing these regions integrate information over long timescales (Hasson et al., 2015; Hasson et al., 2008; Honey et al., 2012). For instance, Lerner et al., (2011) presented participants with auditory narratives that were scrambled either at the word, sentence or paragraph levels. They observed that early auditory cortices showed reliable responses even to stories scrambled at word level (participants did not hear coherent sentences in this condition). On the other hand, parietal and frontal regions showed reliable responses only when the story contained coherent paragraphs. These results suggest that frontal and parietal regions are integrating information over longer periods of time (seconds to minutes), which is necessary for event cognition. This cortical hierarchy of differing temporal receptive windows has been shown also with electrocorticography data and data-driven fMRI analysis techniques (Baldassano et al., 2017; Honey et al., 2012; see also Huntenburg et al., 2018).

Previous studies strongly support the involvement of DMN regions in event cognition. However, effects are often wide-spread across large regions of the cortex, and it is still not clear how different aspects of the event models are represented and how we rely on our prior knowledge to comprehend newly incoming information. The complexity of event models makes it difficult to understand what aspects are represented. Two events may differ on the broad topics (schemas) they are referring to (e.g. wedding vs funeral) or only differ on subtle details (e.g. lunch on Monday versus Tuesday). The previously observed effects might partly be due to differences in broad schematic representations

between events (e.g. 'meeting in a restaurant' or 'a car chase'). Such schematic knowledge provides the building blocks for comprehending and remembering events but might not be very helpful in differentiating between similar events (e.g. going to a restaurant on different dates). More specific information, such as the goal of the actors or topic of conversation is required to distinguish between similar events. However, only recently have researchers started to examine the neurobiological effects of prior knowledge on event processing.

A recent fMRI study used a design similar to Bransford and Johnson's (1972) paradigm (see also Dooling & Lachman, 1971). Ames and colleagues (2015) presented participants with ambiguous or confusing vignettes. Prior to reading some of the vignettes participants were presented with pictures that provided context and allowed participants to fully comprehend the vignettes. This manipulation allowed them to examine the effects of provision of prior knowledge on brain activity. They found that when participants shared the same prior knowledge they showed increased synchronization in the ventromedial prefrontal cortex (vmPFC) and posterior cingulate cortex (PCC) (Maguire et al., 1999; see also van Kesteren et al., 2010). It should be noted that in such experiments the manipulation often results in participants either being able to construct a very detailed mental representation of what is happening in the current situation or not being able to understand at all what the story is about. As such, the effects of such manipulations could be due to fundamental differences between the conditions, such as comprehending versus not comprehending. These manipulations often prevent participants from constructing an event model at all or even prevent them from activating the situation appropriate schematic knowledge.

However, our comprehension of everyday events is not necessarily binary. We could understand an event only partially, which possibly would be associated with a less detailed event representation. For instance, if a person walks into a conversation midway through, they might comprehend vaguely what is happening but still have less detailed understanding on what the people were talking about. Apart from affecting their interpretation, this can also influence their memory for the event. On the other hand, a person that listened

to the first half could integrate the incoming information with the previously established topic of conversation, which could result in better understanding of the situation. Indeed, having heard the first half of the conversation could also improve later memory for the second half, by making the relevant information more accessible.

In the Chapter 2 of this thesis I examined how the prior knowledge of the topic of conversation affected comprehension and memory for complex events. I presented participants with clips that were separated into two halves. The language in some of the first half clips was made incomprehensible which prevented people from knowing the specific topic of conversation. However, the first half clips, even without comprehensible speech, provided some general/schematic context about the situation (e.g. number of people involved, location etc.). This manipulation allowed me to examine how prior narrative knowledge specific to a situation will affect encoding of newly incoming information. Specifically, I examined whether having more detailed understanding of the narrative would result in widespread differences in event representations as measured with fMRI. I also used behavioural measure to examine whether hearing the first half of the conversation would lead to better memory for the second half. The chapter also provides a more detailed overview on the more recent studies that have utilised naturalistic fMRI designs to examine event cognition and effects of prior knowledge (e.g. Chen et al., 2016; Keidel et al., 2017; Lahnakoski et al., 2012; Nguyen et al., 2019; Saalasti et al., 2019; Yeshurun et al., 2017).

Apart from prior knowledge specific to a certain situation, our prior knowledge could also be more general. For instance, our knowledge of how a friend typically acts can help us understand him. However, the effect of this type of schematic knowledge has rarely been examined using naturalistic stimuli (but see Baldassano et al., 2018). There has been quite a few studies that have examined schema effects using simple stimuli (see Gilboa & Marlatte, 2017 for review). Some of them have relied on participants' pre-existing knowledge and have presented participants with familiar vs unfamiliar stimuli to examine schema effects (e.g. Bein et al., 2014; di Oleggio Castello et al., 2017; Liu et al., 2016). These types of studies often have difficulty controlling for

differences in the extend of prior knowledge across participants. Another type of studies have trained participants on arbitrary rule-based associations (e.g. Schlichting & Preston, 2015; Sommer, 2016; Wagner et al., 2015). These paradigms allow for strong experimental control, but often involve learning simple associations over short periods of time, which does not resemble the rich schematic representations that we often acquire over multiple episodes of exposure.

In Chapter 3 and 4 I utilised a new paradigm where I trained participants outside of the scanner on one of two TV shows over the course of a week. This allowed me to match the amount of prior knowledge across participants, whilst they were learning complex schematic representations (e.g. how the main characters typically act). In Chapter 3 I examined how familiarity with the characters acquired over multiple episodes affected processing of still pictures of trained and untrained characters. The data was used to better understand current neurobiological theories of schematic processing. To briefly summarise, various neurobiological theories have suggested that vmPFC and hippocampus are particularly important for schema processing (Gilboa & Marlatte, 2017). However, whereas some theories suggest that they have complementary roles (Preston & Eichenbaum, 2013; Robin & Moscovitch, 2017), others have suggested competing roles for these regions (van Kesteren et al., 2012). For instance, van Kesteren et al., (2012) suggested that in the presence of information congruent with prior knowledge vmPFC would exhibit higher activation, which in turn would be associated with decreased activation in medial temporal lobes (including hippocampus). According to the SLIMM ("Schema-Linked Interactions between Medial prefrontal and Medial temporal lobes" - SLIMM van Kesteren et al., 2012) model, the hippocampus would show higher activity for information incongruent with prior knowledge, since it is involved in incidental learning of such information (see also Greve et al., 2019). The design in Chapter 3 allowed me to directly examine this theory and investigate vmPFC and hippocampal activity when participants were processing new information that was related to their training or not.

In Chapter 4 I examined how schematic knowledge about the TV show affected encoding and retrieval of naturalistic stimuli. It is important to

understand that when processing complex events, we could have schematic knowledge about multiple elements of the situation. For instance, at a restaurant meeting we could have schematic knowledge of what to expect from a restaurant, but also, we can have schematic knowledge about the friend we are out with (e.g. how do they typically act). In this study, I examined how person specific schema effects affected event cognition. In particular, I focused on how schematic knowledge of people impacted on the encoding and retrieval of naturalistic events.

Apart from schematic knowledge specific to an individual we also have stereotypical knowledge about people from certain social groups. In Chapter 5 I present a pilot study where I examined how knowledge about social categories (e.g. occupations) is represented. This was partly inspired by previous behavioural literature showing that stereotypical or person schema knowledge can affect participants' memory (see Cohen, 1981; Klatzky et al., 1982). I designed this study to investigate whether we will observe effects suggesting that social categories are represented by the same brain regions that support general schematic knowledge. I implemented word and picture stimuli associated with certain professions and applied cross-modal classification analysis (Kaplan et al., 2015) in order to search for amodal semantic representations of social categories.

In chapter 6 I applied the analytic techniques I employed in the study from Chapters 2, to investigate event processing in healthy older adults and patients diagnosed with mild cognitive impairment (MCI). Specifically, I used ISCs to examine whether MCI patients would process the clips differently from older adults with subjective memory impairments and healthy controls. MCI patients often experience memory problems and behavioural evidence suggests they have problems processing naturalistic stimuli (Johnson et al., 2003; Zacks et al., 2006). Such patients are at increased risk of developing Alzheimer's disease (AD) (Flicker et al., 1991; Petersen et al., 2000; Royall et al., 2007). Apart from episodic memory problems AD, might be associated with difficulty performing everyday tasks, and orienting oneself in space. Indeed, at later stages of the disorder patients may even struggle to provide answers to some of the questions posed in the beginning of this introduction.

In this thesis I aimed to examine how different types of prior knowledge affect event processing. I show that both specific and more generic prior knowledge was associated with some memory benefits. I found evidence that medial prefrontal regions may be particularly important for processing schematic knowledge. Furthermore, I demonstrate that angular gyrus and inferior frontal gyrus might be particularly important for supporting situation specific prior knowledge that can affect the interpretation of the event.

Chapter 2: Shared contextual knowledge strengthens inter-subject synchrony and pattern similarity in the semantic network

2.1 Abstract

Events are understood with reference to what has happened before. However, the effects of previously acquired knowledge on the processes supporting event cognition are poorly understood. Here, we selectively manipulated knowledge about the narrative content of events. Narrative knowledge boosted memory for the events and had two effects on fMRI markers of neural processing: (1) it strengthened temporal inter-subject correlations in left angular (AG) and inferior frontal gyri (IFG), and (2) it increased spatial inter-subject pattern similarity in the bilateral anterior temporal lobes (ATL). We argue that shared narrative knowledge constrains participants' interpretation of the videos, resulting in greater alignment of neural processing of the events. We propose a division of labour between semantic control brain regions (IFG and AG), which coordinate the moment-by-moment activation of relevant semantic concepts, and the ATL, which represents the overarching narrative gist of an event.

2.2 Introduction

Understanding events as they unfold requires our attention over multiple timescales (Hasson et al., 2015). Following a conversation or a complex sequence of actions involves attention to moment-by-moment changes in incoming information. It is also thought that we extract and represent more slowly changing features of the event such as the location and the people present as overarching "event models" (Zacks et al., 2007). These event models provide coherence to our experiences, even in the face of rapidly changing sensory input (Zacks et al., 2007). Our prior knowledge affects both our ability to comprehend conversations and to construct event models. However, the effects of prior knowledge on the brain systems that underpin event processing are poorly understood.

Recently, MRI scanning combined with the use of naturalistic materials, has begun to shed light on the brain regions that support processing of lifelike events (Ben-Yakov et al., 2013; Bird et al., 2015; Chen et al., 2017; Zacks et al., 2001). Various studies have described both transitory responses, corresponding to discrete events within a continuous video (Zacks et al., 2001), as well as patterns of activity that persist over time and which may correspond to representations of a currently active event model (Baldassano et al., 2017; Bird et al., 2015; Oedekoven et al., 2017).

Interestingly, effects are not only seen within individual subjects, but some aspects of event processing are shared across brains. Hasson and colleagues (2004) found significant correlations in the timecourse of activity elicited by a movie across subjects (inter-subject correlations: ISC). In more recent work, Chen et al. (2017) demonstrated the existence of shared multivoxel representations of events. Participants watched and recalled a full movie in the scanner and the authors analysed multivoxel patterns of activity averaged across sub-events within the movie. The authors found that activity patterns were correlated across participants, both when they watched, or recalled, specific events from the movie (inter-subject pattern similarity: ISPS). Similar effects have been seen when people construct an event in their mind's eye while listening to it being described (Zadbood et al., 2017). The authors

suggested that the "units" of information being shared across participants were event models.

Effects in these studies are typically seen across large regions of sensory cortex as well as throughout the brain's so-called default mode network (DMN; Raichle et al., 2001). However, a major challenge is to dissect what are often widespread effects into the processes and representations supported by different brain regions. For example, the complexity of event models makes it difficult to confidently ascribe pattern similarity effects to any particular aspect of the model. Thus, observed effects could reflect very broad schematic representations of the content of the scenes (e.g. 'a conversation in a café', or 'a chase down the street'). While such schematic representations provide an essential scaffold for comprehending and remembering short events, by themselves they provide no means of differentiating similar events (e.g. talking to different people on different days while having a coffee in the same café). Instead, much more specific information is required, such as the specific actions being carried out by the actors or the topic of the conversation.

A number of classic studies have investigated narrative comprehension of prose passages by manipulating prior knowledge (e.g. Bransford & Johnson, 1972; Dooling & Lachman, 1971; Maguire et al., 1999). In such experiments, ambiguous or confusing narratives can be understood with the provision of specific background contextual information before the narrative is read. Ames and colleagues (2015) used such a manipulation to investigate the effect of prior contextual knowledge on ISCs. The authors found that participants sharing the same background knowledge showed increased synchronization in BOLD response in the ventromedial prefrontal cortex (vmPFC) and posterior cingulate cortex (PCC). However, the key contrast in such paradigms involves comparing meaningful passages with passages that are very difficult to understand and it is therefore unclear whether the effects reflect this more fundamental difference in the conditions (coherent versus incoherent narratives).

Several recent studies have tried to address this issue by presenting participants with identical comprehensible narratives and manipulating the prior

knowledge participants receive beforehand (Chen et al., 2016; Keidel et al., 2017; Lahnakoski et al., 2012; Nguyen et al., 2019; Saalasti et al., 2019; Yeshurun et al., 2017).

Yeshurun et al., (2017) manipulated the interpretation of ambiguous narrative in two groups of participants by presenting them with different prior context. Both groups of participants listened to the same story about a phone conversation between two friends, Arthur and Lee. However prior the story, one group was led to believe that the Arthur's wife was cheating on him with Lee, whereas the other group were provided with a different context in which Arthur was overreacting and being paranoid.   Yeshurun et al. (2017) found that participants that held different interpretations showed different brain activations in extended network largely overlapping with the DMN, which further supported that DMN areas are representing content about the event models. Yeshurun's et al. (2017) manipulation led to very different interpretations of both the semantic and emotional content across groups. Furthermore, it did not address how we integrate incoming information with relevant prior knowledge to aid comprehension, since both groups were provided with equally likely contexts.

A recent study more directly examined how prior knowledge is integrated with on-going narrative processing to aid comprehension (Keidel et al., 2017). Participants saw first and second half clips taken from TV situational comedies (sitcoms). The second half clips could either be a direct continuation of the first half clips, or be clips taken from the same show involving the same characters and location, but a different episode of the show (and consequently depicting a different narrative storyline). The first half clips always provided some general semantic information about the relationship between the characters but did not always provide relevant topic of conversation for the second half clips. When examining the second half clips the provision of narrative context resulted in increased activation in regions of the SN, including the inferior frontal gyrus (IFG), middle temporal gyrus (MTG) and angular gyrus (AG). It was argued that this reflected the reactivation of linked semantic concepts that were created when watching the first half videos. However, because the non-continuation clips clearly showed a different event, the activation differences may have reflected other differences between the conditions, such as the appearance of

the characters and the contents of the scene. This study only examined within-subject univariate effects.

In the current study, we examine how prior narrative context affects the cognitive and neural substrates of event processing. We presented participants with video excerpts taken from sitcoms that were divided into first and second halves. In the high context condition, the first-half clips were presented with normal speech, whereas in the low context condition we spectrally rotated the speech to render it unintelligible. Under this design, all the pairs of clips were clearly taken from the same occasion and differed only in the provision of the narrative context. Importantly, all second-half clips, which were the focus of the analyses, were the same for both conditions, allowing us to detect differences in inter-subject synchronization and pattern similarity while participants viewed an identical set of stimuli. Both temporal synchronisation and spatial pattern analyses require the comparison of activity across more than one event - either two or more events within a subject, or the same event across multiple subjects. Since our manipulation is hypothesised to affect processing only during the second-half clips, these analyses can only be carried out across subjects.

The study aims to test a number of hypotheses. First, we predict that provision of comprehensible narrative contextual information will aid the comprehension and memory for the subsequent event. Second, a narrative context will constrain the interpretation of the second-half clips, resulting in greater inter-subject similarity within semantic processing regions. ISCs examine the temporally varying BOLD signal and are therefore suited to detecting moment-to-moment processing of the narrative content. These effects may therefore be particularly apparent in regions associated with semantic control processing (Noonan et al., 2013). Conversely, ISPS is based on spatial patterns of activity averaged across the video clips and is therefore more likely to detect stable aspects of the narrative (e.g. overarching themes) that contribute to the overall event model. These effects are predicted to be apparent in regions representing abstract and amodal semantic knowledge (Fairhall & Caramazza, 2013b; Rice et al., 2015).

2.3 Methods

2.3.1 Participants

Twenty-four right-handed native English speakers with normal or corrected to normal vision were included in the study. Four participants were not included in the final analysis due to artefacts in the MRI scans and 1 further participant did not complete the experiment. One participant had corrupted post-scanning behavioural data for the memory questions and was not included in the behavioural analysis. The project was approved by the Brighton and Sussex Medical School Research Governance and Ethics Committee (RGEC) and all participants gave informed consent and were paid £20.
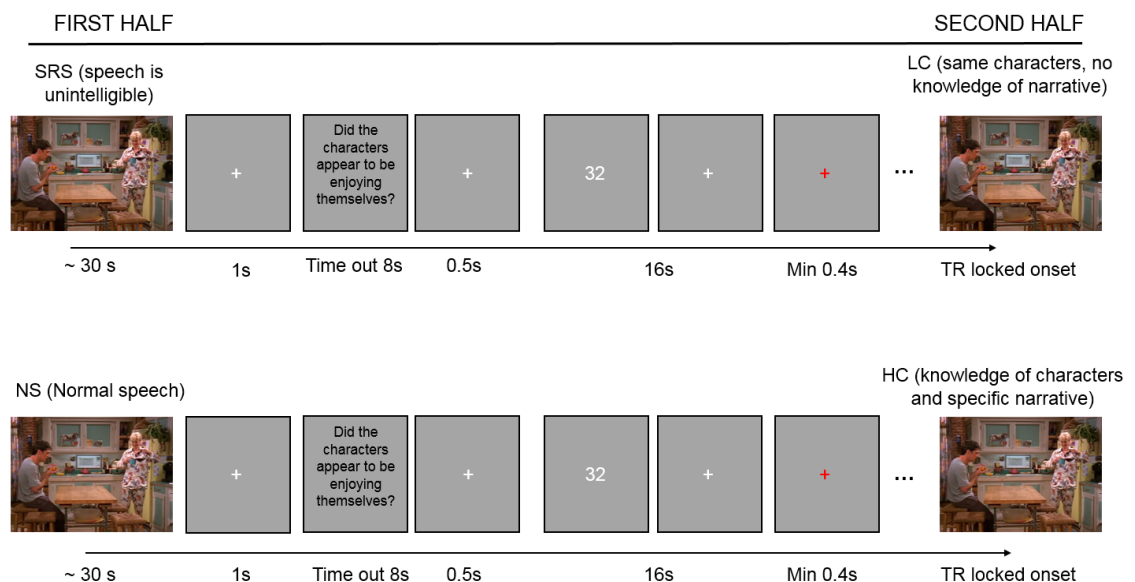
Figure 2-1 *Study design*. Schematic of study design. Participants viewed videos from unfamiliar TV sitcoms that were divided into two halves. Participants viewed a set of 5 first half videos followed by a set of 5 corresponding second half videos presented in random order. Ten of the first halves had comprehensible speech, whereas the other 10 had unintelligible speech, created by spectrally rotating the audio. Videos were counterbalanced across participants in a within-subjects design. SRS – spectrally rotated speech; NS – normal speech; HC – high context; LC – low context.

2.3.2   Stimuli

Twenty video clips from different US and UK television shows were used in the experiment. The TV shows originally aired between 1970 and 2003 and were selected to be unfamiliar to our sample. Each video was divided into first and second halves. The scene location and characters remained constant across the two halves. For our main experimental manipulation, the speech in 10 of the first half videos was made unintelligible. This was done with Praat (version 6.0.15) (Boersma, 2001) by spectrally rotating the audio of the videos with a sinusoidal function with maximum frequency of 4 KHz. This keeps the intonation and rhythm of the speech but makes it incomprehensible. The audio for all videos was scaled to have the same mean decibel intensity. The mean duration of all the excerpts was 32.47(±3.88) seconds. The first half videos (30.57±4.38) were on average shorter than the second half videos (34.37±2.02). Three different video clips, all with spectrally rotated audio, were used in the practice task with total video length of 4.36 minutes.

2.3.3   Procedure

Participants were informed they would see first- and second-half videos in four separate runs (five videos in each). They were told that the speech in some of the first-half videos would be unintelligible and were asked to watch the clips as they would watch television at home. Participants were also informed that their memory for the clips would be tested after the scanning session. They completed an 8-minute practice session outside the scanner, to familiarise themselves with the task and the sound of spectrally rotated speech.

Four lists were created to fully counterbalance the conditions and presentation order. For instance, a first half video was presented with normal comprehensible speech (NS see Figure 2-1) for half of the participants and the same video was presented with spectrally rotated speech (SRS see Figure 2-1) for the other half participants. This meant half of the participants had knowledge of the narrative theme for a second half clip (HC see Figure 2-1) and the other half did not (LC see Figure 2-1). Apart from counterbalancing the conditions which created two lists we also counterbalanced the order in which

the videos were presented both across runs and within run. This created two more lists leading to 4 counterbalancing lists.

The scanning session started with a 4-minute resting state scan (data not reported here). Following this, the task was presented in four functional runs, each approximately 10 minutes long. Each run consisted of 5 first half and 5 second half clips and every clip was followed by a question and an active baseline task. Participants initially watched the set of 5 first half clips and afterwards watched the set of corresponding second half clips in random order. This meant that a second half clip did not immediately follow its' corresponding first-half clip. In each run there were either two or three clips with rotated speech. Clip onsets were time-locked to the repetition time (TR). After each clip, a white fixation cross was presented for 1 second. Each video was followed by a question about the general relationship between the characters in the scene (e.g. Did the characters appear to be enjoying themselves?). Behavioural piloting confirmed that participants could answer the questions regardless of whether speech was rotated or not. The questions were presented for 8 seconds or until participants made a Yes/No response and were followed by a 500 milliseconds fixation. Participants made an odd/even number judgement during an active baseline task (Stark & Squire, 2001), which was presented in 16-second blocks between clips. Six randomly chosen numbers, between 1 and 98, were each presented for 2 seconds, followed by a fixation cross presented for 667 milliseconds. The active baseline task was used to prevent participants from rehearsing the information presented in the clips. After the baseline task a red fixation cross was presented for a minimum of 400 milliseconds to signal that the next video was about to begin.

Outside of the scanner, participants completed a questionnaire about their familiarity with the shows. Only 6 participants reported any familiarity with 1-3 of the 20 shows. This represented only 3.9% from the data used in the analysis. None of the participants were familiar with the particular scenes used in the experiment, which was our main interest as the first half clips provided some familiarity with the social relationships between characters in the second half clips. Afterwards, participants carried out a computer-based memory task, in which the first 4-6 seconds of the second half videos were presented as a

memory cue. Participants were then asked to rate from 1 to 10: (1) the vividness of their memory of the video, (2) how coherent they found the story in the videos, (3) how engaging they found the video. Participants were also asked an open-ended memory question specific to each second half video (e.g. What was the address on his chest written in?). All memory questions concerned only material presented in the second half of the videos.

2.3.4   MRI acquisition

Data were acquired on a 1.5 T Siemens Avanto MRI scanner. Functional T2* weighted BOLD-sensitive images were acquired with EPI sequence with the following parameters: FOV = 192mm, TR = 2.62 seconds, TE = 42 milliseconds, 90 degree flip angle, slice thickness = 3mm, 35 interleaved ascending slices with .6 mm gap, and 3.0x3.0x3.0 mm voxels. A high resolution T1-weighted image was acquired with the following parameters: FOV 256mm, TR = 2.73 seconds, TE = 3.57ms, 1.0x1.0x1.0mm voxel size.

2.3.5   Image pre-processing

All EPI images were pre-processed using SPM 12 (Wellcome Department of Imaging Neuroscience, London, UK). Field maps were used to correct for image distortions and susceptibility-by-movement effects using the Realign and Unwarp option (Andersson et al., 2001; Hutton et al., 2002). All EPI images were aligned to the first image of the first session. The anatomical image of each subject was co-registered to their mean realigned EPI image. The anatomical images were then segmented into grey and white matter maps. Anatomical and EPI images were normalized to the MNI space using DARTEL (Ashburner, 2007) and smoothed with an 8 mm FWHM kernel. Images for the inter-subject pattern similarity were pre-processed as above with the exception that a 6 mm FWHM smoothing kernel was applied to the normalised images, as previously used by Chen et al. (2017).

2.3.6   Data Analysis

Data were analysed with SPM 12, the CoSMoMVPA toolbox (Oosterhof et al., 2016) and custom scripts in MATLAB (Version 2016b, The MathWorks, Inc., Natick, MA, USA). Permutations tests for whole brain analyses were

conducted with command-line functions in FSL (Nichols & Holmes, 2002; Winkler et al., 2014). All analyses were conducted on MNI normalised images within a grey matter mask. Segmentation of the high-resolution structural images provided us with grey matter tissue probability map for each subject. These probability maps were normalised to MNI, averaged across participants. The averaged mask was smoothed with an 8mm FWHM kernel. We selected all voxels within this average probability map higher than a threshold of 0.3 (Nastase et al., 2019). To describe and visualise our data we used the Bspmview toolbox (www.bobspunt.com/bspmview), which implements the MNI coordinates from the Anatomical Automatic Labelling 2 toolbox for SPM 12. Significance was tested with a one-sample random effects t-test against zero. Unless otherwise stated, images were whole brain cluster corrected for FWE p < 0.05 at voxel height-defining threshold of p < 0.001.

2.3.7 GLM analysis

A single task regressor for each of the four conditions (SRS, NS, LC and HC: see Figure 2-1) was included in the first-level models. For all GLM first level models the questions after each video were modelled with a single regressor of no interest and the odd/even number judgment task was left unmodelled to represent the implicit baseline. A block design first level analysis was conducted to replicate previous findings. In this analysis, all video stimuli were modelled with boxcar functions whose durations matched the stimulus duration. The models also included the six motion parameters, a regressor for the mean session effects, and a high-pass filter with a cut-off of 1/128 Hz. We also ran an analysis identical to the above but modelled only the onset of the videos with a gamma function, rather than including the whole duration of the video. This was done to replicate previous findings by Keidel et al. (2017). First-level models for the inter-subject pattern analysis included the same nuisance regressors as the previous analysis. However, each video was represented with its own block regressor that covered the whole duration of the video. This allowed us to examine video specific patterns.

2.3.8   Inter-Subject Analyses

2.3.8.1   Inter-subject correlation (ISC)

The ISC allowed us to examine how dynamic processing of the second half videos was modulated by previous knowledge. ISCs were computed voxelwise over second half videos (HC and LC videos, which contained coherent speech). To examine the similarity across participants under the same condition we constructed 2 condition lists. To construct 2 condition lists from 4 counterbalancing lists we combined the lists in which videos were seen under the same condition, but in a different order. There were 9 and 10 people in the two condition lists. It has been shown that averaging over at least 4 people's time courses provides reliable ISC estimation (Hasson et al., 2004). The first 2 TRs (5.24 seconds) of each video were removed in order to remove transient onset effects that can lead to artificially high ISCs (Ames et al., 2015).

The raw time course for each video and each subject were extracted. These time-courses were used to compute the Fisher-transformed correlations across subjects for each video. For a given subject we computed the correlation between the subject's specific video time-course and the average time-course for the rest of the participants watching the same video in the same condition (e.g. the participants in the same condition list). This resulted in 20 (10 HC and 10 LC videos) time-course correlations for each subject, which represented the time-course similarity across participants watching the same videos (diagonal values in Figure 2-3 A & C).

The time-course correlations across participants watching different videos (e.g. correlating the time-course of a subject watching 'Dharma and Greg' with the average time-course of other subjects watching 'Just Shoot Me') were also computed for the general ISC analysis (see off-diagonal in Figure 2-3 A). The general ISC analysis allowed us to examine ISCs while participants watching the same videos irrespective of whether the context was familiar or not (see Figure 2-3 A). We compared the time-course correlations across participants watching the same video versus different videos. The mismatching videos (off-diagonal in Figure 2-3 A) acted as a baseline, since participants were experiencing different sensory stimulation whilst watching different videos.

It allowed us to see if we can observe synchronisation across participants watching the same videos regardless of context.

Next, we examined how narrative themes affected ISCs. We examined whether participants were more synchronised when they were watching the HC clips versus when they were watching the LC clips. Each subject had 10 ISCs for the HC clips and 10 ISCs for the LC clips (see Figure 2-3 B). These subjects' values represent his similarity with the rest of the people that watched the same clips under the same conditions. The HC vs LC contrast was performed for each subject by averaging over the 10 Fisher transformed correlations across HC videos and subtracting the average of the 10 LC coefficients. This condition difference was computed for each voxel and for each subject. Therefore 19 subject specific brain maps were used in the group analysis.

The resulting 19 subject specific brain maps however are not necessarily independent. This is due to the fact that when comparing the correlation between a subject's time-course and the mean of the "others" there is overlap in the information used to compute the mean "others" across subjects. To illustrate this if we have 1-20 subjects within a group, the ISCs for subject 1 is between subject 1 and the average time-course of subjects 2, 3-20. The ISCs for subject 2 involves the average of everyone else, which is 1, 3-20. Therefore, the data for subjects 3-20 was used to calculate the ISCs for both subjects 1 and 2, which means that their ISCs are not independent. Indeed for n subjects in a group any pair will share n-2 elements (Aly et al., 2018). Because of this, we used non-parametric permutation tests to compute the significance at the group level. The difference in Fisher transformed ISCs between conditions (same vs different videos and HC vs LC) was computed for the general and context specific ISC analyses respectively. To perform the permutations the sign of the resulting difference was flipped for a random subset of subjects before computing the group mean. This effectively is the same as shuffling the conditions for different subjects. 5000 permutations were run (per analysis) to obtain the null distribution with which to compare our observed data and obtain p-values. Cluster corrected images at FWE $p < 0.05$ at voxel height-defining threshold of $p < 0.001$ are presented in Figure 2-3 and Figure 2-4

2.3.8.2 Inter-Subject Pattern Similarity (ISPS)

This analysis was performed to examine spatial pattern similarity across participants experiencing the same events. The inter-subject pattern (ISPS) analysis was conducted on the normalised t-maps generated for each subject and each 2nd half video. For each subject, a searchlight map was generated by centring a spherical searchlight with radius of 3 voxels (mean size 110 voxels) at each voxel. For a given participant the activity patterns for a specific video were correlated with the average activity pattern across participants watching the same video in the same condition. This resulted in 20 (10 HC and 10 LC videos) correlations for each subject representing the video specific pattern similarity across subjects (see diagonal Figure 2-4 A). The across participants pattern similarity was also calculated for non-matching videos resulting in 380 correlation coefficients for each searchlight (see off-diagonal Figure 2-4 A). Contrast matrixes were used to weight the resulting Fisher-transformed spatial-pattern correlations for each searchlight. The summed correlations were assigned to the central voxel of each searchlight. Two ISPS analyses were conducted by specifying different contrast matrixes (see Figure 2-4). Therefore, the central voxel of each searchlight represented the difference between conditions (same vs different videos or HC vs LC) for the general and context specific ISPS respectively. For each of the two analyses we obtained a single condition difference brain image per subject. These brain maps were used in the group analyses.

First, we conducted a "General Show" ISPS analysis to examined the similarity across participants watching the same clip versus when they were watching non-matching clips, irrespective of their prior knowledge (see Figure 2-4).

Then we examined whether participants showed more highly correlated patterns for HC videos than for LC videos (see Figure 2-4). Due to stimulus counterbalancing, there were two groups (n = 9 and n = 10) of people who saw the same videos in the same condition. Therefore, similarly to the ISC analysis, for the ISPS we compared the similarity between a subject's patterns and the

average patterns of the other subjects in their group who viewed the same video under the same condition.

Similarly, to the ISC images the ISPS images were not necessarily independent. Therefore, we again used non-parametric permutation testing to examine the group significant results for the ISPS analyses. This was done by flipping the sign of the ISPS condition difference images for a random subset of subjects. 5000 permutations were run. Results were cluster corrected at FEW $p < 0.05$ with voxel height defining threshold of $p < 0.001$.

Both ISCs and ISPSs analyses were also calculated separately for the first half videos using identical procedures as described above. These analyses examined the synchronization across participants watching the same first half videos. We also contrasted whether participants were more synchronized when they were watching the normal speech (NS) first half videos when compared to videos with spectrally rotated audio (SRS). These analyses showed higher synchronization (both ISC and ISPS) across participants when watching the NS videos compared to the SRS videos in bilateral ATL and other regions often associated with the DMN or semantic processing (see Supplementary Figures 2-4 and 2-5).

2.4 Results

2.4.1 Behavioural results

Participants had an overall accuracy of 72.2% for the memory questions, which is high level of performance given the fact that the questions were open ended. Participants responded more accurately to the same questions when in the HC condition (80%) than in the LC condition (64.4%: $t_{17} = 3.39$, $p = 0.003$). The memory questions were specific to the 2nd half videos and did not require information from the 1st half videos. HC videos were also rated as being remembered more vividly ($t_{17} = 7.15$, $p < 0.001$), more coherent ($t_{17} = 6.88$, $p < 0.001$) and more engaging ($t_{17} = 6.23$, $p < 0.001$).
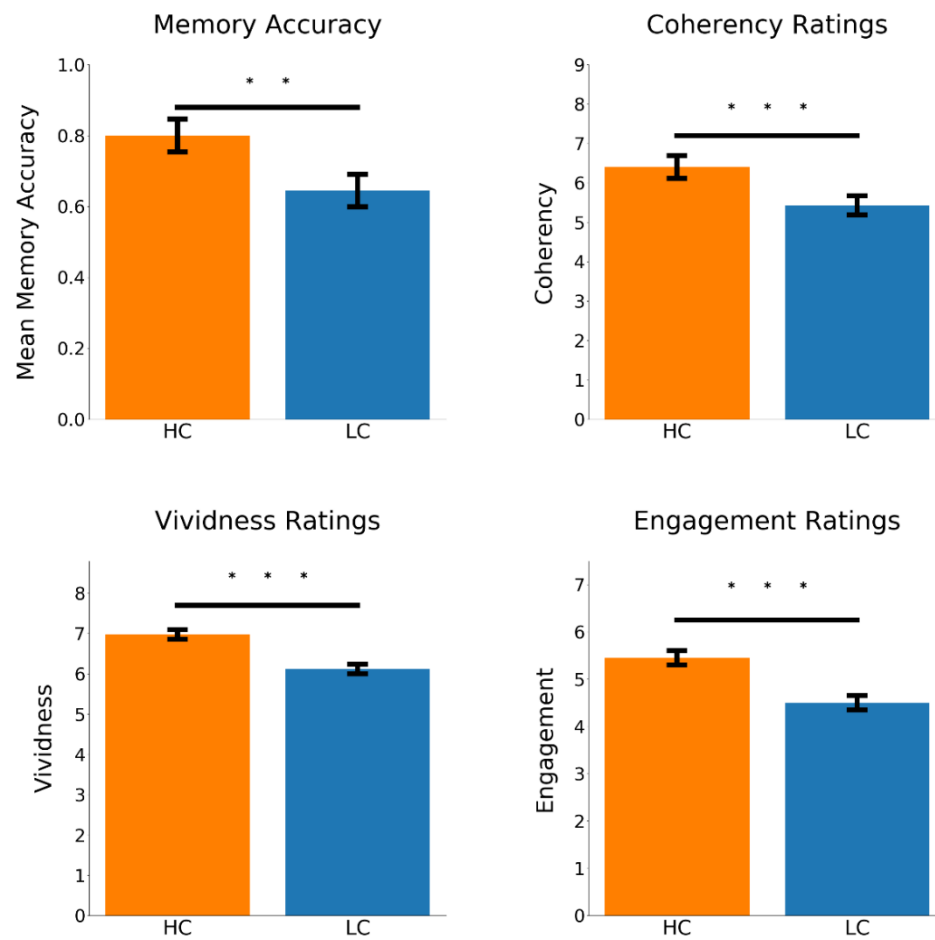
Figure 2-2 *Behavioural results.* A) Shows average memory performance for questions on HC versus LC videos. B) Shows that participants on average found HC videos more coherent. C) Higher vividness ratings were observed for HC videos. D) Participants reported HC videos as more engaging. ** p < .01; *** p < .001

2.4.2 fMRI Results

2.4.2.1 GLM

The contrast of watching videos versus the active baseline task revealed higher activation in visual, auditory, medial and anterior temporal cortices (see Supplementary Figure 2-1). This is consistent with previous studies using videos (e.g. Bartels & Zeki, 2004). Brain areas that showed higher activation for the onset of the videos versus baseline are shown in Supplementary Figure 2-3. These results replicate Keidel et al.'s (2017) findings and indicate that retrosplenial cortex (RSC) and parahippocampal cortex (PHG) extending into the ventral precuneus showed transient activation associated with the onset of the videos. The results of the time-course analysis were also consistent with this previous study in showing higher activation in the middle temporal gyrus (MTG), supramarginal gyrus (SMG) and angular gyrus (AG) for videos depicting a continuation of a previous narrative (HC clips). See Supplementary Material for further discussion.

2.4.2.2 Inter-Subject Correlation

The ISC analysis allowed us to examine synchronization of the BOLD response across participants. ISCs for watching videos irrespective of the context manipulation were found in extensive regions of the occipital and superior temporal lobes, encompassing visual and auditory processing regions. Higher synchronization was also observed in bilateral IFG, medial prefrontal cortex, AG and precuneus (see Figure 2-3).

The ISC comparison between HC and LC videos showed stronger coupling in the left AG, IFG, superior parietal lobule (SPL), superior frontal gyrus, and right precentral gyrus (see Figure 2-3).

2.4.2.3 Inter-Subject Pattern Similarity

The general ISPS allowed us to examine where spatial patterns of activity were more similar across participants watching the same videos versus watching different videos irrespective of the context manipulation. The results are shown in Fig. 4. This analysis revealed significant video-specific similarity across participants in the primary sensory areas and areas associated with

higher cognitive processes, such as the bilateral IFG, precuneus, the MTG, the inferior portion of the anterior temporal pole (ATL) and the medial prefrontal cortex. The video-specific pattern similarity results reported here strongly resemble the scene-specific cross-subject similarity reported by Chen et al. (2017).

However, our main interest was to examine whether narrative theme modulates this effect. We expected higher spatial pattern similarity for people watching HC videos as they had shared narrative knowledge and were, potentially, better able to interpret the videos. Indeed, for the HC > LC contrast we found that left and right anterior temporal lobe (ATL) to show higher pattern similarity across participants. Surprisingly, the reverse contrast showed that the precentral gyrus exhibited higher pattern similarity across subjects for LC clips.

Figure 2-3 *Inter-subject correlations*. A) The weight matrix (General ISC) tests for video specific time course similarity across participants. Each cell represents the correlation between subjects' time course for a particular video with the average time course of all remaining participants for a particular video. The diagonal represents correlations between time courses for the same videos. The off diagonal represents temporal correlations between mismatching videos within the same run. B) Brain map from video specific analysis, which shows extended synchronization across the brain for people watching the same videos. C) Weight matrix that tests for the time-course similarity across the same videos, depending on the prior knowledge provided for them. D) Brain map showing how time-course synchronicity was modulated by prior knowledge. Both brain maps show clusters significant at FWE p < 0.05 after permutation testing.

Figure 2-4 *Inter-subject Pattern Similarity*. A) The weight matrix (General ISPS) tests for video specific spatial pattern similarity across participants. The diagonal represents spatial similarity for the same videos. The off diagonal represents spatial correlations between mismatching videos within the same run. B) Brain map from video specific analysis, which shows extended pattern similarity across the brain for people watching the same videos. C) Weight matrix that tests for the spatial similarity across the same videos, depending on the prior knowledge provided for them. D) Brain map showing how spatial pattern similarity was modulated by prior knowledge. Both brain maps show clusters significant at FWE $p < 0.05$ after permutation testing.

2.5 Discussion

This study examined the cognitive and neural effects of prior knowledge of a narrative storyline on the processing of novel events. Participants viewed videos for which they either were, or were not, provided with knowledge of the preceding narrative (HC and LC respectively). Prior knowledge increased participants' memory performance and subjective comprehension and vividness ratings. Several regions showed higher coupling in the moment-to-moment BOLD response across participants in the HC condition, particularly in regions associated with the brain's semantic network (including the left superior and inferior frontal gyrus, and left AG). In addition, we observed greater cross-participant multivoxel pattern similarity for HC videos in another region strongly associated with semantic knowledge, the bilateral anterior temporal lobes. The results show that increasing the amount of "common ground" with which to interpret a new event increases the degree to which neural responses in regions of the semantic network are shared across participants. More generally these results highlight the role of the semantic network in processing narrative content, a central element of naturalistic events.

Prior knowledge about a particular situation enables subsequent new information to be comprehended more easily and remembered better (Ames et al., 2015; Bransford & Johnson, 1972; Chen et al., 2016; see also Yeshurun et al., 2017). It also constrains how the new information is interpreted. For example, in one of the second half videos in our experiment (taken from the show "Just Shoot Me") two of the main characters (Jack and Maya) discuss the fact that penguins cannot fly. Jack claims that "penguins once filled the skies", but one day their confidence was shattered, and they never flew again. A participant viewing this clip in the HC condition can relate this discussion back to the first half of the video, in which Jack explains how Maya hurt her colleague's confidence and the negative effect this has had on his work. However, because participants viewing this clip in the LC condition were familiar with the general setting (Jack and Maya in an office), but not the specifics of the narrative, they would be likely to have formed more idiosyncratic interpretations of what the scene is really about. Thus, while participants in both conditions shared the general "scaffold" of the event model, only in the HC condition could

participants bring the more specific information gained from the first half of the video to their understanding of the second half.

Previous studies using ISC and pattern similarity measures to investigate event processing have generally compared participants watching similar, or the same events to different events (Bird et al., 2015; Chen et al., 2016; Chen et al., 2017; Oedekoven et al., 2017; St-Laurent et al., 2014). These studies have found widespread effects throughout sensory brain regions and the DMN. We found similar effects when we compared the similarity across participants watching the same show, regardless of prior knowledge. These effects are likely to be driven by the common elements of the same shows, including the location, the people present or the overarching schemas (see Baldassano et al., 2018). Indeed, a recent study showed that the neural representation of events in the DMN, indexed by multivoxel patterns of activity, is dominated by the spatial context (Robin et al., 2018). Our findings comparing the HC with the LC condition reveal a much more restricted set of regions are involved in integrating prior knowledge of the narrative. These effects were found predominately within the semantic network. Furthermore, different regions were highlighted with the ISC analysis to the ISPS analysis, which may reflect the different processing roles of these regions.

ISC effects were seen in regions, which have been associated with semantic processing, particularly in "semantic control" (Binder et al., 2009; Noonan et al., 2013). These were the superior and inferior frontal gyri, the AG, and premotor cortex. The fact that ISCs are based on temporal correlations in activity, suggest that these regions are involved in moment-by moment integration of knowledge gained by watching the intact first half of each video (for participants watching in the HC condition) with the incoming information provided by the second half of the video. Of note, the MTG, IFG and AG were recently highlighted in a recent study of narrative context processing (Keidel et al., 2017). Activity in these regions was higher, and in the case of the MTG, peaked earlier, when a narrative context was provided. The authors suggested that these regions processed the "on-the-fly" links between semantic concepts necessary to comprehend the storyline.

It is worth mentioning two recent studies that examined how similarity in narrative interpretation affected ISC across participants (Nguyen et al., 2019; Saalasti et al., 2019). Nguyen et al., (2019) for instance presented participants with ambiguous narrative and later asked them for their interpretation of the narrative. They found higher ISCs for participants that had more similar interpretations of the narrative in AG and other areas of the DMN. Saalasti et al., (2019) used a similar approach where they presented participants with a narrative and asked them every 3-5 seconds to report 3 words that came to their mind. They also found higher ISCs in AG for participants that had more similar interpretations of the narrative. These findings resonate well with our results since the provision of narrative context potentially constrained the possible interpretations of the second half clips. Furthermore, the AG, IFG, ATLs and SPL regions have been recently shown to continuously integrate information in the scale of seconds to minutes (Hasson et al., 2015, Hasson et al., 2008; Lerner et al., 2011). Here we extend these findings demonstrating that these regions are also involved in the integration of narrative context even when multiple narratives were presented in an interleaved manner (second half videos did not immediately follow the first half videos) (see also Lahnakoski et al., 2017). Whether these regions process any previously acquired information (such as people or locations), or they more specifically process the abstract concepts necessary to understand a narrative, is a question for future research.

We additionally carried out ISPS analyses to see where the spatial patterns of BOLD activity were more consistent between participants sharing narrative contextual information. These effects were localised to the anterior temporal lobes bilaterally. Although these results are due to the same contrast as the ISC results discussed above (greater similarity for the HC compared to the LC clips), they are possibly driven by subtly different mechanisms. While ISC effects reflect temporal variations in activity during the clips that are more synchronised across participants, the ISPS effects are driven by spatial variation in the activity patterns for each clip, where the patterns reflect time-averaged responses. Therefore, these effects might represent shared representations of the overarching narrative themes rather than more dynamic processing of concepts relating to the ongoing narrative. This information,

together with information about the location and people present, is a core element of the event model describing a particular situation. The importance of the ATL for semantic memory and conceptual knowledge is well-established (L. Chen et al., 2017; Patterson et al., 2007; Rice et al., 2015). Within the ATL, the anterior and ventral regions identified in our study have been argued to act as a semantic "hub", supporting amodal conceptual representations that are independent of specific sensory input (Murphy et al., 2017; Patterson et al., 2007). Our results extend this theory, suggesting that the region supports abstract representations of information as complex as narrative themes.

Of course, we would expect multimodal events to be represented across many cortical regions. If we take together these previous findings and the results of the current study, it appears that there is a division of labour in the instantiation of event models in the brain. Regions of the DMN, notably posterior midline regions, represent the stable core of the model, such as the location and identity of the people present (Chen et al., 2017; Robin et al., 2018). By contrast, the ATL may play a central role in representing the overarching narrative gist. Finally, other regions of the semantic network, particularly the IFG and AG, may more tightly track the changing aspects of the associated narrative and link then to prior knowledge. This framework is similar to that proposed by Ranganath and Ritchey (2012).

In summary, we have shown how manipulation of knowledge about a narrative storyline impacts on the cognitive and neural processing of events. The availability of narrative information led to increases in intersubject synchronization and spatial pattern similarity in regions associated with semantic processing. Moment-by-moment tracking of narrative information and linking it to prior knowledge was associated with several regions of the semantic control network. Conversely, global updating of the event model with the central narrative themes was linked to representations supported by the ATLs. These results provide important new insights into how the brain represents and updates narrative information as well as highlights an important case of functional specialisation within the wider network of brain regions that are involved with event processing.

2.6 Supplementary Materials
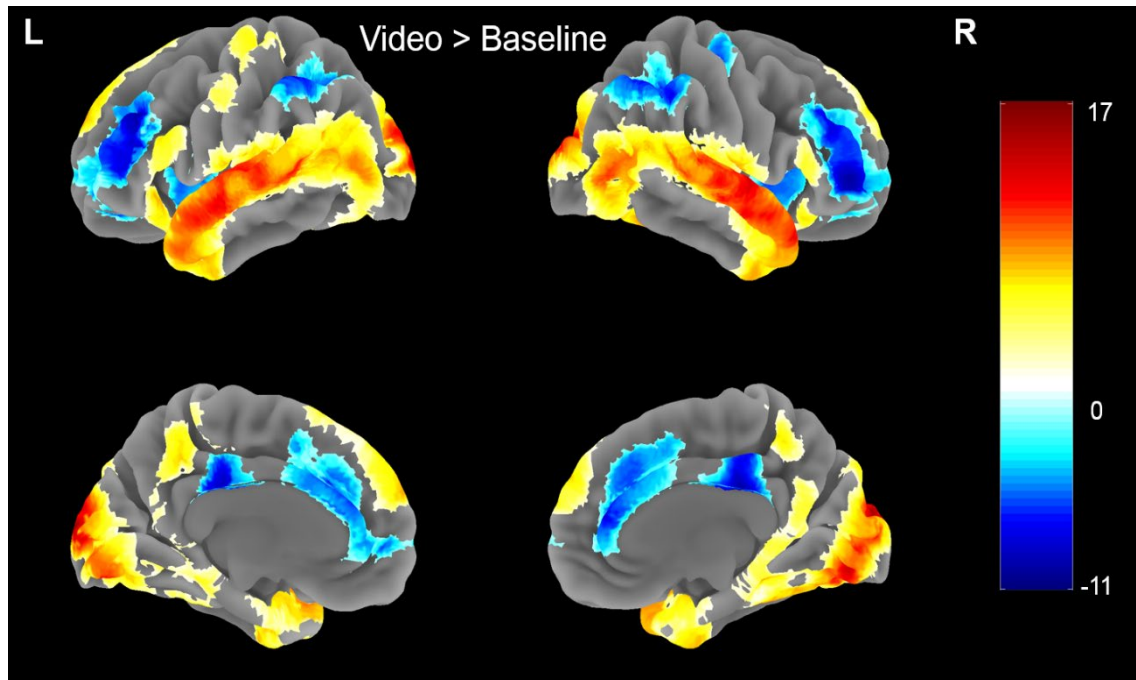
Supplementary Figure 2-1 *Video vs Baseline analysis.* The map shows brain regions active throughout the duration of the videos (from all conditions) versus baseline.
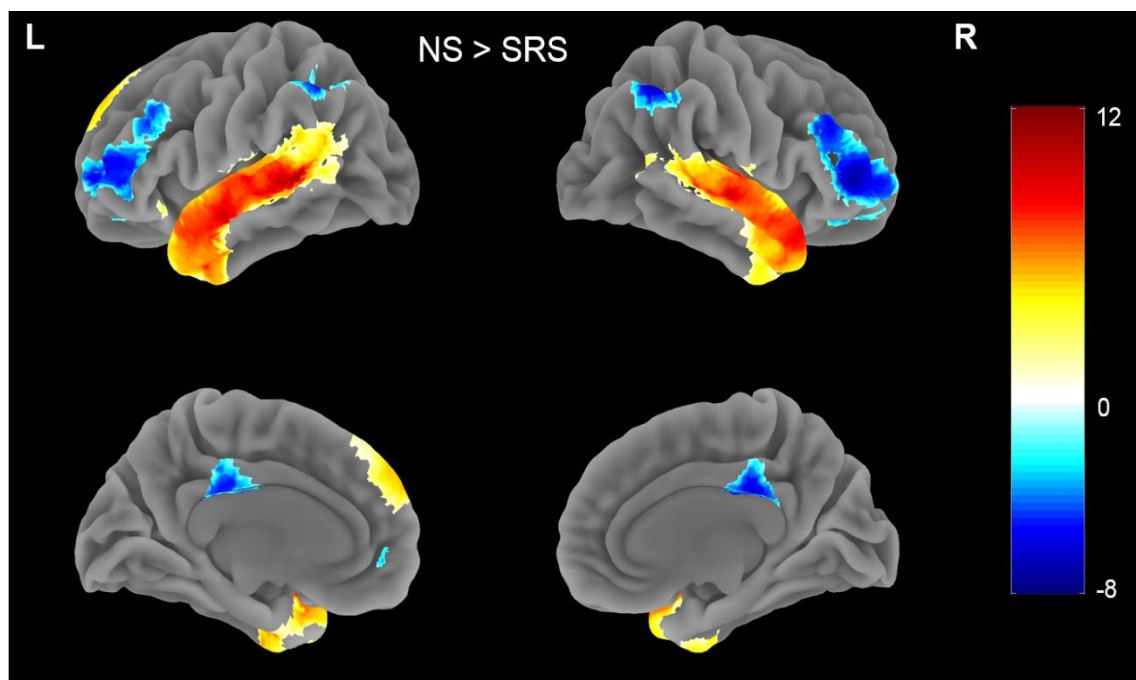
Supplementary Figure 2-2 *Language contrast.* Brain map showing contrast of first half videos with intact speech (NS) versus first half videos without comprehensible speech (SRS).
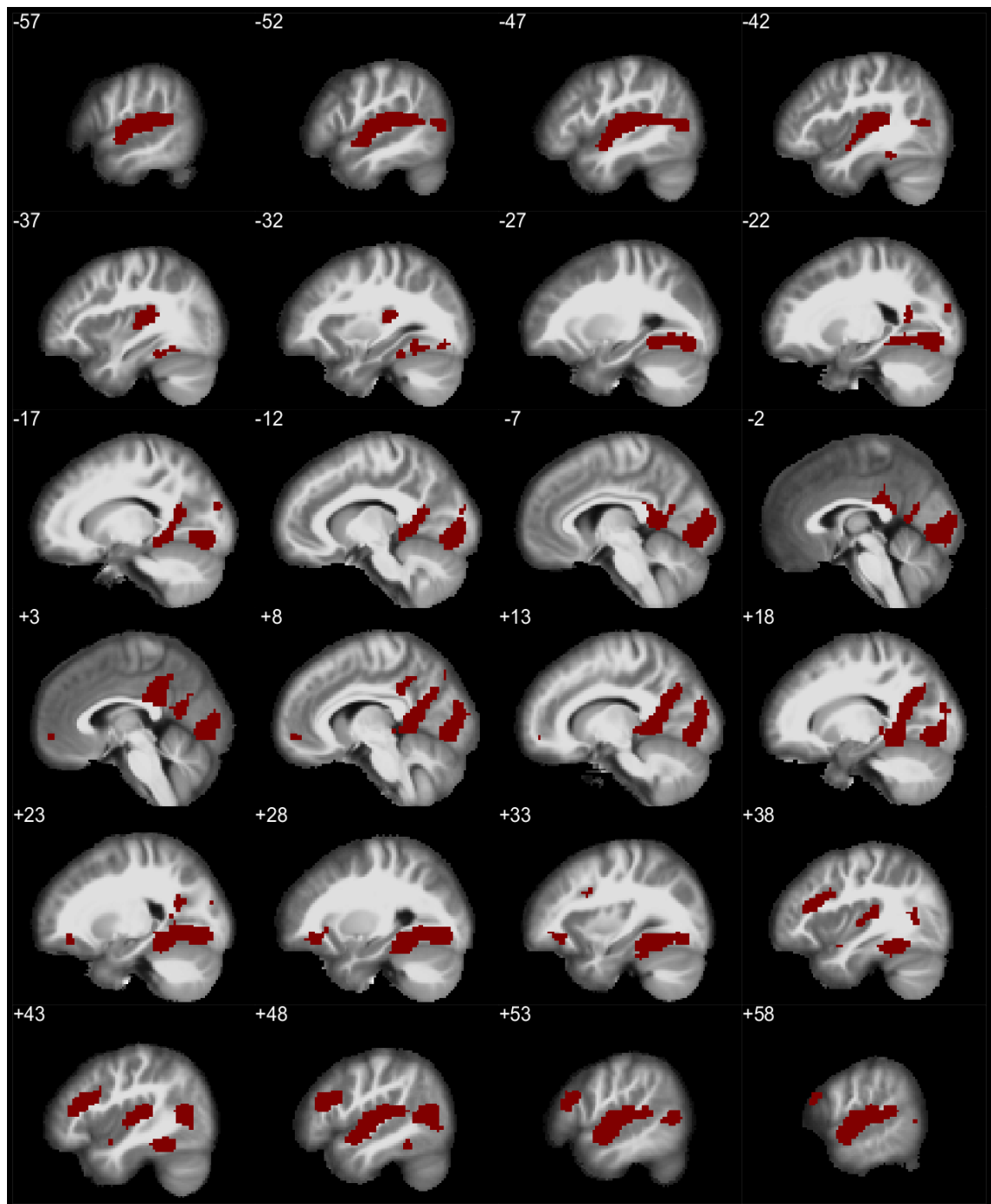
Supplementary Figure 2-3 *Analysis of video onsets*. Conjunction analysis showing the positive onset responses for HC, LC and NS videos. Voxels in red represent whole-brain significant (p < 0.001) responses to all 3 conditions.

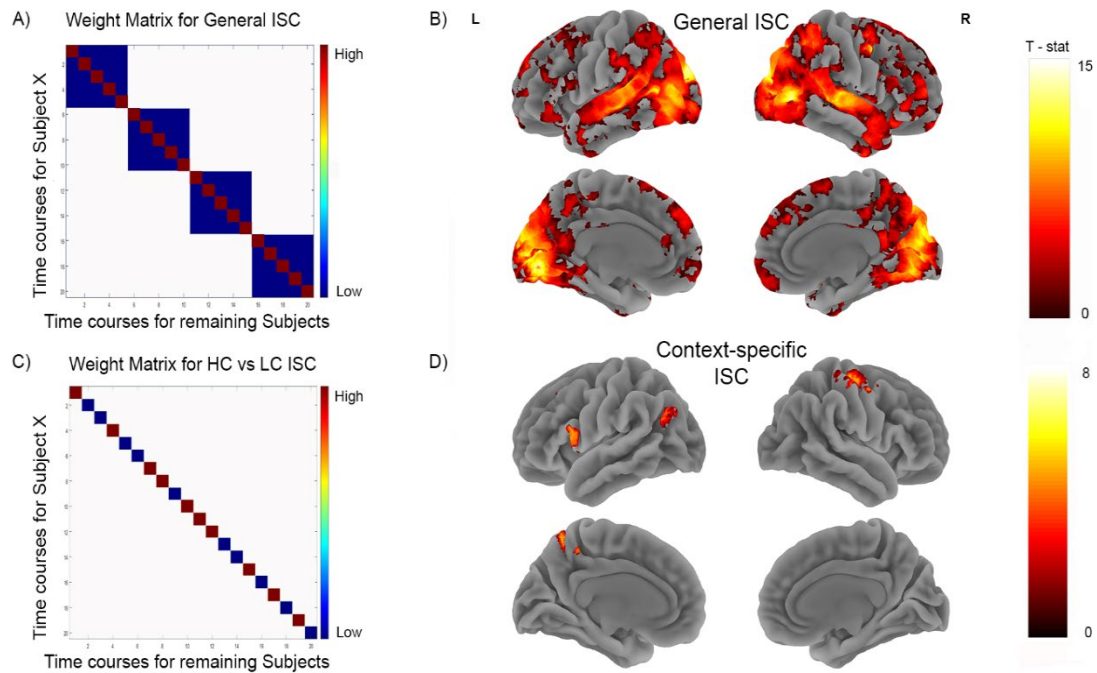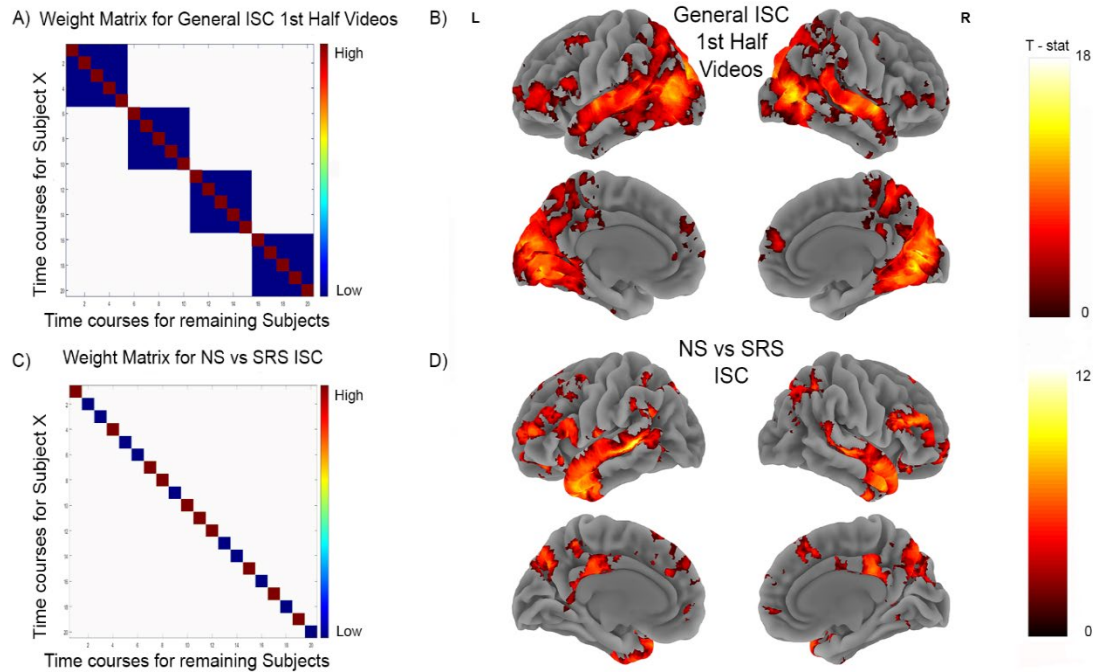**Supplementary Figure 2-4** *Inter-subject correlations for first half videos.* A) The weight matrix (General ISC) tests for video specific time course similarity across participants. Each cell represents the correlation between subjects' time course for a particular video with the average time course of all remaining participants for a particular video. The diagonal represents correlations between time courses for the same videos. The off diagonal represents temporal correlations between mismatching videos within the same run. B) Brain map from video specific analysis, which shows extended synchronization across the brain for people watching the same videos. C) Weight matrix that tests for the time-course similarity across the same videos, depending on whether the language in the videos is intelligible (NS) or not (SRS). D) Brain map showing how time-course synchronicity was modulated by provision of comprehensible language in the videos. Both brain maps show clusters significant at FWE p < 0.05 after permutation testing.

A) Weight Matrix for General ISPS 1st Half Videos

B) L   General ISPS 1st Half Videos   R

C) Weight Matrix for NS vs SRS ISPS

D) NS vs SRS ISPS
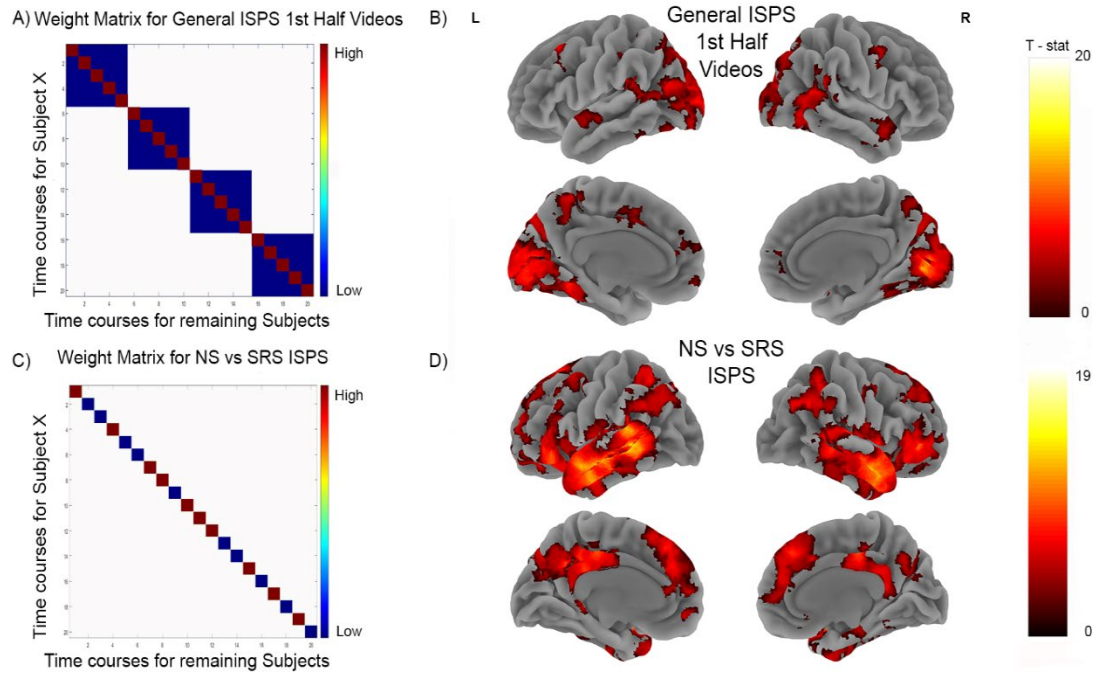
Supplementary Figure 2-5 *Inter-subject Pattern Similarity for first half videos.* A) The weight matrix (General ISPS) tests for video specific spatial pattern similarity across participants. The diagonal represents spatial similarity for the same videos. The off diagonal represents spatial correlations between mismatching videos within the same run. B) Brain map from video specific analysis, which shows extended pattern similarity across the brain for people watching the same videos. C) Weight matrix that tests for the spatial similarity across the same videos, depending on the whether the language is comprehensible (NS) or not SRS. D) Brain map showing how spatial pattern similarity was modulated by presence of comprehensible narrative. Both brain maps show clusters significant at FWE p < 0.05 after permutation testing.

2.6.1 Supplementary Methods

We implemented a time-course analysis in order to analyse how activity differed over the duration of the videos. A set of 12 piecewise linear tent functions were used to model the first 26.2 seconds of each of the 4 conditions. Keidel et al. (2017) found significantly greater activation in MTG, AG, SMG and IFG for HC as compared to LC videos. To attempt to replicate this finding we averaged the results of the time course analysis in these clusters. Significant differences in the time-course were found in the left MTG, AG, and supramarginal gyrus (SMG) replicating the previous findings, while no significant difference was observed in the left IFG.
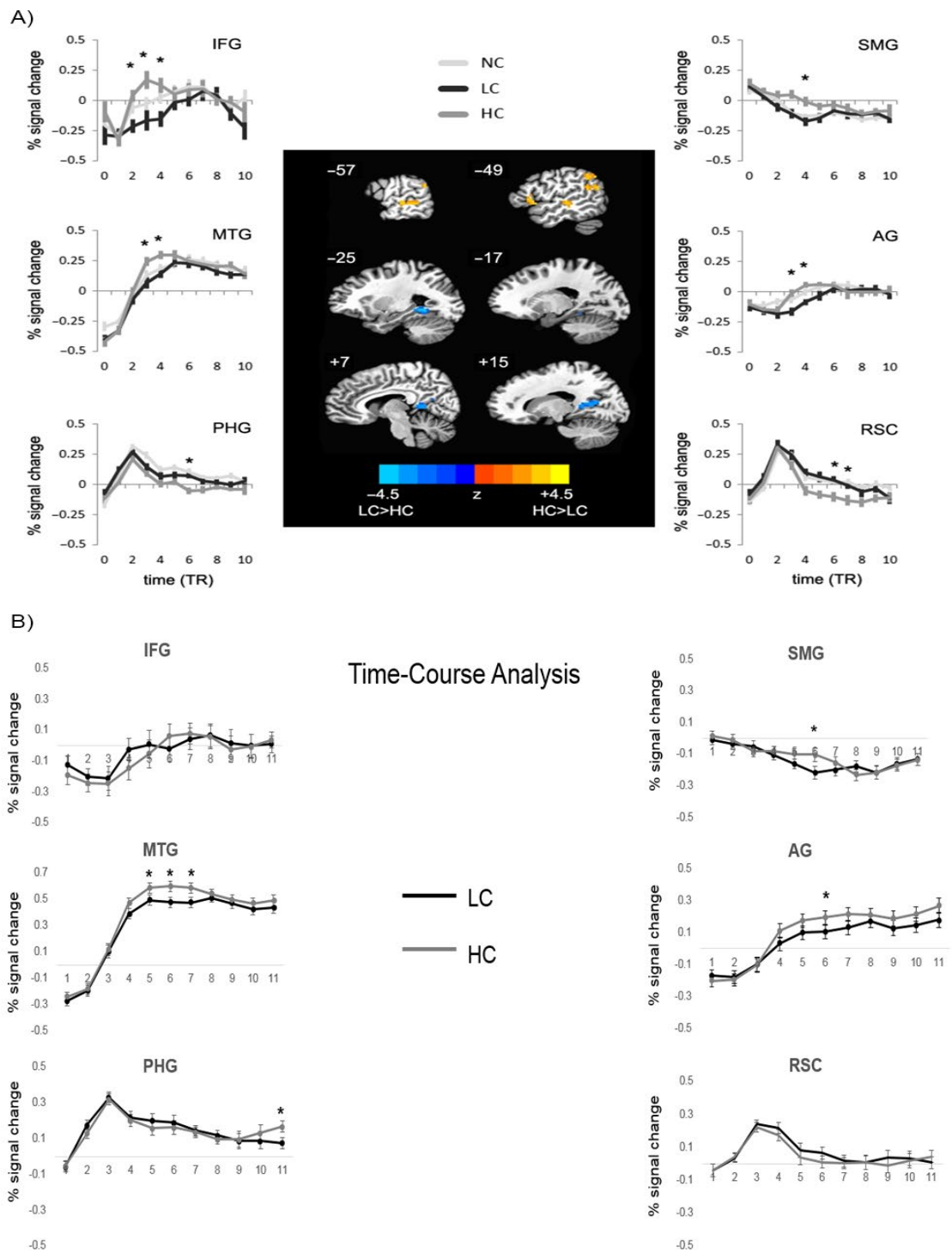
Supplementary Figure 2-6 *FIR analysis*. Deconvolution analysis examining response to the initial 26.2 seconds for HC and LC videos. A) Results reported by Keidel et al. (2017). B) Time courses in ROIs identified in Keidel et al. (2017) for HC versus LC videos.

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Chapter 3: The brain regions supporting schema-related processing of people's identities

3.1 Abstract

Schematic knowledge about individual people enables us to predict and understand their behaviour in novel situations. The ventromedial prefrontal cortex (vmPFC) and hippocampus have been identified as playing key roles in schema-based processing of new experiences. Nevertheless, their precise roles and their interactions with each other remain poorly understood. We manipulated schematic knowledge by familiarising participants to the lead characters of one of two TV shows, both of which featured young couples. Familiarisation involved watching episodes of the show over a period of at least a week. Then participants viewed pictures of all 4 characters in an MRI scanner and performed a recognition memory test afterwards. They also performed a memory test for short novel videos from the two shows. Schematic knowledge boosted performance on both of the memory tests. Whole-brain analyses revealed that schematic knowledge increased activation in the vmPFC and the retrosplenial cortex, while a region-of-interest analysis additionally found increased activity in the hippocampus. The size of the effects in the vmPFC and hippocampus were not significantly different. Representational similarity analyses found evidence for person-specific patterns of activity in the vmPFC but not hippocampus, but neither region showed an effect of training on representational similarity. Our findings suggest complementary roles for the vmPFC and hippocampus in processing schematic knowledge that has been recently acquired over multiple occasions.

3.2 Introduction

The world and people around us can be confusing. To understand what is happening in our environment we rely on our prior schematic knowledge. Schemas are abstracted knowledge structures learned over multiple episodes (Ghosh & Gilboa, 2014; see for review Gilboa & Marlatte, 2017). A schema for a well-known friend might include their appearance, likes and dislikes and their personality traits. This knowledge helps us understand and predict other peoples' behaviour in new situations (Ramon & Gobbini, 2018). The present study investigates the impact of schematic knowledge - acquired in a naturalistic manner - on both episodic memory processes and on brain activity in regions that support these processes. In this introduction, we will first highlight the findings from different types of studies that have been used to investigate the brain-basis of schematic knowledge. We will then summarise current views on how schematic processing is carried out in the brain before introducing the current study.

A range of tasks have been used to examine the neurobiology of schemas. These fall broadly into three different types. The first are studies that rely on participants' pre-existing knowledge, contrasting behavioural and physiological responses to stimuli that are familiar versus unfamiliar (Bein et al., 2014; di Oleggio Castello et al., 2017; Liu et al., 2016; McAndrews et al., 2016; van Kesteren et al., 2013; van Kesteren et al., 2014). For example, Liu et al., (2016) required participants to learn face-house associations, where the faces were of either famous or non-famous people. Such studies consistently find positive effects of prior knowledge on memory performance. It has been argued that this boost in performance is due to the rich associations that exist for familiar items which enables new memories to be organised efficiently as well as increasing the distinctiveness of individual items (e.g. Bird et al., 2011; Van Overschelde et al., 2005).

The second class of studies involve teaching participants new arbitrary rule-based associations (Schlichting et al., 2015; Schlichting & Preston, 2016; Sommer, 2016; Wagner et al., 2015; Zeithamova et al., 2012). In one such study, Sommer and colleagues (2016) trained participants on 10 distinctive

object-location arrays each containing 20 locations. During training, only some of the locations in each array were associated with an object. Participants were then presented with novel object-location pairs that were either related or unrelated to the previously learned spatial structure. In these types of paradigms, memory is better for new items that conform to the learnt rules.

The last types of studies use naturalistic video- or text-based tasks and expose participants to information that aids the interpretation of novel events (e.g. Ames et al., 2015; Keidel et al., 2017; Raykov et al., 2018; van Kesteren et al., 2010). In a study by van Kesteren et al., (2010), participants watched a movie for which prior knowledge was manipulated. On the first day of the experiment participants watched the first part of the movie in either scrambled or unscrambled order. On the next day both groups watched the last 15 minutes of the movie in unscrambled order. Thus, participants who had watched the unscrambled first half of the movie had a more coherent knowledge base within which to interpret the second half clip. Once again, the provision of knowledge consistently results in improved memory for the subsequent movie or narrative text.

All the studies mentioned above have combined manipulations of prior knowledge with functional MRI to investigate the brain regions involved schema processing. Overall there is a general consensus that when participants engage schematic knowledge, brain activity is modulated in certain key regions. These are the ventromedial prefrontal cortex (vmPFC) and hippocampus, as well as other regions such as the anterior temporal lobes, posterior midline regions, and - particularly in the case of faces - the fusiform gyrus (see Gilboa & Marlatte, 2017). Despite this overarching similarity across studies, there is still inconsistency in the specific pattern of BOLD activity effects. For example, whereas some studies find that processing stimuli related to prior knowledge is associated with higher activity in vmPFC and hippocampus (e.g. di Oleggio Castello et al., 2017; Liu et al., 2016; Sommer, 2016; Zeithamova et al., 2012), other studies find a different pattern showing that the hippocampus is more active whilst processing schema-incongruent associations (McAndrews et al., 2016; van Kesteren et al., 2013, see also van Kesteren et al., 2014). For instance, using paradigms reliant on pre-experimental knowledge, Liu et al.,

(2016) found that known faces engaged both the vmPFC and hippocampus, but van Kesteren et al., (2013) found that while schema-consistent associations activated medial PFC, the hippocampus was more active when viewing schema-inconsistent associations. While the former result suggests that the two regions are part of a single functional unit, the later finding suggests that the two regions play distinct roles (for reviews see Ghosh & Gilboa, 2014; Gilboa & Marlatte, 2017; McCormick et al., 2018; Preston & Eichenbaum, 2013; Robin & Moscovitch, 2017; van Kesteren et al., 2012).

Various theoretical frameworks have been proposed to explain how different brain regions interact during schema-based processing of new information. Van Kesteren and colleagues proposed the "SLIMM" framework ("Schema-Linked Interactions between Medial prefrontal and Medial temporal lobes", van Kesteren et al., 2012). SLIMM proposes that the vmPFC and hippocampus have competing roles in the presence of prior knowledge (see also Greve et al., 2019). According to this framework, incoming information congruent with prior knowledge is associated with increased medial PFC engagement and inhibition of medial temporal lobe (including hippocampal) activity. By contrast, processing information incongruent with prior knowledge should be associated with increased hippocampal activity. However, other models suggest that the hippocampus and medial PFC play complementary roles in relating new experiences with prior knowledge (e.g. Preston & Eichenbaum, 2013). In a recent formulation, Robin and Moscovitch (2017) argued that the posterior hippocampus, anterior hippocampus and vmPFC play roles in processing detail, gist and schema information respectively, and that these regions act cooperatively when retrieving episodic memories.

The lack of consensus in the roles different brain regions play in schema processing is unsurprising, given the variability in findings from different fMRI studies. It is possible that some of this variability is a consequence of the paradigms used. Studies that capitalise on schematic knowledge acquired outside of the laboratory have a strength in that the knowledge is acquired in real-world settings. However, it is difficult to equate the amounts of information known about the different stimuli across participants. Consequently, the type, and richness, of information activated by a "familiar" stimulus is likely to be

highly variable (see also Westmacott & Moscovitch, 2003). Studies that require the learning of rule-based schemas enable careful control of the amount of schema-relevant information learnt, but the schemas involve highly abstract information and the rules are often learnt rapidly in one or two sessions close to when scanning takes place. This is very different from real-world situations where schematic knowledge is acquired over weeks, months and years. Lastly, paradigms that manipulate knowledge of a single event or narrative are not necessarily targeting the more general and abstract schematic knowledge that is acquired over multiple episodes.

For these reasons, the present study uses a novel method to acquire new schematic knowledge under a naturalistic, yet carefully controlled, training regime. Over the course of a week, participants watched six episodes from one of two television shows. This allowed participants to gradually build up their knowledge of the show's main characters across multiple episodes over several days, in a manner similar to our acquisition of person-specific semantic knowledge in everyday situations. Both shows were US situation comedies (henceforth, "sitcoms") that aired in the early 1990's and were previously unfamiliar to our participants. The trained show was counter-balanced across participants to control for potential stimulus-specific confounds between the two shows. Before scanning, we checked that all participants had complied with the training regime by examining their memory for the training videos.

The main purpose of the study was to identify the brain regions that are engaged when schematic knowledge is activated. Familiar faces are thought to automatically activate "identity-specific semantic codes" (Bruce & Young, 1986). We therefore assume that after training, participants will spontaneously activate their schematic knowledge about the characters when viewing them in both static photos and short video clips. We therefore contrast the BOLD response when people view pictures of the trained characters compared to when they view characters from the untrained show. To engage participants in the in-scanner task and to obtain an index of schematic knowledge, participants performed a recognition memory test for the specific pictures they viewed in the scanner. Participants also watched and then answered questions about short video clips taken from unseen episodes of both sitcoms. Although these tasks

do not directly assess schematic knowledge learnt about the trained characters, numerous studies have demonstrated a memory advantage for memoranda associated with pre-existing schematic knowledge (e.g. Bird et al., 2011; Klatzky & Forrest, 1984; Liu et al., 2016).

We carried out three types of analyses. Univariate analyses investigated differences in overall brain activity for pictures of familiarised versus unfamiliar characters. Differences could reflect the direct effects of activation of schematic information or related processes (such as activation of episodic memories involving the characters or the rewarding effects of seeing a familiar person). Multivariate representational similarity analyses (RSAs) aimed to identify regions where person-specific information was represented – and critically, regions where person-specific representations existed only for the trained characters. Lastly, functional connectivity analyses were used to identify whether the connectivity between different brain regions was modulated by the presence of schematic knowledge about the characters. Our analyses focussed particularly on effects within and between the vmPFC and hippocampus. We predicted schema-related effects due to training in the vmPFC. Additional training-related effects within the hippocampus would be supportive of views that the vmPFC and hippocampus work in concert when prior knowledge can support new learning (Preston & Eichenbaum, 2013; Robin & Moscovitch, 2017). By contrast, stronger engagement of the vmPFC compared to the hippocampus for trained material would be more in line with the SLIMM model.

3.3 Methods

3.3.1 Participants

Thirty right-handed native English speakers (15 female), between ages 18-29 (21.71 ± 3.08) were included in the experiment. One participant was not included in the fMRI analysis, as they did not complete the task due to a technical issue with the scanner. One additional person was excluded from the behavioural analysis of the video memory test due to a technical issue. Before taking part, participants were screened to be unfamiliar with other shows/films where the main characters played a major role. Informed consent was obtained from all participants and they were all paid £40.

3.3.2 Stimuli

Sixty-four colour pictures taken from two US shows ("Mad about you" - MaD and "Dharma and Greg" - DG) were used in the scanning session. The shows were chosen to be previously unfamiliar to our participants. Both shows represent fictional situations happening in the everyday life of a couple in their 30s living in USA. There were 16 pictures for each of the four main characters (two for each show). The pictures were selected from unseen clips from the shows. Each picture represented a single character in the living room or in the kitchen. The camera angle and clothes differed across pictures of the same character. 10 short videos for each show were also used for a memory test. Videos from MaD show (32.7secs ± 6.73) were on average the same duration as videos from the DG show (33.4secs ± 7.87) (p = .833). The videos were selected from previously unseen episodes and represented self-contained situations happening in unfamiliar locations (e.g. the museum). All clips were presented in black and white and the audio was scaled to the same mean decibel intensity with Praat (version 6.0.15).
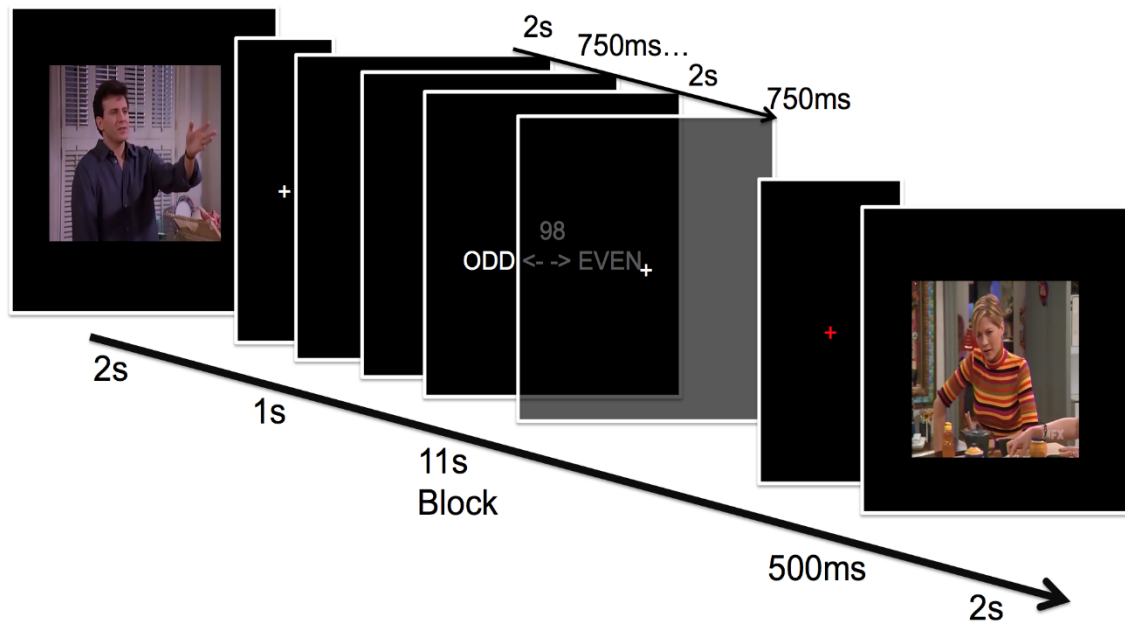
Figure 3-1 *Schematic of picture task*. Participants viewed pictures of the 4 main characters taken from unseen episodes from two TV shows. Before the experiment participants were familiarised with one of the shows (2 of the characters). Each picture represented only one character in their kitchen or living room. The view angles and clothes of the characters differed across different pictures. Participants made an odd-even number judgment task in between presentation of pictures, which acted as an active baseline task.

3.3.3 Procedure

Participants were asked whether they had seen either of the two shows or other shows including the same actors in leading roles. Participants who reported seeing either of the shows (or shows with the same actors in main roles) were not included in the experiment. Participants were then randomly assigned to one of the two training conditions (MaD or DG). This counterbalancing allowed us to control for stimuli effects at the group level. Each participant was allocated 6 episodes to watch at their own time. Participants were asked to watch the episodes over a week rather than binge watch all episodes in one sitting. To ensure participants followed the instructions their memory for the 6 training episodes was tested before continuing with the scanning session. Participants freely recalled the 6 episodes. When necessary, cues were provided for certain details (e.g. what was said, the intentions and emotions of the characters, their location) about scenes in the episodes. Participants that required many cues and could not

recall specific details about one or more episodes were asked to re-watch them. Only one of the included participants needed to re-watch a single episode. This screening procedure was done at least 2 days before scanning and took approximately 45 minutes.

Participants carried out 4 functional runs within the scanner; 2 runs involved viewing pictures (run 1 and run 4) and 2 runs involved watching short videos (runs 2 and 3). Each run of the picture task lasted 9 minutes and participants saw 8 pictures for each of the 4 main characters (2 characters from the trained and 2 from the untrained show). Presentation order was randomized within runs. Each picture was presented for 2 seconds on a black background followed by a 12 second inter-stimulus-interval during which participants made an odd/even judgment, which served as active baseline task (Stark & Squire, 2001; Visser et al., 2010). See Figure 3-1 for a schematic of the procedure. The odd/even task comprised a sequence of four numbers randomly chosen from the range 1-98. Each number was presented for 2 seconds followed by a fixation cross lasting 750 milliseconds. A red fixation cross was presented for 500 milliseconds before the presentation of the next picture. Participants were informed their memory for the pictures would be tested outside of the scanner. To further ensure participants attended to the pictures, there was an oddball target detection task where participants pressed a target if they saw a picture of an adult older than the 4 repeated characters (4 targets per run). Each run of the video task lasted approximately 16 minutes. Ten videos were presented in each of the two video task runs (5 trained, 5 untrained). Videos were presented in an interleaved order. There was a 13 second inter-trial interval between each video.

Outside of the scanner participants first completed a memory test for video task. We used a three-alternative forced-choice test for the details from the video (see Supplementary Figure 3-2). There were 5 questions for each video. The sets of 5 questions were presented in a pseudo-random order so that there were no more than 3 sets of questions in a row for the same show. Performance was measured as the proportion correct, with chance level being 0.33. We report the behavioural data from the video memory test below. The

fMRI data collected during these runs is the focus of a separate manuscript and will not be described further here.

Participants then completed a yes/no recognition memory test with 40 old (studied) pictures and 62 new (unstudied) pictures. The new pictures were selected from previously unseen episodes. Each picture was presented for 5 seconds or until the participants made a response. A white fixation cross was presented for 2 seconds between each picture and a red fixation cross preceded the next picture by 400 milliseconds. To characterise performance, whilst accounting for response bias, we used the non-parametric discrimination index A' (Snodgrass et al., 1985). The index was calculated separately for each participant for the trained and untrained pictures. The index was calculated as 0.5 + ((H - FA)*(1 + H - FA))/4*H*(1-FA), where H stands for hits - correct old responses to previously presented pictures, and FA stands for false alarms - incorrect old responses to new pictures. A' ranges from 0-1 and 0.5 indicates chance level performance.

3.3.4 Behavioural analysis

For both the video and pictures task accuracy on the trained and untrained stimuli was compared using a paired samples t-test.

3.3.5 MRI acquisition

A 3T Siemens Prisma scanner with a 32-channel head-coil was used to acquire all images. Soft cushions were inserted into the head coil to minimize head movement. Functional images were acquired with a gradient-echo EPI sequence with multiband acceleration factor of 8 with the following parameters (TR = 0.8 seconds; TE = 33.1 ms; 52 degree flip angle; FOV = 208x180mm; 72 slices with sliced thickness of 2mm and isotropic 2mm voxels). Two SpinEcho Field map runs with reversed phase-encode blips in both Anterior to Posterior and Posterior to Anterior were acquired with the same parameters as the functional images. A high-resolution structural T1-weigthed image was acquired with 3D MPRAGE sequence (TR = 2.4 seconds; TE = 2.14 seconds; 8 degree flip angle; FOV = 224x224mm and 0.8mm isotropic voxels).

3.3.6   Image pre-processing

All images apart from the field maps were pre-processed with SPM 12 (Wellcome Department of Imaging Neuroscience, London, UK). Images from both runs were initially spatially realigned to the mean image. Field maps were estimated and applied to the motion corrected data with command-line functions from FSL (Smith et al., 2004). Field maps were used to correct for image distortions (Andersson et al., 2001; 2003). The anatomical image was coregistered to the mean functional image and segmented into grey, white and cerebrospinal fluid using tissue probability maps. The segmented images were used to estimate deformation fields, which were applied to the functional data to transform them to MNI space. A 6mm FWHM smoothing kernel was applied to the functional images for the whole-brain GLM analyses.

3.3.7   Data analysis

Data were analysed with SPM 12, the CosMoMVPA toolbox (Oosterhof et al., 2016) and custom scripts in MATLAB (Version 2017b, The MathWorks, Inc., Natick, MA, USA). All analyses were conducted on MNI normalised images. The RobustWLS toolbox in SPM 12 was used to estimate the first level models (Diedrichsen & Shadmehr, 2005). This method downweights volumes with high variance estimates, which leads to a "soft" exclusion of bad volumes. We used the Bspmview toolbox (www.bobspunt.com/bspmview) to visualise and describe our data. The toolbox implements MNI coordinates from the Anatomical Automatic Labelling 2 toolbox for SPM 12.

3.3.8   Whole-brain analyses

We first carried out whole-brain random-effect analyses across participants. Contrast images in MNI space were evaluated with one-sample t-tests. Results were thresholded in SPM using a cluster-level family-wise error correction (p < .05), with a cluster-defining voxel threshold of p < .001.

3.3.9   ROI definition and analyses

Predefined ROIs were used in follow-up analysis, as a seed for functional connectivity analysis and for representational similarity analysis. These ROIs were in the hippocampus and the vmPFC.

We investigated separately the head, and the combined body and tail, of the hippocampus since theories of schematic processing have suggested differentiation between these sub-regions of the hippocampus (Preston & Eichenbaum, 2013; Ritchey et al., 2015; Robin & Moscovitch, 2017). These regions were defined based on a segmentation carried out by Ritchey and colleagues (2015) and available at www.neurovault.org. This ROI was used for (1) univariate activity analyses, (2) functional connectivity, and (3) representational similarity analysis.

In order to compare activations between vmPFC and hippocampus, while avoiding circular voxel selection, we used a leave-one-participant out (LOSO) method (Esterman et al., 2010). The voxels for an vmPFC ROI for a given participant were identified by using the suprathreshold voxels in a whole-brain group analysis that excludes the participant. For instance, the ventromedial prefrontal cortex ROI for participant 1 is identified from suprathreshold voxels from a group analysis of all the other participants excluding participant 1. This was repeated for each participant.

We also used an anatomical mask of the ventromedial prefrontal cortex to perform representational similarity analysis (RSA). We used the WFU atlas pick toolbox and the AAL to identify ventromedial prefrontal cortex following the procedure presented in Liu (2016). The ventromedial mask included the left and right gyrus rectus and the left and right medio-orbital section of the frontal cortex.

3.3.10 GLM analysis

For the univariate analyses we modelled all of the trained pictures (32 trials) with a single regressor and a separate regressor included the information about the untrained characters (32 trials). We also included a regressor of no interest for the odd-ball pictures and modelled the six motion parameters. To estimate patterns to use in the subsequent RSA we modelled each of the characters with a single task regressor (Trained male, Trained female, Untrained male, Untrained female; 8 trials per run per character). This meant that a regressor for a character included pictures of the same character in different locations and from different viewpoints. We implemented a slow event

related design, which allowed us to sample the whole duration of the HRF and we used multiple trials per character to estimate robust patterns for each character (Zeithamova et al., 2017). Estimated patterns for all four characters were used in the general identity and trained vs untrained RSAs. An additional regressor of no interest was used for the oddball images. The odd/even judgment task was not modelled and served as an implicit baseline. The six motion parameters, mean session effects, and a high pass filter with a cut-off of 1/128 Hz were also included in the models. The contrasts of interest from the first-level models were subjected to a group analysis.

To compare BOLD activity between the hippocampal and vmPFC ROIs whilst accounting for regional differences and across-participants variability of the BOLD signal we computed a differentiation index (see Koen et al., 2019). For each trial and for each separate ROI we extracted the mean signal over all voxels within the ROI. Thus, we had a single value for each ROI and each condition. This allowed us to compute a differentiation index separately for each ROI. The individual trial values were used to estimate the mean (μ) and variability (σ^2) for each condition (trained and untrained). Positive values of the differentiation index indicate the ROIs preference for the trained versus the untrained condition. The differentiation index was calculated with the following formula:

$$\text{Differentiation Index} = \frac{\mu_{trained} - \mu_{untrained}}{\sqrt{\frac{\sigma^2_{trained} + \sigma^2_{untrained}}{2}}}$$

3.3.11 Connectivity analyses

Based on prior findings of modulated connectivity in the hippocampus when processing schematic knowledge (van Kesteren et al., 2010) we ran generalized psychophysiological interaction (gPPI) analysis (McLaren et al., 2012) to examine whether the anterior (head) and/or posterior (combined body and tail) hippocampus would show connectivity with the rest of the brain that is modulated by prior knowledge. We also used the significant vmPFC cluster as

a seed to examine whether there are changes in connectivity modulated by training over and above the increased univariate response in the vmPFC.

3.3.12 Representational similarity analysis (RSA)

We ran exploratory RSAs (Kriegeskorte et al., 2008) to investigate whether activation patterns were specific to the identities of the four main characters presented and whether pattern similarity was modulated by training. Whole-brain searchlight analyses were performed using a searchlight sphere with radius of 4 voxels (mean 235 voxels). Images for the RSAs were pre-processed as described above but were not smoothed before estimating the first-level models. All RSAs were performed for each subject separately in normalized space and the resulting maps were subjected to a one-sample group t-test against zero.

For each searchlight sphere, the multi-voxel response patterns (*t*-statistics) for each character for run 1 and run 2 were extracted and vectorised to compute their similarity using Pearson correlation. The resulting correlation coefficients were then Fisher transformed and assigned to the center voxel of each searchlight sphere. The resulting matrix of 16 correlations represents the neural similarity between the four characters across the two runs. The four diagonal values representing the matching identities across runs and the 12 off-diagonal values representing the correlations between non-matching identities (see Figure 3-2).

To identify brain regions that show higher similarity for matching identities we compared the correlation matrices calculated above with the similarity matrix shown in Figure 3-2 (left). This is equivalent to computing the mean average similarity for matching identities minus the mean average similarity for non-match identities ('Identity RSA').

A second RSA compared only the similarities of the matching identities to investigate brain regions where similarity was greater for the trained characters compared to the untrained characters (see Figure 3-2, right; 'Trained versus untrained RSA').

It is possible that any observed similarity to characters could be driven in part by the background scene (e.g. the character Dharma was always pictured in her living room or kitchen, but never the rooms from the other show). To ensure any observed effects are specific to character identity an additional RSA was run to examine the similarity across matching locations versus mismatching locations, irrespective of the character in the picture. There were two locations within each show (kitchen and living room). The first-level models included a single regressor for each of the all four locations (trained kitchen, trained living room; untrained kitchen; untrained living room) in each run. The regressor trained kitchen averaged over pictures of the trained characters in the kitchen. The similarity matrix was the same as the Identify RSA, but the patterns were specific to the locations rather than the characters. We also ran an RSA comparing the similarity for the trained and untrained locations.

In addition to whole-brain searchlight analyses we ran the RSAs described above in the hippocampal and vmPFC ROIs using all voxels within the ROI as activity patterns.
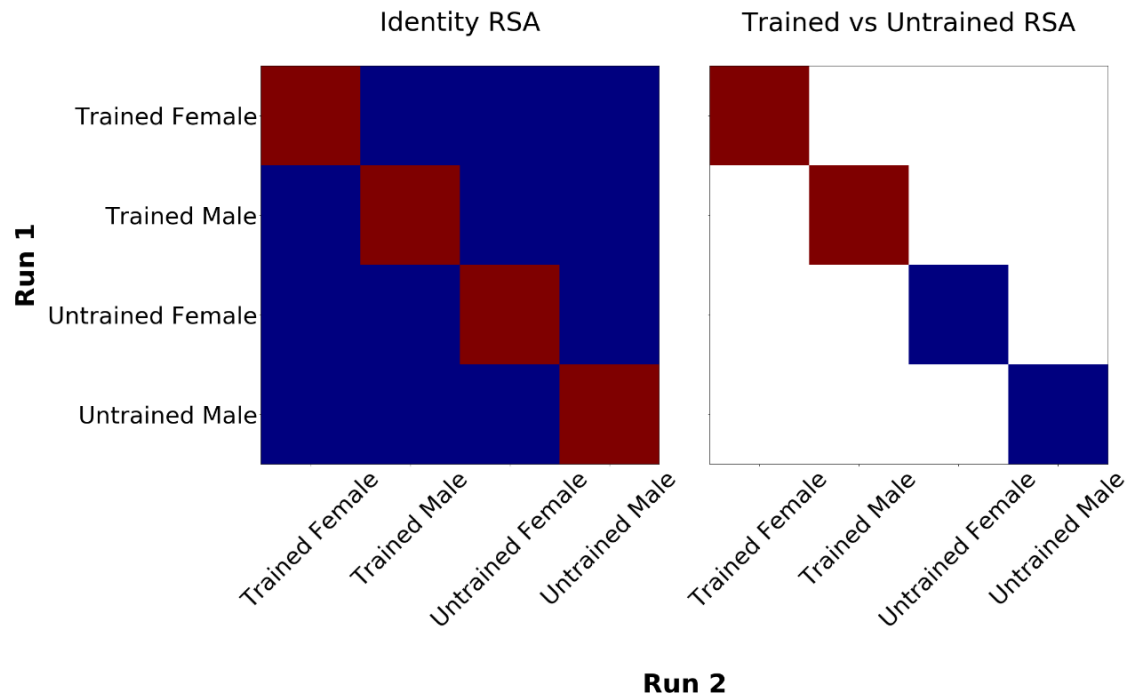
Figure 3-2 *Contrast Matrices.* The contrast matrixes used for the RSA analyses are shown above. Red indicates positive and blue indicates negative contrast values. In the identity RSA the main contrast was comparing for higher similarity for matching identities (across runs) versus mismatching identities. The second analysis examined modulations by training and which regions show more similar patterns (across runs) for the trained matching identities versus the untrained matching identities

3.4 Results

3.4.1 Behavioural Results

In the pictures task participants showed higher old/new discrimination, measured with A' (Snowgrass et al., 1985), for the trained pictures compared to the untrained ones (t_{28} = 2.07; p = 0.047) (see Figure 3-3). This effect is in line with previous findings of better recognition of familiar faces (Bird et al., 2011; Klatzky & Forrest, 1984). Overall, accuracy on the video memory questions was high (mean = 0.75 SD = 0.11 chance level = 0.33). Consistent with the results from the recognition memory test, performance on the video memory test was higher for the clips taken from the trained show (mean = 0.78) versus the untrained show (0.72: t_{27} =3.5; p = 0.002).

Participants showed high overall performance on the odd-even task in the scanner with average accuracy of 97% (sd = 0.02). There were no differences in accuracy or reaction times on the odd-even task trials following the trained or untrained pictures (ps > 0.42).
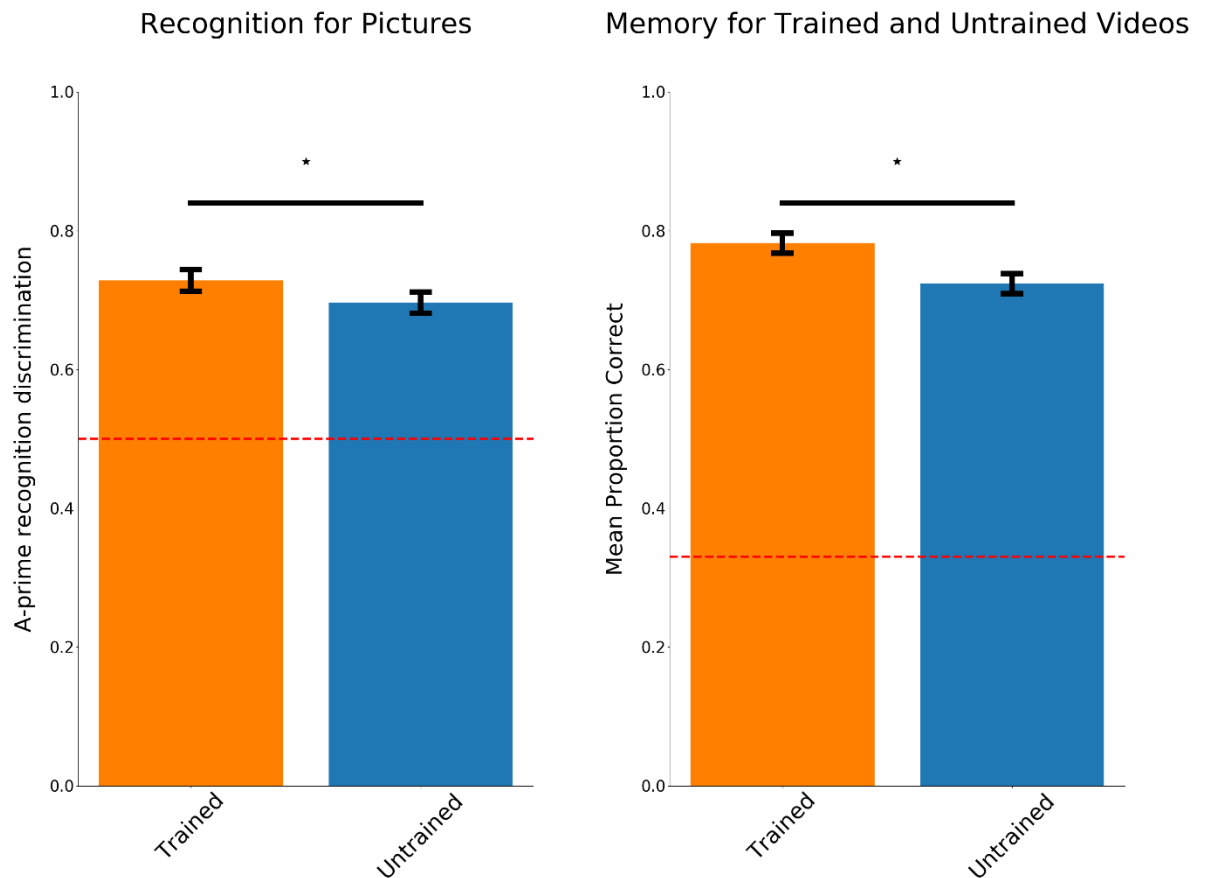
Figure 3-3 *Behavioural results.* Bar graph shows discrimination performance on the picture task, memory accuracy for the videos. Both measures were significantly higher for the trained show. Bar graph shows mean and standard error. Red dashed line indicates chance performance for each of the two tests. The star indicates a significant difference between the trained and untrained conditions at p < 0.05.

3.4.2 Imaging results

3.4.3 Univariate analyses

The contrast of viewing pictures versus the odd-even baseline task showed extensive activations including visual cortex, anterior temporal poles, ventromedial prefrontal cortex (vmPFC) and hippocampus (see Supplementary Figure 3-1).

In our main univariate analysis of interest, we compared activity while participants viewed the trained versus the untrained characters. The revealed whole-brain significant increases in BOLD activity in the vmPFC (cluster size = 185; peak voxel x = -4, y = 42, z = -12 t_{28} = 5.35) and RSC (cluster size = 183; peak voxel x = 12, y = -48, z = 18; t_{28} = 5.06)(see Figure 3-4).

Apart from whole brain effects we also focused on a priori defined regions of the anterior and posterior hippocampus. We examined the average BOLD response within our ROIs over all voxels. The head (t_{28} = 2.42, p = 0.02) and the body (including tail; t_{28} = 2.49; p = 0.02) of the hippocampus showed higher activations for the trained versus the untrained characters.

We were particularly interested to examine if there were any differential effects in processing pictures of trained versus untrained people between the vmPFC and the hippocampus. The vmPFC region maximally sensitive to the trained versus untrained effects was identified using a LOSO method (see above). Effects in this region were compared to the effects in the head and body of the hippocampus using the differentiation index method (for details see Methods). The across regions repeated ANOVA did not show any significant difference in differentiation index method across regions ($F_{1,83}$ = 0.95, p = 0.33)(see Figure 3-5).
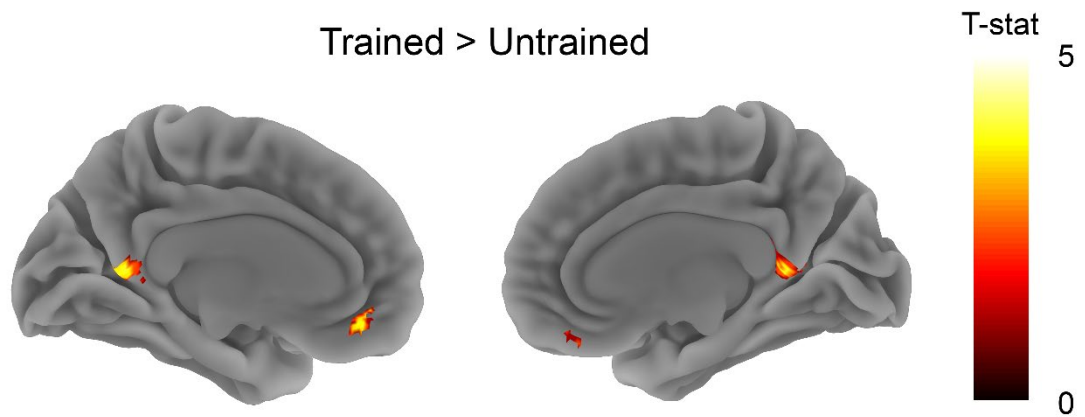
Figure 3-4 *Trained vs Untrained pictures.* The maps shows brain regions more active for the trained pictures when compared to the untrained pictures. Map is thresholded at p < 0.001 with FWE cluster size correction.
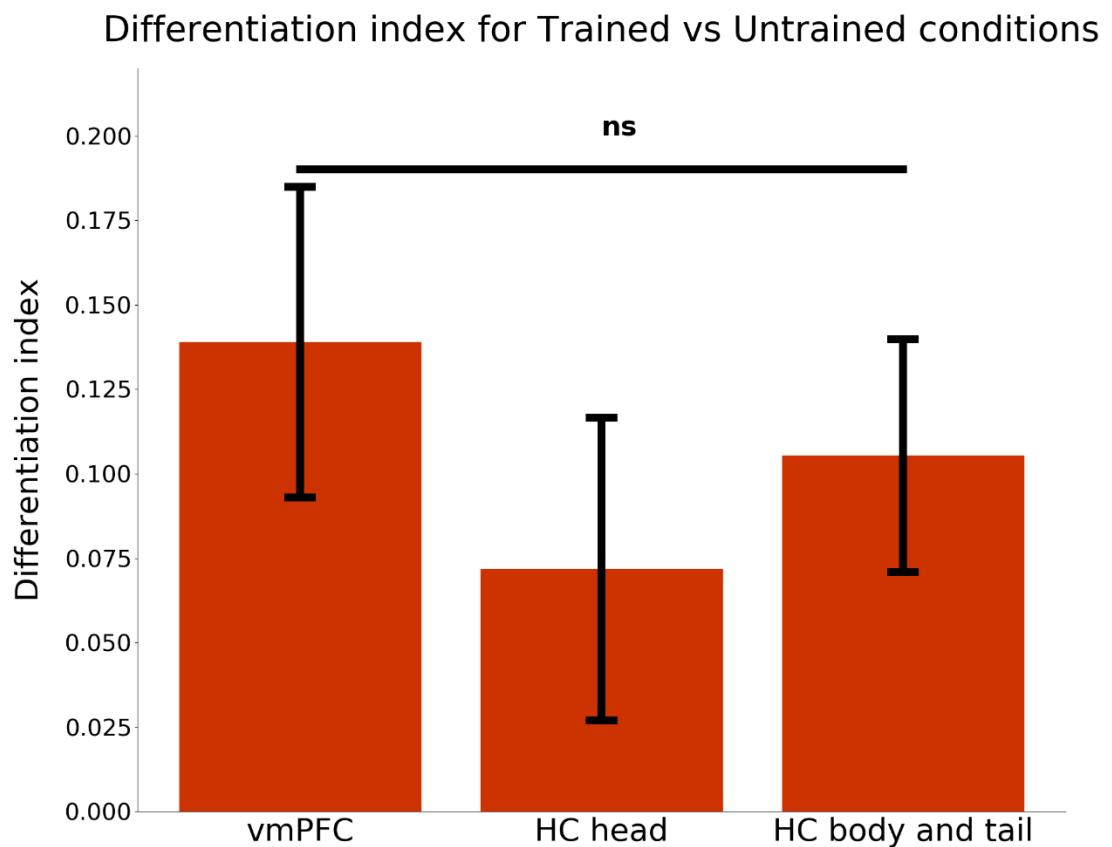
Figure 3-5 *Within ROI* Trained vs Untrained differentiation index. The plot shows the average differentiation index in the vmPFC, head of the hippocampus (HC head) and body plus tail of the hippocampus (HC body and tail). A positive differentiation index indicates that the regions shows greater activation for the trained condition. Bar graph shows mean and standard error.

3.4.4 Connectivity analyses

Contrary to our expectations, we did not observe any modulation of hippocampal connectivity by our training manipulation. Additionally, we did not observe any differences in connectivity between training conditions when we used the significant vmPFC cluster as a seed. Our result is in line with a recent finding from Brod and colleagues (2016) who also did not observe significant modulation of connectivity of hippocampus and vmPFC (but see Liu et al., 2016).

3.4.5 RSA

The Identity RSA searched for brain regions that showed consistent local patterns of activity for the four different characters. This analysis revealed a significant cluster in the vmPFC (cluster size = 273; peak voxel x = -10, y = 38, z = -2; t_{28} = 5.46), a cluster in the occipital cortex (cluster size = 264; peak voxel x = 16, y = -90, z = 16; t_{28} = 5.34), and a smaller cluster in the right occipital cortex (cluster size = 98; peak voxel x = 36, y = -72, z = -4; t_{28} = 4.69) (see Figure 3-6). A follow-up RSA for locations did not reveal any significant effects across the brain, suggesting that the Identity-RSA results are driven by the characters themselves and not the locations that they are pictured in.

The Trained vs Untrained RSA revealed a single cluster in the left inferior temporal gyrus (cluster size = 79; peak voxel x = -40, y = -44, z = -12; t_{28} = 4.98) where activity patterns were more similar for the characters for whom schematic knowledge was available (see Figure 3-7). The location of this cluster corresponds to the well characterised fusiform face area. When comparing similarity for trained and untrained locations at the whole brain level we found a significant cluster in left postcentral gyrus (cluster size = 134; peak voxel x = -20, y = -42, z = 66; t_{28} = 5.74).

In addition to whole brain searchlight analysis we ran both the Identity RSA and the Trained vs Untrained RSA in our predefined regions of interest. The anatomically defined vmPFC ROI showed higher similarity for matching identities versus mismatching ones (t_{28} = 2.76; p = 0.01), echoing the whole brain searchlight analysis. Neither the head (t_{28} = -1.22; p = 0.23) or the body (t_{28} = -0.21; p = 0.83) of the hippocampus showed significant multivariate effects

of identity. Surprisingly, none of our regions of interest showed significantly higher similarity for the trained versus the untrained characters (all *ps* > 0.3).
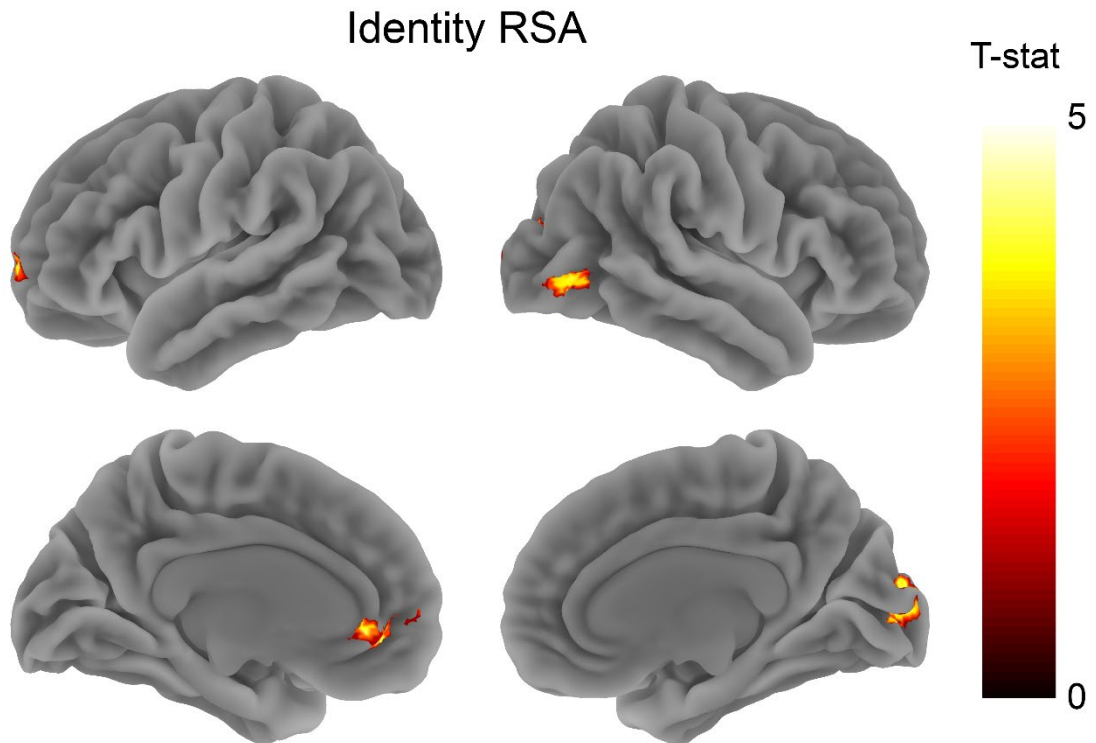
Identity RSA

Figure 3-6 *Identity RSA*. Searchlight map shows regions that showed higher similarity for matching identities when compared to mismatching identities. Map is thresholded at p < 0.001 and FWE cluster size corrected.
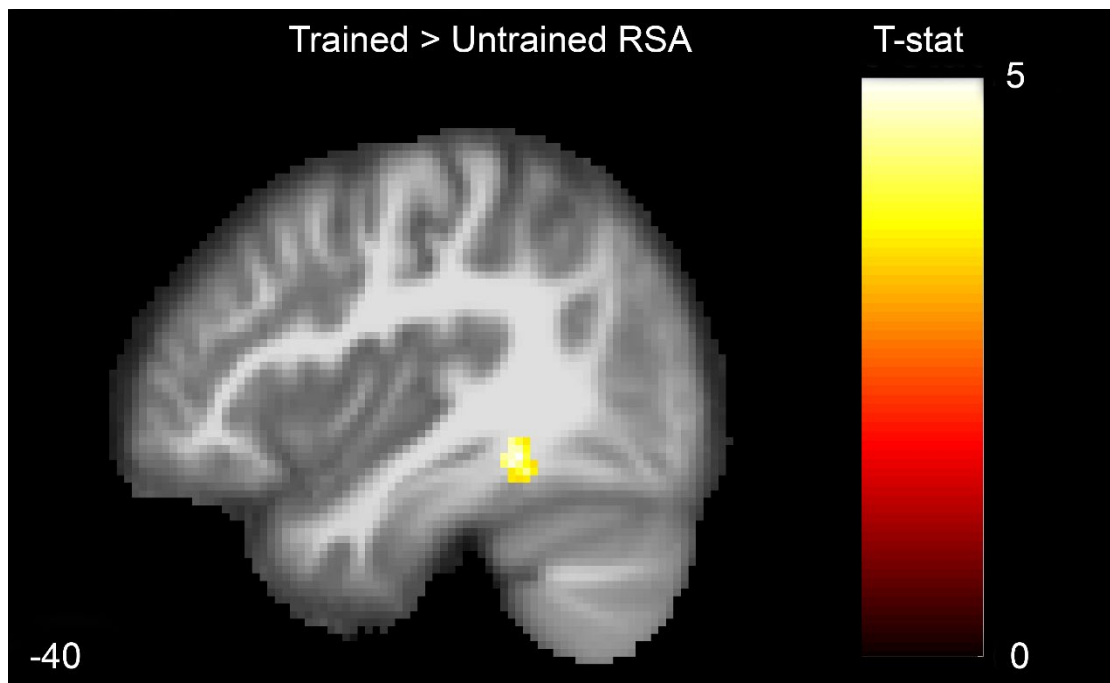
Figure 3-7 *Trained vs Untrained RSA*. Searchlight analysis revealed one region (the left fusiform gyrus) showing higher similarity for the trained identities when contrasted with the untrained identities. Map is thresholded at p < 0.001 and FWE cluster size corrected.

3.5 Discussion

The current study aimed to investigate the effects of recently acquired schematic knowledge on the processing of pictures of people. Before scanning we trained participants on one of two TV shows, which allowed us to examine brain regions that are associated with processing of knowledge that has been acquired across multiple occasions in a naturalistic manner. Whole-brain analyses revealed the vmPFC and retrosplenial cortex were more active when viewing trained versus untrained characters. To a lesser extent, but significant within our pre-specified regions of interest, both the head and the combined body and tail of the hippocampus also showed increased activation for the trained characters. We did not observe an inter-regional interaction between the vmPFC and the hippocampus suggesting a similar level of preference for the trained stimuli in both regions. Furthermore, we observed representational similarity identity effects in the vmPFC, but not in the hippocampus. Our results are consistent with theories implicating vmPFC and hippocampus in processing of schematic knowledge, but do not support a differential processing role for these regions in the face of prior knowledge.

Participants learned about the characters of a TV show over the course of a week. The training show was counterbalanced across participants allowing us to control for low-level visual differences between the shows and other potential confounds, such as the attractiveness or distinctiveness of the characters. Participants had to integrate information from multiple episodes to learn about the home, personalities, relationships and occupations of the main protagonists. This resembles how we acquire schematic knowledge in our everyday life and differentiates our design from previous studies that have relied on participants' pre-experimental knowledge without matching it across people or studies that have trained participants on rule-based associations. Furthermore, our design was different from other studies using naturalistic stimuli that have provided prior knowledge only specific to a single situation or narrative. Our finding of stronger activations in the vmPFC for the trained characters supports this region's proposed role in processing of schematic knowledge.

Notwithstanding the differences in study designs, our results are consistent with previous findings that have showed vmPFC involvement in prior knowledge effects (Baldassano et al., 2018; Liu et al., 2016; Preston & Eichenbaum, 2013; Tse et al., 2007, 2011; van Kesteren et al., 2013, 2010; Zeithamova et al., 2012). For instance, Liu et al., (2016) found higher vmPFC activation for famous versus non-famous faces (see also di Oleggio Castello et al., 2017; Von Der Heide et al., 2013). Using a weather prediction task trained over two days, (Wagner et al., 2015) observed higher vmPFC activity when participants were retrieving the rules after a 24-hour delay. Interestingly, lesions to the vmPFC have been associated with subtle schematic processing deficits (Ghosh et al., 2014). For instance, patients with vmPFC lesions have difficulty linking words ("receptionist") to their appropriate everyday schemas ("visit to the doctor") (Ghosh et al., 2014). Moreover, on word lists that contain thematically linked information ("bed", "tired", "rest", "dream"), healthy participants often have false memories for schematically linked but not presented targets ("sleep"). In contrast patients with vmPFC damage often do not make such false memory errors for schema congruent words (Ciaramelli et al., 2006; Melo et al., 1999; Warren et al., 2014). The paradoxically more accurate performance of patients with frontal lesions could be due to their reduced ability to instantiate a schematic representation that biases the encoding of related words (see Gilboa & Marlatte, 2017).

We note that the orbitofrontal cortex, which overlaps with the vmPFC, is implicated in social cognition, in person-trait processing (Benoit et al., 2010; Jenkins et al., 2008; Krienen et al., 2010), and in representing stereotypes about people (Stolier & Freeman, 2016). These findings are compatible with a role for the region in schematic processing. Stereotypes and trait judgments are likely based on schematic-like knowledge acquired across multiple occasions. Future studies could test whether different types of schemas (e.g. social versus non-social) are more associated with different sub-regions of the medial prefrontal cortex. For instance, it is possible that vmPFC is more involved in prior knowledge when it involves social or evaluative aspects (see for similar suggestions Liu et al., 2016).

Apart from univariate training effects we found evidence for character-specific patterns of fMRI activity within the vmPFC, suggesting that the region contains information about people's identity. Interestingly, this effect was found for both the trained and the untrained characters. This finding is consistent with previous studies reporting successful identity decoding for both friends and unfamiliar others in the vmPFC (di Oleggio Castello et al., 2017). Surprisingly, we did not observe higher pattern similarity for trained identities versus untrained identities across runs. This might initially appear to be in contrast with the univariate effect in the vmPFC, however, it should be noted that correlation-based RSA analyses rely on the voxel level variability across conditions. On the other hand, univariate effects sensitive mainly to the mean activation differences across conditions (Davis et al., 2014). Future studies will be needed to better understand the neural coding mechanisms of schematic processing. One potential explanation for this pattern similarity finding is that the repeated exposure to the untrained characters allowed participants to make impressions about their identities (Todorov et al., 2015). Nevertheless, taken at face value, our RSA results, and the finding of di Oleggio Castello et al., (2017), are inconsistent with the view that the vmPFC plays a preferential role in processing stimuli associated with schema-related knowledge.

We also observed training effects on overall activation level in both the anterior (head) and posterior (body and tail) hippocampus. These effects were not significant at the whole-brain level but were present when considering average activity levels within the pre-defined ROIs. According to recent suggestions, these two sub-regions of the hippocampus process information at different levels. The posterior hippocampus is thought to process information at more detailed perceptual level, whereas the anterior hippocampus might support coarser gist-level semantic information (Poppenk et al., 2010; Preston & Eichenbaum, 2013; Robin & Moscovitch, 2017). Based on these suggestions we might have expected that the anterior hippocampus might better differentiate between training conditions as it might reflect the gist-level information. Moreover, several studies contrasting responses to famous and non-famous faces have found effects in the anterior hippocampus and adjacent regions of the amygdala (Elfgren et al., 2006; Trinkler et al., 2009; Von Der Heide et al.,

2013). However, our photo stimuli depicted not only the characters themselves, but also their apartments, which were familiar to participants after training. Since the posterior hippocampus is more associated with processing spatial contexts (Nadel et al., 2013; Ranganath & Ritchey, 2012; Strange et al., 2014), this might explain why activity in this region was also modulated by training.

The higher hippocampal activation for the trained characters may be due to spontaneous reinstatement of episodic memories about the show (see also Ishai, 2008; Ishai et al., 2002; Trinkler et al., 2009), rather than simply the activation of associated schematic knowledge. This suggestion is in accordance with findings that famous names can be associated with personal memories (Renoult et al., 2012; Louis Renoult et al., 2015; Westmacott et al., 2004; Westmacott & Moscovitch, 2003). This in turn might contribute to the (modest) boost in recognition performance for the pictures of trained individuals. Indeed, a number of studies have shown that learning new information which is related to prior experience was supported by the hippocampus (Liu et al., 2016; Poppenk et al., 2010; Preston et al., 2004; Sommer, 2016; Tse et al., 2007, 2011). However, the present study cannot provide direct evidence for the nature of the relationship between episodic recollection, schematic knowledge activation and memory for new information.

Some models propose that the hippocampus and vmPFC have competing roles. The SLIMM model proposes that the vmPFC monitors whether the current experience is related to prior schematic information and engages different memory processes depending on the amount of congruency with prior knowledge. By contrast, the medial temporal lobe, including the hippocampus, is involved in memory processing of novel information, but not of information strongly related to prior knowledge (van Kesteren et al., 2012). Therefore, according to the SLIMM model we might have expected to have seen stronger vmPFC response for the trained pictures and a stronger hippocampal response for the untrained pictures. In fact, we found that (1) the response in both the anterior and posterior hippocampus was greater for trained versus untrained pictures, and (2) that the trained versus untrained effects were not significantly different between the vmPFC or either hippocampal ROI. These findings are inconsistent with the SLIMM model. However, our findings are

consistent with other studies reporting increased hippocampal involvement for prior knowledge effects from a range of tasks (Liu et al., 2016; Sommer, 2016; Zeithamova et al., 2012). More broadly, our findings lend support to accounts of memory processing that view the roles of the vmPFC and hippocampus as being complementary (e.g. Robin & Moscovitch, 2017) or working together under situations with moderate levels of prior knowledge (Gilboa & Marlatte, 2017).

Given that prior schematic knowledge modulates activity in the vmPFC and hippocampus to a similar degree, future studies will be needed to better understand the nature of their roles in schema-based semantic and episodic memory processes. For example, both the vmPFC and the hippocampus have been shown to be involved in episodic memory retrieval (e.g. see McCormick et al., 2018). However, they seem to process information at different levels of abstraction. Partial damage to hippocampal regions is associated with loss of detailed memories, but preserved gist, or story level memories (St-Laurent et al., 2014). On the other hand, damage to vmPFC is often associated with problems in schematic processing (Ciaramelli et al., 2006; Melo et al., 1999; Spalding et al., 2015; Warren et al., 2014). Nonetheless, it is important to note that schematic processing has rarely been examined in patients with hippocampal damage and more research is needed to understand how vmPFC lesions affect episodic memory (see McCormick et al., 2018 for review). An open question for future studies is to examine to what extent encoding of new information related to prior schematic knowledge depends on episodic memory retrieval (see Zeithamova et al., 2012).

Beyond the effects in the vmPFC and hippocampus, two further regions warrant mention. First, there was an increase in activation for pictures of trained versus untrained characters in the retrosplenial cortex. Posterior midline regions including the retrosplenial cortex are strongly implicated in processing known versus unknown entities (e.g. Liu et al., 2016; Von Der Heide et al., 2013) and are also frequently identified in studies that have manipulated prior knowledge (e.g. Ames et al., 2015; Maguire et al., 1999). Although posterior midline regions have attracted less attention than the vmPFC in schema processing, it is possible that they nevertheless play an important role in linking

incoming information with prior knowledge (see also Bird et al., 2015). The second region is the left fusiform gyrus, as this was the only brain region in our study to show significant identify-specific RSA effects that were greater for trained compared to untrained characters. This is a region strongly implicated in face processing (Kanwisher et al., 1997) and other studies that have examined prior knowledge for faces have also often observed effects here (e.g. see Brod et al., 2016; Liu et al., 2016; Schlichting & Preston, 2016). Interestingly, a study by Axelrod & Yovel (2015) also found that a region in the fusiform gyrus was the only place where the identify of famous faces could be decoded from patterns of BOLD activity. The mechanism underpinning these findings is unclear, but it is possible that familiarity with a person "sharpens" the representation in this region, resulting in increased pattern similarity. Follow-up studies could examine whether different types of category-specific schematic knowledge result in representational similarity effects in other specialised cortical regions (e.g. locations in the parahippocampal gyrus).

It may seem surprising that we did not observe more widespread RSA effects of location. Only one region (within the left postcentral gyrus) showed greater similarity for the same compared with different locations. However, it should be noted that all of the locations were highly similar – all being apartments belonging to a young married couple. Although the locations could be living rooms or kitchens, during the training episodes participants saw a lot of scenes involving the characters moving from one to another. This could have led to a highly associated representation of these locations. Our result contrasts with studies that have observed robust and widespread location similarity effects, which have often used locations that are distinctive and unique to different episodes (e.g. Robin et al., 2018). Furthermore, the participants' task was to detect the oddball pictures of elderly individuals, which potentially directed their attention more to the faces present in the picture rather than the locations.

In sum: our results further support the neurocognitive theories that suggest a role for both the vmPFC and hippocampus in schema-based processing of new information and they also identify the posterior midline cortex in as an additional region associated with person-specific schematic knowledge.

Our study employed a novel paradigm to enable participants to acquire novel schema in a naturalistic manner. New schematic knowledge boosted performance on tests of episodic memory for previously unseen pictures and short videos. The finding that prior knowledge increased activity in both the vmPFC and the hippocampus to similar extent is at odds with the SLIMM account of memory processing. Future studies are needed to establish the effects of the specific content and richness of schema knowledge on the involvement of particular brain areas.

3.6 Supplementary Materials
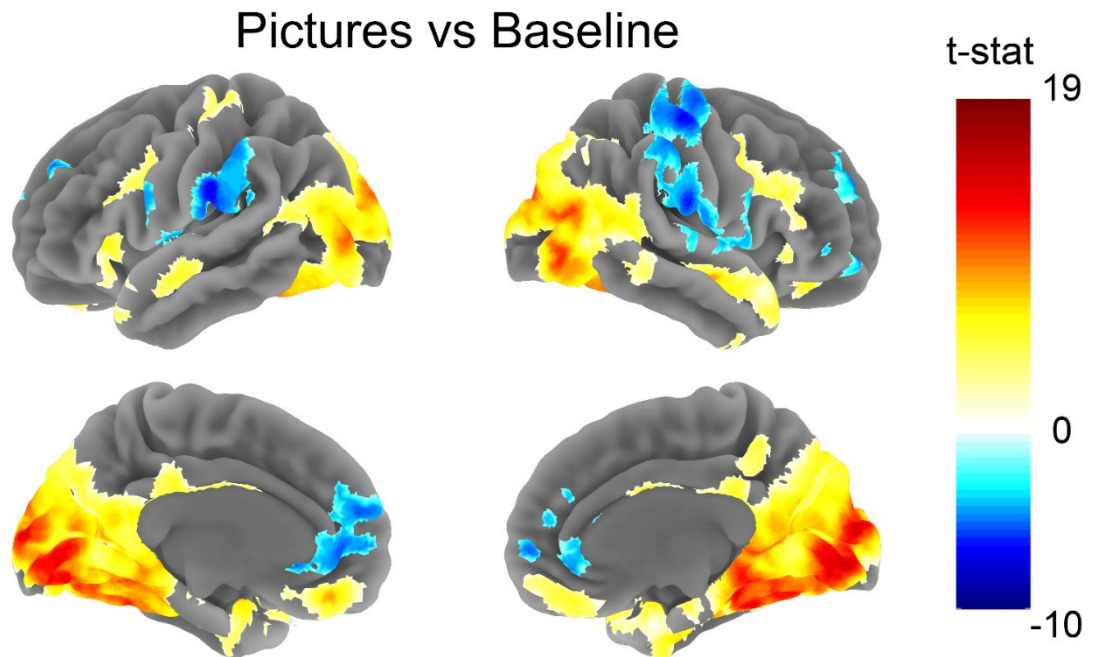
Supplementary Figure 3-1 *Picture Contrast*. Brain regions with higher activation for watching pictures (both trained and untrained) versus the odd-even number judgment baseline task. The map is FWE cluster corrected with a voxel threshold p < 0.001.

A Stranger's Death				
	Who did Dharma Meet?	**1. George**	2. David	3. Britney
	Where did she meet him?	1. On the street	2. In their apartment	**3. On the roof**
	Why does he have to die here?	1. Because it is where he was born	2. Because it is his old place	**3. Because the spirits could guide his soul**
	How does Dharma respond when Greg says it is incredible	**1. She says it is awesome**	2. She says it sounds bad	3. She argues with him
	What is Greg wearing?	**1. A suit**	2. A T-shirt	3. Winter Jacket

Supplementary Figure 3-2 *Example questions for a single video clip.* The title indicates for which video the questions are. The participants see each question one after the other and have to make a choice between three provided options. The highlighted options are the correct answers (they were not presented to the participants).

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Chapter 4: Person related schema knowledge during processing of complex events

4.1 Abstract

To comprehend the world around us we often rely on our prior knowledge. Schema knowledge about a friend can help us understand and predict how they will typically act. Apart from our perception, schemas could also affect how we later remember information. Here we focused on how person related schematic knowledge will affect the encoding and retrieval of naturalistic events. Participants were familiarised with the lead characters of one out of two TV shows. Over the course of a week, participants watched 6 episodes in order to acquire schematic knowledge about the main characters from one of the shows. Inside the scanner, participants watched and retrieved novel short clips taken from both the show they were trained on and the show that was completely unfamiliar to them. Outside the scanner participants performed a memory test for the clips. Schema knowledge boosted memory performance. Surprisingly, we did not observe any modulation of memory reinstatement effects by schema knowledge. However, we show shared patterns of activity for the trained clips in medial prefrontal cortex (mPFC), angular gyrus (AG) and superior frontal gyrus (SFG). These results further extend previous work showing that mPFC, AG and SFG might be particularly important for supporting schema representations during naturalistic perception.

4.2 Introduction

The use of video stimuli, in Chapter 2, allowed me to examine how situation specific prior knowledge affects ongoing processing of events. Apart from examining situation specific knowledge, I also used naturalistic stimuli in a week-long familiarization procedure to examine the effects of schematic prior knowledge (Chapter 3). In Chapter 3, I used still picture stimuli in order to have a better comparison with previous literature on schematic knowledge. However, a sensible extension is to also examine the effects of schema knowledge on complex stimuli. Here I report, data from the same participants (as in Chapter 3), who underwent the week-long familiarization with a TV show, but performed a video task inside the scanner. The use of a video task allowed me to examine what effects schematic knowledge would have on the processing of dynamic stimuli, which is something that has not been extensively examined previously. In this chapter I report data from participants who watched and retrieved novel short clips taken from a familiar or unfamiliar show (see Figure 4-1). Below I introduce some of the rationale for the study.

Schema knowledge is thought to bias how we process new information that is related to our prior knowledge. However, this has rarely been examined using naturalistic stimuli. A recent study by Baldassano et al., (2018) investigated the brain regions that are involved in a particular aspect of knowledge schemas – "scripts" (Bower et al., 1979; Mandler, 1984; Schank & Abelson, 1977). Scripts describe familiar situations and comprise the locations, likely individuals and objects present, as well as the typical order of actions (see also Ghosh & Gilboa, 2014). Baldassano and colleagues scanned participants while they listened to audio clips or watched video clips which depicted scenes taking place at an airport or in a restaurant. Although the scenes were taken from different genres and featured very different characters, remarkably consistent patterns of fMRI activity were observed when the clips corresponded to the same underling scripts. For example, the pattern of activity across medial prefrontal cortex, angular gyrus and posterior midline regions was similar when participants viewed or listened to clips involving the ordering of food in a restaurant.

Scripts constitute a major framework for understanding events, with Schank and Abelson (1977) arguing that "most of understanding is script-based". However, schemas can also relate to particular individuals, enabling us to anticipate how an individual is likely to act in a particular situation. For example, we may have a script for "waiting for a delayed train to arrive" but predicting how a specific individual will act in this situation will depend on our knowledge of their temperament, which is typically acquired after observing that individual in a range of different situations. How is such knowledge activated when processing novel events and what are the brain regions responsible? Here we address this question.

We further examined whether schema knowledge about people will affect retrieval of complex events. Recent neuroimaging experiments have shown that patterns of activity during retrieval of a stimulus are similar to patterns that were elicited during encoding of the same stimulus. Such pattern reinstatement effects during retrieval have been observed in a range of tasks (Danker & Anderson, 2010; Deuker et al., 2013; Staresina et al., 2013). Indeed, they have been demonstrated for complex video stimuli (Bird et al., 2015; Chen et al., 2017; Oedekoven et al., 2017; St-Laurent et al., 2015). Interestingly, higher reinstatement has been associated with better memory performance (Bird et al., 2015; Oedekoven et al., 2017). Schemas can affect how we learn and later retrieve new events (see for reviews see Gilboa & Marlatte, 2017; van Kesteren et al., 2012). Information that is consistent with our schema knowledge is often remembered better (DeWitt et al., 2012; Gilboa & Marlatte, 2017; Liu et al., 2016; Sommer, 2016), but see (Bartlett, 1932; Oren et al., 2017). Therefore, we hypothesised that person related schema knowledge would be associated with better retrieval and stronger reinstatement effects for complex events. Specifically, we hypothesised that we would observe higher pattern similarity between encoding and retrieval of trained versus untrained events.

We investigated the effects of training using univariate and multivariate analyses. Apart from whole-brain analyses we also examined the univariate response in ventromedial prefrontal cortex (vmPFC), hippocampus and retrosplenial cortex (RSC). Based on previous findings (Liu et al., 2016; Chapter 3), we predicted that vmPFC and hippocampus would show higher

activity for the trained clips. We also ran exploratory analyses examining whether these regions would also differentiate between retrieving trained and untrained clips. Multivoxel analyses allowed us to replicate previous reinstatement effects and examine whether our training manipulation affected how activity is reinstated during retrieval. Using a conceptually similar analysis to Baldassano et al. (2018) we were also able to investigate whether there are spatial patterns of activity shared across all trained encoding videos when compared to the untrained videos. Our reasoning for this analysis was that if there is schema instantiation for the trained clips, they should be more similar to one another compared to the untrained clips.

4.3 Methods

4.3.1 Participants

Here we report data from participants that were also included in Chapter 3. Twenty-eight participants (15 females) were included into the analyses. Mean age was 21.71 (± 3.08). For more details see Chapter 3.

4.3.2 Stimuli

Twenty short clips were taken from two US shows ("Mad about you" – MaD and "Dharma and Greg" - DG) to be used in the scanning session. All clips used in the scanning session were chosen to represent unrelated self-contained short situations. The clips were taken from previously unseen episodes and were all in unique and unfamiliar locations (e.g. the museum). The duration of the 10 clips from the MaD show (32.7 ± 6.73) were on average the same duration as clips from the DG show (33.4 ± 7.87) (p = .833). The audio for the clips was scaled to the same mean decibel intensity with Praat (version 6.0.15) (Boersma, 2001). All clips were made black and white.

4.3.3 Procedure

See Chapter 3 for more detailed procedure on the familiarization. Participants carried out 4 functional runs within the scanner. The first and last of the 4 runs included a picture task and the results from these data are reported elsewhere (see Chapter 3). The middle 2 runs are the focus of this chapter. Each run was approximately 16 minutes long. In each run participants viewed and recalled 10 clips in total (5 from trained show and 5 from untrained show). Participants viewed and recalled the clips in sets of 5 (e.g. encode 5 videos and then recall these 5 clips) (see Figure 4-1A). Within each set there were both trained and untrained clips presented in random order. Before each video participants were presented with a title associated with the video (e.g. A Stranger's Death) for 3s (see Figure 4-1B). Participants were made aware the title would act as a memory cue later on and were asked to pay attention to it. The title was followed by a red cross that allowed us to TR lock the onset of the clips. Each clip was followed by a 2s white fixation cross after which participants were asked to make an odd/even number judgment during an

active baseline task (see Chapter 3 for task description) (Stark & Squire, 2001). A white fixation cross lasting for 400ms was presented before the onset of the next title. After encoding the 5 videos participants had to silently recall the videos in random order. Participants were presented again with a title associated with one of the videos they just watched (A Stranger's Death) for 3 seconds in blue font (see Figure 4-1C). The title was then followed by a text cue asking them to recall the video. The recall cue stayed on the screen until participants made a response to indicate finishing recalling or until 30 seconds. The recall cue was followed by a white fixation cross presented for 1500ms. In-between the recall trials, participants again made odd/even number judgments for 4 numbers accumulating for a total of 11s. After completing each of the four sets of 5 encode and 5 recall videos participants were presented with 4 visual analogue scales on which they rated their familiarity with the 4 main characters. Each scale was presented for 6 seconds and participants rated from 0 to 100 how familiar they felt with each character (e.g. Dharma). Familiarity ratings for the characters were than averaged separately for each show and each set (4 sets in total).
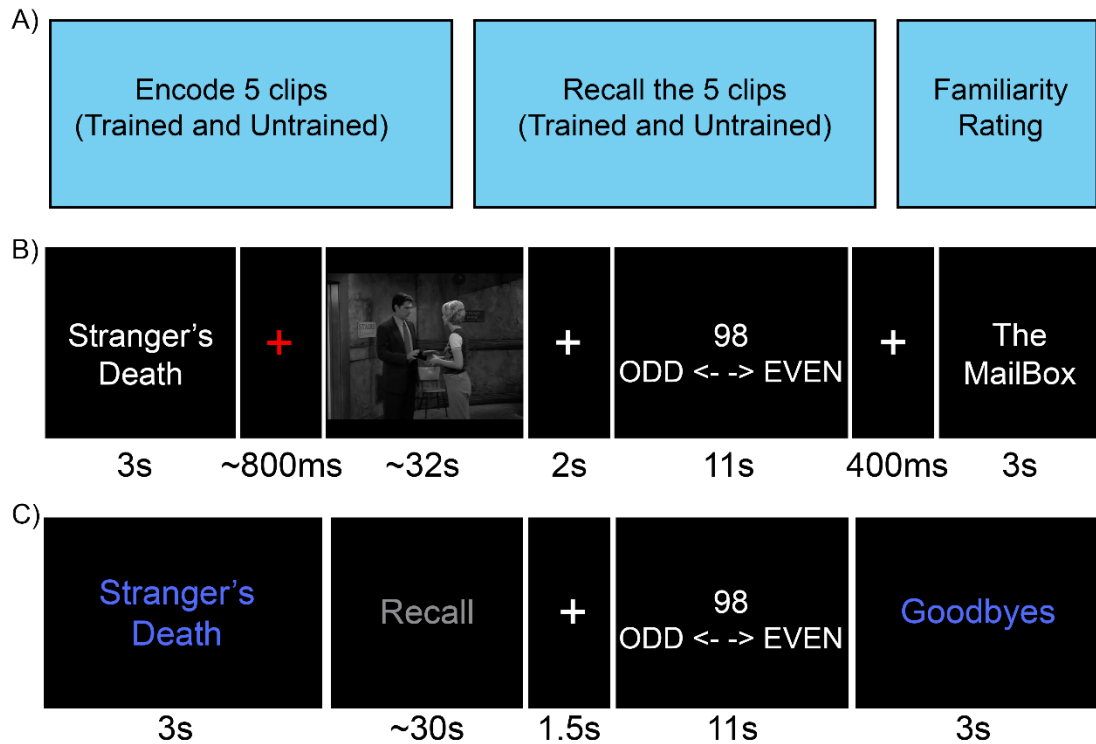
Figure 4-1 *Schema of Study Design*. Before the experiment participants were familiarised with one out of two shows. Participants viewed and recalled novel clips from the trained and untrained show. A) Participants initially viewed 5 clips taken from both the trained and untrained show, and later recalled the 5 clips in random order. After each set of 5 clips participants rated their familiarity with the characters in the videos. A run included two sets of 5 clips and there were four sets for the whole experiment (2 runs; 20 clips in total). B) Shows the timings for encoding part of the experiment. Note all clips were in novel locations not seen in any of the familiarisation episodes and were made black and white. C) Shows the timings for the recall part of the experiment. Participants made an odd-even judgment in between each event (encode/recall).

Memory for the clips was tested outside the scanner (see Chapter 3). The title of the video was used as a memory cue. Participants' memory was tested with a three-alternative forced-choice test concerning details from the video. There were 5 multiple-choice questions for each of the 20 clips (10 trained and 10 untrained). The sets of 5 questions for each clip were presented in a pseudo-random order so that there were no more than 3 consecutive clips from the same show. For each subject the average accuracy for the trained clips was contrasted with the average accuracy for the untrained clips with a paired sample t-test. Participants also made vividness and engagement judgments for each of the clips. These judgments were made before participants completed the accuracy questions.

4.3.4 MRI acquisition

T2*-weighted fMRI images were acquired on a 3T Siemens Prisma scanner using a 32-channel head-coil. To minimise movement, soft cushions were inserted into the head coil. A gradient-echo EPI sequence with multiband acceleration factor of 8 with the following parameters (TR = 0.8s; TE = 33.1ms; 52 degree flip angle; FOV = 208x180mm; 72 sliced with sliced thickness of 2mm and isotropic 2mm voxels). The same parameters were used to acquire two SpinEcho Fieldmap runs with reversed phase-encode blips in both Anterior to Posterior and Posterior to Anterior directions. These pairs of images were used to estimate the distortion field map using a method similar to Andersson (2003) as implemented in FSL. A T1-weighted high-resolution structural image was acquired with 3D MPRAGE sequence (TR = 2.4 seconds; TE = 2.14 seconds; 8 degree flip angle; FOV = 224x224mm and 0.8mm isotropic voxels).

4.3.5 Image pre-processing

We used SPM 12 (Wellcome Department of Imaging Neuroscience, London, UK) to pre-process all of the images except the field maps. Images from both sessions were spatially realigned to the mean functional image to account for any motion. Command-line functions from FSL (Smith et al., 2004) were used to estimate and apply field maps to the motion corrected data in order to correct for image distortions (Andersson et al., 2001). The high-resolution structural image was coregistered to the mean functional image and was segmented into grey, white matter and cerebrospinal fluid using tissue probability maps. The segmented images were used to estimate deformation fields, which were applied to the functional images in order to transform them to MNI space. A 6mm FWHM smoothing kernel was applied to the functional images. Unsmoothed normalised images were used for ROI analyses.

4.3.6 Data analysis

Data was analysed with SPM 12, the CosMoMVPA toolbox (Oosterhof et al., 2016), custom scripts in MATLAB (Version 2017b, The MathWorks, Inc., Natick, MA, USA). All analyses were conducted on MNI normalised images. The RobustWLS toolbox in SPM 12 was used to estimate the first level models (Diedrichsen & Shadmehr, 2005). This method provides a "soft" exclusion of

bad volumes by downweighting volumes with high variance estimates. We used the Bspmview toolbox (www.bobspunt.com/bspmview) to visualise and describe our data. The toolbox implements MNI coordinates from the Anatomical Automatic Labelling 2 toolbox for SPM 12.

4.3.7   Whole-brain analyses

We first carried out whole-brain random-effects analyses across participants. First-level contrast images in MNI space were evaluated with one-sample t-tests. Unless otherwise stated results were thresholded in SPM using cluster-level family-wise error correction (p < .05), with a cluster-defining threshold of p < 0.001.

4.3.8   ROI definition and analyses

Various theories have implicated the hippocampus in schematic processing. Particularly recent theories have argued about a division of labour across subregions of the hippocampus. Anterior hippocampus has been argued to represent more abstracted and gist level information whereas, posterior hippocampus has been proposed to process more detailed information (Preston & Eichenbaum, 2013; Ritchey et al., 2015; Robin & Moscovitch, 2017). We used the bilateral head of the hippocampus as one regions of interest and the combined body and tail of the hippocampus as a separate region of interest. These regions were defined based on segmentation carried out by Ritchey and colleagues (2015) that is available at www.neurovault.org.

We also used the vmPFC and RSC as regions of interest since they have often been associated with schematic processing (Gilboa & Marlatte, 2017; Liu et al., 2016). Both ROIs were defined as the suprathreshold clusters for training effect identified in the group analysis of the picture task from the same participants (see Chapter 3).

Furthermore, in order to keep in line with previous studies, we examined schema effects in a set of regions from the default mode network, including the mPFC, angular gyrus, and posterior cingulate cortex. Similarly to Baldassano et al. (2018), we also examined schema effects in the superior frontal gyrus, superior temporal sulcus and parahippocampal gyrus. The posterior cingulate

cortex (PCC) was defined from previous studies from our lab that have shown reinstatement effects for complex events (Bird et al., 2015; Oedekoven et al., 2017). The mPFC region was defined based on a resting state connectivity atlas (Shirer et al., 2012). Specifically, it was defined as the medial frontal region from the "dorsal default network" set. We used the AAL atlas and the WFU atlas pick toolbox to define the bilateral angular gyrus (AG), and parahippocampal cortex (PHG). The superior frontal gyrus (SFG) and superior temporal sulcus (STS; posterior division) were defined from the Harvard Oxford cortical atlas (https://neurovault.org/images/1699). Any overlap from the superior frontal gyrus (SFG) ROI to the MPFC ROI was removed from the SFG.

4.3.9 GLM analyses

For the univariate analyses we included a single task regressor for each of the 4 conditions (Trained Videos, Trained Recall, Untrained Videos, Untrained Recall). The title cues were modelled with a single regressor of no interest and an additional regressor for the VAS was included. The regressors included the onset and whole duration of events (clip or recall). Unsmoothed contrast maps were used for the ROI analyses. For multivariate analyses we ran separate first-level models where we modelled each video (20) and recall (20) event with a separate block regressor, which covered the whole duration of the video or recall event. This allowed us to examine video specific patterns and whether these patterns were reinstated during recall. These patterns were left unsmoothed for the within subject RSA analyses.

4.3.10 Representational similarity analysis (RSA)

We investigated the similarity between spatial patterns of BOLD activity when people were watching and recalling the same videos using an RSA (Kriegeskorte et al., 2008). Furthermore, we investigated spatial pattern similarity across videos from the same training conditions. We ran whole-brain searchlight analyses on unsmoothed normalised t-map images with a searchlight radius of 4 voxels (mean 235 voxels). In the first type of analyses we were interested in a general reinstatement effect. We compared the spatial pattern similarity between matching encoding and retrieval patterns (encode video 1 and retrieve video 1; see diagonal Figure 4-2A) versus the similarity

between mis-matching encoding and retrieval patterns (encode video 1 and retrieve not video 1; see off-diagonal Figure 4-2A). Higher similarity between matching encoding and retrieval patterns would suggest that there is reinstatement of the video specific encoding patterns during recall.

To investigate how these reinstatement effects were modulated by memory accuracy we focused on the encode-retrieve patterns for matching videos. We weighted these values positively and negatively depending on memory accuracy ratings, such that the diagonal values summed to zero. To achieve this, we subtracted from each video accuracy score the average subject memory accuracy (see Figure 4-2). Therefore, positive values are assigned to videos for which a participant exhibited better than average recall. This contrast allowed us to examine areas where the reinstatement effect correlates with richness of retrieval. These general reinstatement analyses were conducted largely with aim to replicate previous findings (see Bird et al., 2015; Oedekoven et al., 2017). Similarly, to previous studies, we also ran these general reinstatement analyses within a region of interest encompassing the PCC.

One of our main interests was to investigate whether the reinstatement effects were affected by our training manipulation. Specifically, we examined whether encode-retrieve similarity was higher for the trained clips versus the untrained clips (see Figure 4-2B). This analysis focused only on the encode-retrieve similarity patterns for matching videos.

Apart from reinstatement RSAs we also investigated the spatial pattern similarity across videos. We directly compared whether spatial patterns for the trained clips are more similar among each other than patterns for the untrained clips (see Figure 4-2B) during encoding. This analysis allowed us to investigate whether there are regions showing schematic effects during encoding of the trained videos. If participants developed schemas for the trained show but not for the untrained show and they instantiated these schemas for each of the trained clips, we would expect this analysis to show areas with higher spatial pattern similarity across trained clips. Importantly, each clip had a unique topic of conversation and was set in a unique previously unseen location (e.g.

museum). We also ran this analysis in predefined ROIs. Specifically, we ran the analyses in mPFC, hippocampus, PCC, parahippocampal cortex (PHC) and bilateral angular gyrus (AG).

For each searchlight sphere we computed the multi-voxel spatial pattern similarity across pairs of trials using correlation. Normalised unsmoothed t-maps for each of the encoding and/or retrieval videos trials were used. The Pearson correlation values were then Fisher transformed and weighted according to a contrast matrix (see Figure 4-2). The resulting weighted average value was assigned to the center voxel of the searchlight. The searchlights spheres were with a radius of 4 voxels (mean 235 voxels size). Different contrast matrixes were used for different analyses. Note that for the last RSA analyses we compared the similarity across encoding videos within-subject, which resulted in symmetric correlation matrixes with a diagonal of 1s. Therefore, our contrast matrix focused only on the lower triangle of the matrix.
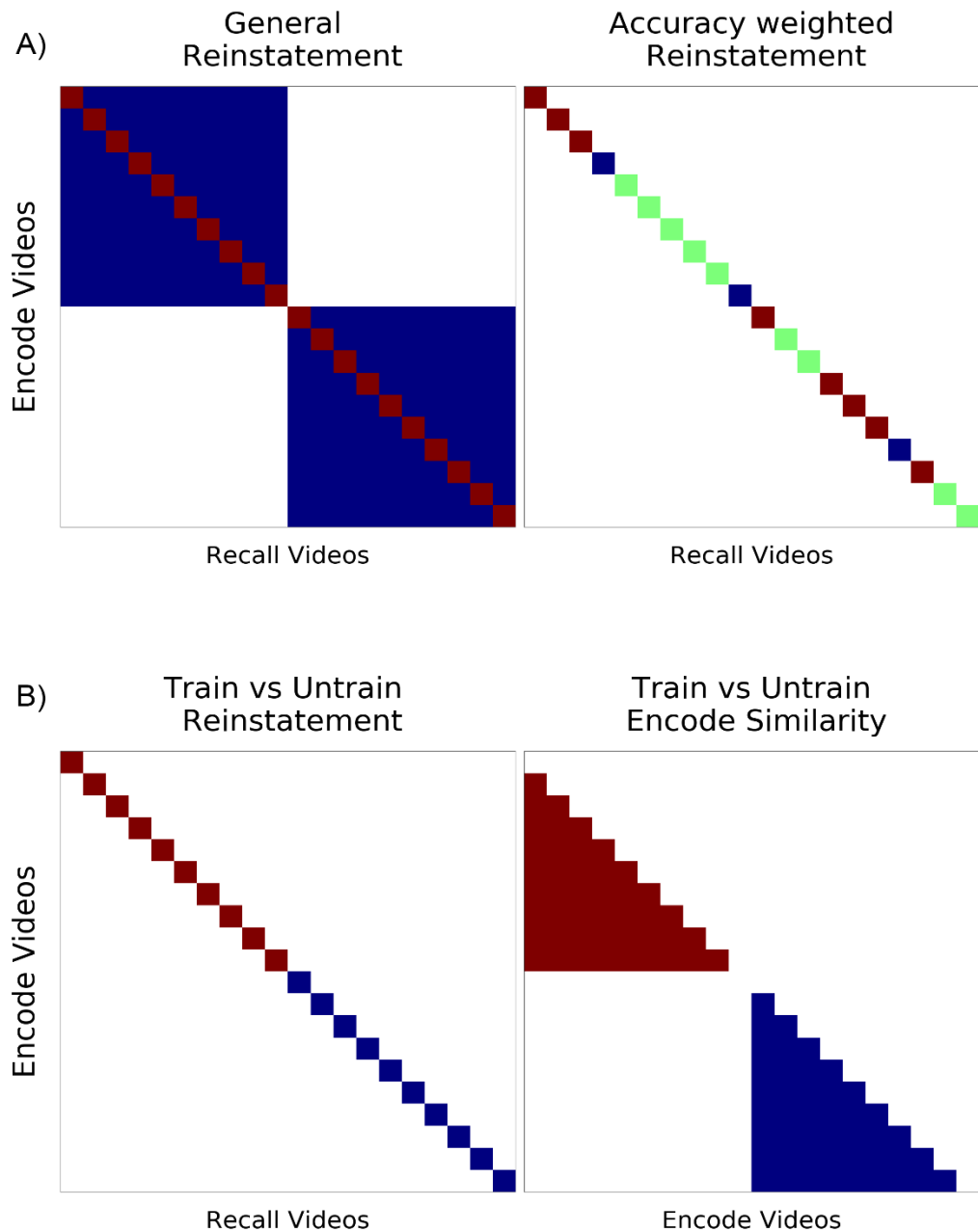
Figure 4-2 *Contrast Matrixes RSA.* The contrast matrixes used for the RSAs are shown above. Red indicates positive weighting and blue indicates negative contrast values. **A)** shows contrast matrixes examining general reinstatement regardless of training. The matrix on the left tests for video specific reinstatement effects. The matrix on the right examines where reinstatement effects are correlated with more accurate recall. Different colours represent positive or negative weighting of reinstatement effects dependent on memory accuracy scores. Red indicates positive weighting, blue and green indicate different magnitudes of negative weighting. A different weight matrix was constructed for each subject to take into account their memory performance. **B)** Shows matrixes testing for training effects. The matrix on the left tests for regions showing higher reinstatement for the trained clips. The matrix on the right examines the similarity between clips during encoding. It tests if clips from the trained show are more similar to each other than clips from the untrained show.
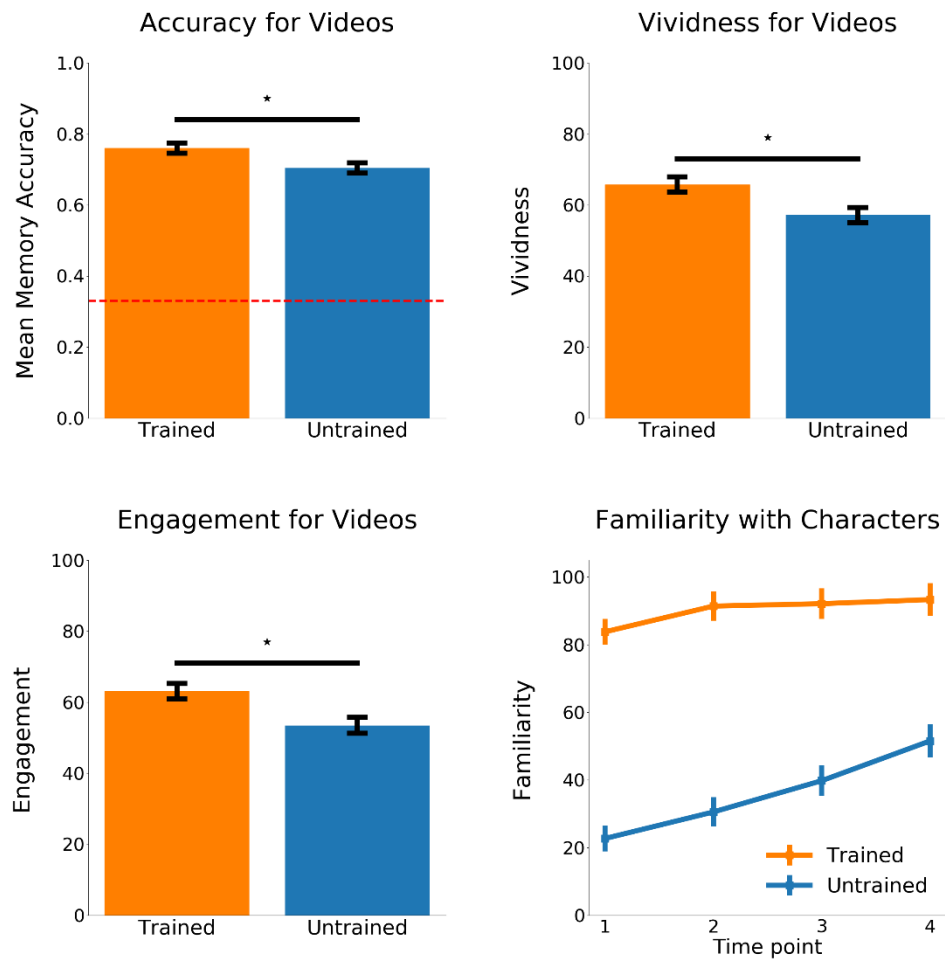
Figure 4-3 *Behavioural Results.* Bar graphs show memory accuracy for the clips from the trained and untrained shows. Subjective vividness and engagement ratings are also shown. Dashed red line indicates chance performance (33%) for the memory test. Stars indicate significance below p < 0.01. The line graph shows familiarity ratings for each show (averaged over the characters in each show) after each set of 5 clips. Familiarity ratings after each set were significantly higher for the trained characters when compared to the untrained characters. Graphs represent means and standard errors.

4.4 Results

4.4.1 Behavioural results

Participants had a high overall accuracy for the memory questions (75%, chance level = 33%). Participants' memory was more accurate for the trained clips (78%) versus clips from the untrained show (72%; t_{27} = 3.5; p = 0.002). Participants also rated remembering the trained clips more vividly (t_{27} = 3.67; p

= 0.001) and found them more engaging (t_{27} = 3.94; p < 0.001) (see Figure 4-3). Familiarity ratings showed that, although participants felt they knew the characters from the untrained show more after watching the videos, they still did not feel as familiar as the characters from the trained show (see Figure 4-3).

4.4.2 Imaging results

4.4.3 Univariate analyses

The whole brain contrast for trained versus untrained videos did not show any significant clusters. Furthermore, the ROI analyses also did not show differences across the trained and untrained videos [VMPFC: t_{27} = 0.86; p = 0.19 one-tailed; Hippocampus Head: t_{27} = 0.36; p = 0.36; Hippocampus body and tail: t_{27} = -0.11; p = 0.45; RSC: t_{27} = 1.50; p = 0.07 one-tailed]. These results are somewhat in contrast to previous work (Liu et al., 2016; see also Chapter 3). However, we note that modelling the whole duration of a clip with a box-car might not be optimal. We ran exploratory analysis examining the BOLD responses at the onset of the videos. This contrast showed that there was higher BOLD activity in vmPFC, the head of the hippocampus and the RSC ROIs for the trained versus the untrained clips (see Supplementary materials). Given the exploratory nature of this analysis future work will be needed to if confirm such onset effects are robust. The contrast between trained and untrained recall events did not show any significant clusters at the whole brain level or across the ROIs (all ps > 0.30).

4.4.4 RSA

The general reinstatement RSA analysis identified regions in which there was video specific reinstatement of encoding spatial patterns during retrieval. This analysis revealed significant clusters in bilateral angular gyrus, left middle temporal gyrus, left medial frontal gyrus, and right middle cingulate (see Figure 4-4 and Table 4-1). These results largely replicate previous whole brain findings from our lab (Bird et al., 2015; Oedekoven et al., 2017). We also examined the general reinstatement effect in an independently defined PCC ROI and found a significant video specific reinstatement effect (t_{27} = 2.47; p = 0.02), which is in line with previous findings.

The general reinstatement weighted by memory performance revealed significant clusters through large parts of the brain. Spatial patterns of reinstatement correlated with memory accuracy in bilateral temporal poles, inferior frontal gyrus (IFG), left middle temporal gyrus, middle cingulate, left medial frontal gyrus and right middle frontal gyrus (see Figure 4-5 and Table 4-2). The PCC ROI also showed a significant correlation between reinstatement effects and memory accuracy ($t_{27} = 3.54$; $p = 0.001$), replicating previous results from our lab (Bird et al., 2015; Oedekoven et al., 2017).

Surprisingly, we did not find any significant clusters at whole-brain level and none of our ROIs showed different reinstatement effects for the trained videos when compared to the untrained videos.

When we compared similarity during encoding for the trained videos, we found several clusters showing significantly higher similarity for clips from the trained show. Trained clips were more similar to each other during encoding in right orbital frontal cortex, right IFG, right superior and middle frontal gyrus (see Figure 4-6 and Table 4-3). When we ran these analyses in our ROIs, we also found that mPFC ($t_{27} = 2.33$; $p = 0.02$), AG ($t_{27} = 2.32$; $p = 0.02$), SFG ($t_{27} = 2.38$; $p = 0.01$) showed significantly higher spatial pattern similarity across the trained clips when compared to the untrained clips. We did not observe these effects in either the head of the hippocampus ($t_{27} = 0.76$; $p = 0.45$), the combined body and tail of the hippocampus ($t_{27} = 1.20$; $p = 0.23$), the PHC ($t_{27} = 0.75$; $p = 0.46$) or the STS ($t_{27} = -0.68$; $p = 0.5$). The PCC ROI showed higher similarity for the trained clips but this effect did not reach statistical significance ($t_{27} = 1.817$; $p = 0.08$).

General Reinstatement
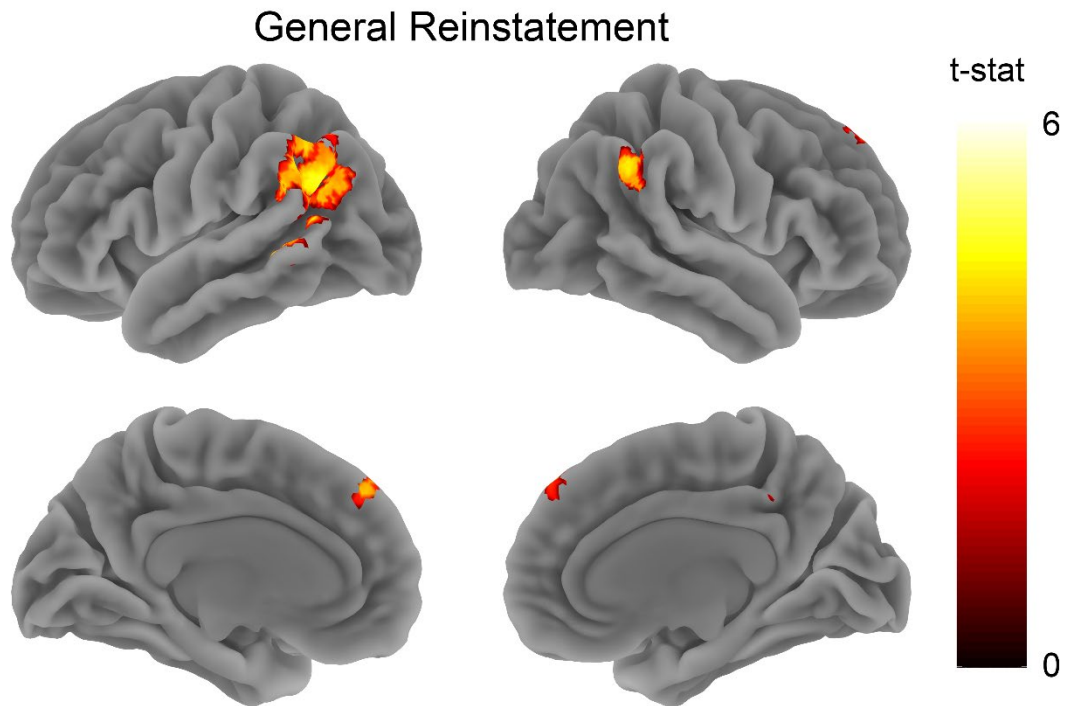
Figure 4-4 *General Reinstatement.* The analysis tested for areas showing higher spatial pattern similarity between encoding and retrieving the same clip vs different clips. Map shows clusters significant after FWE correction at p < 0.05 with voxel defining threshold of p < 0.001.

Accuracy weighted Reinstatement
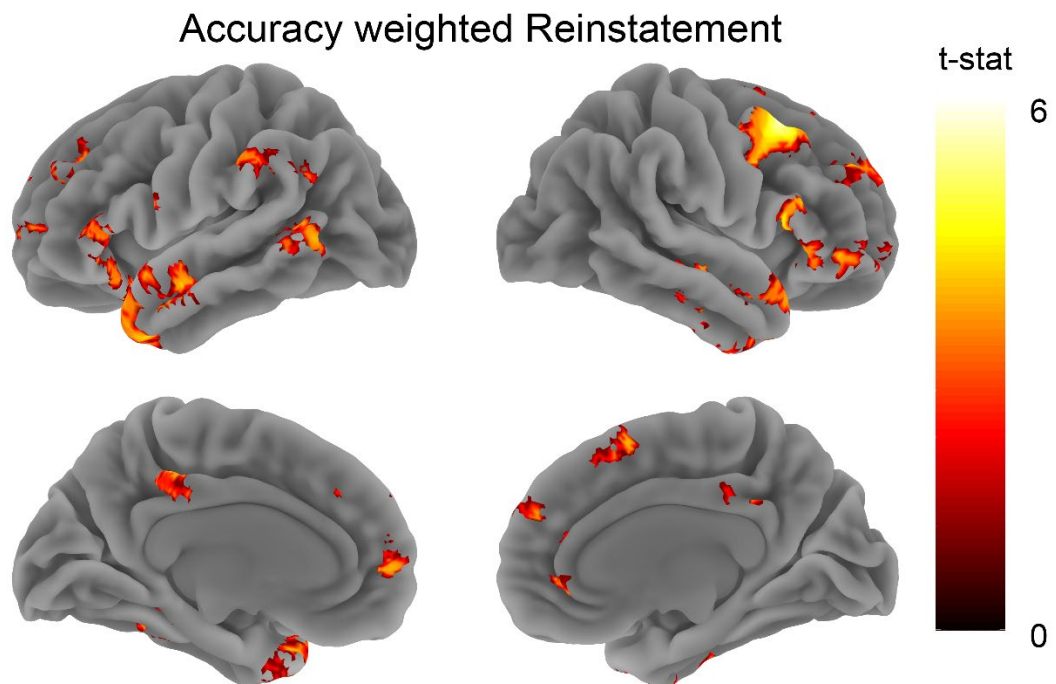
Figure 4-5 *Accuracy weighted reinstatement.* Map shows brain areas where reinstatement effects correlated with memory performance. Map is FWE corrected at p < 0.05 at voxel threshold p < 0.001
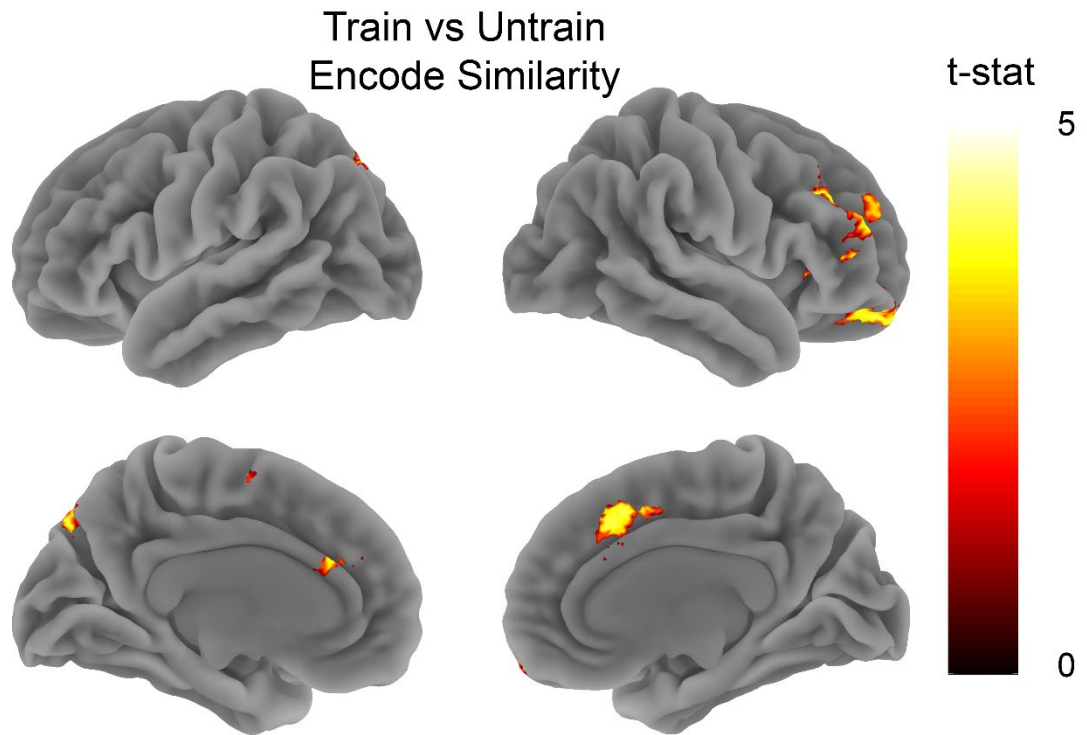
Figure 4-6 *Train vs Untrained Encode Similarity.* Analysis tested for areas showing higher spatial pattern similarity for clips from the trained show when compared to the untrained show during encoding. Map is thresholded at FWE p < 0.05 with voxel threshold of p < 0.001.

Table 4-1 Significant clusters identified for the General reinstatement RSA contrasting encode-retrieve pattern similarity for matching vs mismatching videos. Clusters showing video specific reinstatement effects

Region	x	y	z	Size (voxels)	T
Right Angular gyrus	62	-54	32	394	6.35
Left Angular gyrus	-54	-52	32	1632*	6.11
Left Middle Temporal gyrus	-50	-56	12	1632*	5.42
Left Medial Frontal Gyrus	-2	58	26	494	4.89
Right Middle Cingulate	4	-42	36	74	4.24

Table 4-2 Significant clusters identified for the encode-retrieve Reinstatement RSA correlating with memory accuracy. Clusters are significant after FWE correction at $p < 0.05$ and voxel defining threshold of $p < 0.001$

Region	x	y	z	Size (voxels)	T
Right Middle Frontal gyrus	38	16	52	934	6.85
Left VIII Lobule of Cerebellum	-26	-68	-48	720	6.06
Left Angular gyrus	-50	-60	28	189	4.97
Left Supramarginal gyrus	-60	-32	36	189	4.11
Right Inferior Frontal gyrus	52	20	12	338	5.45
Right Superior Temporal Pole	40	24	-30	242	5.32
Left Middle Temporal gyrus	-52	-2	-18	913	5.11
Right Superior Frontal gyrus	28	64	-2	641	4.20
Left Middle Temporal gyrus	-56	-66	-4	257	5.10
Right Superior Frontal gyrus	22	48	36	485	4.98
Left Temporal Inferior gyrus	-42	-34	-22	259	4.96
Right Middle Temporal pole	38	8	-38	176	4.91
Left Superior Frontal gyrus	-20	40	42	502	4.63
Left Medial Frontal gyrus	-6	56	6	295	4.79
Left Inferior Frontal gyrus	-52	10	18	81	4.45

Table 4-3 Significant clusters identified for the Train vs Untrained Encode similarity. Analysis identified areas showing higher spatial pattern similarity during encoding of trained clips when compared to untrained clips. Clusters showing video specific reinstatement effects.

Region	x	y	z	Size (voxels)	T
Right Middle Frontal gyrus	38	32	34	1025	4.48
Right Medial Orbitofrontal cortex	10	64	-16	542	5.26
Right Inferior Frontal gyrus	46	10	36	121	4.77
Left Anterior Cingulate	-6	30	24	434	4.16
Left Superior Motor Area	-4	-6	62	87	4.55
Left Superior Occipital	-16	-80	40	86	4.45

4.5 Discussion

In this study we investigated the effects of recently acquired schemas on the encoding and retrieval of naturalistic stimuli. We trained participants on one out of two TV shows and afterwards scanned them as they were watching and recalling short clips. This design allowed us to examine how people process new information related to previously acquired knowledge. Behaviourally we found that participants remembered more details about the clips from the trained show and rated them as more vividly remembered and more engaging. During encoding we found out that clips from the trained show were more similar to each other in mPFC, AG, SFG and a set of other frontal regions. Our results are consistent with recent suggestions that mPFC and AG play a special role in schematic processing and further highlight the need for using naturalistic stimuli in such designs.

Although mPFC and AG have often been associated with episodic memory (see Rugg & Vilberg, 2013), we speculate that our results are not due to episodic recall of the training episodes, whilst watching the clips from the trained show. The higher similarity across the encoding clips might imply that participants represented similar information. We think it unlikely that each of the unique clips acted as a memory cue to the same episodic information from the training episodes. Furthermore, our results are largely in agreement with a recent study that placed very little episodic memory demands to examine schema knowledge (Baldassano et al., 2018). Baldassano and colleagues (2018) presented participants with clips taken from different TV shows and clips, but largely associated with two different schemas (airports and restaurants). They observed higher similarity in a set of regions including mPFC, SFG, and AG for clips taken from the same schema. These and our results support proposals arguing that the mPFC and AG are involved in representing abstracted schema information that is not necessarily specific to a single episode (Gilboa & Marlatte, 2017).

Previously little work has been done to better understand whether we maintain schematic representations throughout the whole duration of an event. This was partly due to the use of stimuli that do not contain information

unfolding in time. One of the main advantages of the current design was that we could start addressing questions about the timing of schema representations. For instance, since the whole duration of the clips was modelled our results suggest that the schema representation was maintained throughout the whole clip. According to schema theories people can maintain a general "template" that can act to structure and potentially bias information processing towards schema relevant features present in complex events (Ghosh & Gilboa, 2014; Thorndyke & Yekovich, 1980).

Early evidence that person knowledge can bias information processing comes from a study by Cohen (1981). Participants watched a video clip about the everyday activities of a woman and were told that she was either a waitress or a librarian. Participants remembered better the features from the clip consistent with the occupation label they were provided with before watching the clip. Further support that mPFC may be involved in selecting relevant information comes from a recent study that showed goal-relevant compression of information in mPFC (Mack et al., 2019). It is important to note our design does not allow us to generalize whether schema representations would always be maintained for the whole duration of an event. For instance, it is possible that the role of schema representations varies over events that extend over prolonged periods of time. It would be particularly interesting for future studies to examine how person knowledge is represented in extended clips.

Although the schema information learned in our study was mainly revolving around the main characters, it is likely that mPFC, SFG and AG are involved in processing other types of schema information. For instance, Baldassano et al. (2018) also found that these regions were associated with schema processing using schemas related to locations (airport and restaurant). Furthermore, mPFC and AG have been associated with schematic processing in various studies (see Gilboa & Marlatte, 2017) and these regions have been shown to maintain and integrate complex narrative information at long time scales (Hasson et al., 2015). Interestingly, here although we observed qualitatively higher similarity among trained clips in PCC this effect did not reach significance. This result contrasts with the results of Baldassano et al. (2018) who found evidence for schematic processing in PCC and PHC. One

possible explanation for this discrepancy is the type of schema knowledge used. The airport and restaurant schemas used by Baldassano et al. (2018) are strongly associated with spatial contexts. Both PCC and PHC have been suggested to have preference for processing locations and scenes, which might account for the discrepancy between studies (Epstein & Baker, 2019; Epstein & Vass, 2014; Robin et al., 2018). However, we also note that the schemas used in our experiment were learned over a much shorter span than the restaurant and airport schemas, which are often learned over the course of ones' life. Future studies will be needed to better understand how consolidation can affect schema representations and how different types of schema knowledge are represented in the brain.

Surprisingly, we did not observe schema effects for reinstatement. Given that previous literature has suggested that schema knowledge can affect retrieval (Gilboa & Marlatte, 2017; Liu et al., 2016; Sommer, 2016), we expected to see higher pattern similarity between encoding and retrieval of the trained clips when compared to the untrained clips. Indeed, behaviourally we found higher memory accuracy for the trained clips versus the untrained clips. However, we did not observe reinstatement effects modulated by our training manipulation. Although it is difficult to interpret a null result, we speculate that during retrieval participants focused more on remembering the specific details of the situation and did not rely strongly on the schemas acquired during training. Since the spacing between encoding and retrieval was very small, it is possible that participants had good memory for the clips and did not rely on schematic or semanticised memory representations.

One possibility given our results is that participants maintained a schema representation about the characters during encoding, but later did not rely on such person schema representations for retrieval, as much. Indeed, the use of trained and untrained videos referring to salient situations could have made participants adopt a retrieval strategy that prioritised retrieval of situation specific information rather than schematic information. This suggestion is partly supported from the observed high memory accuracy performance for both the trained and untrained clips. Future studies will be needed to examine how schemas affect retrieval of complex events and whether schema knowledge

should be central to the retrieval task in order to observe schema effects during recall (e.g. Brod et al., 2016).

Notably, when examining general reinstatement regardless of training we largely replicated previous work (Bird et al., 2015; Chen et al., 2017; Oedekoven et al., 2017). We observed memory reinstatement effects in PCC, angular gyrus, middle temporal gyrus and middle frontal gyrus. Furthermore, reinstatement effects were positively correlated with memory accuracy in a set of regions including angular gyrus and PCC.

In summary our results largely support the involvement of mPFC in schema-based processing and further highlight the potential involvement of SFG and posterior regions such as AG. Our results further suggest the need to use naturistic stimuli to better understand everyday schema processing. Indeed, we observed a set of frontal regions showing schema effects. These results are in line with the only other study that used naturalistic stimuli to investigate schema knowledge. It is possible that these regions support maintenance of schema information through the duration of the videos, however, future studies are needed to elucidate this.

4.6 Supplementary Materials

We note that when we modelled only the BOLD response to the first 2 seconds of the videos, we did observe difference between the onset responses for trained and untrained videos (see Supplementary Figure 4-1). The ROI analyses showed that there was a higher response for the onset of trained videos when compared to the untrained videos in the head of the hippocampus (t_{27} = 2.79; p =0.004 one-tailed), vmPFC (t_{27} = 2.07; p = 0.023 one-tailed) and the RSC (t_{27} = 2.53 ; p = 0.008; one-tailed). There was also qualitatively higher onset response for trained videos in the posterior hippocampus (t_{27} = 1.45; p = 0.079 one-tailed), but the effect was not statistically significant. These results are largely in agreement with previous work (Liu et al., 2016; see also Chapter 3). The contrast for recall onsets between trained and untrained events did not show any significant effect at our ROIs (all ps > 0.60). One potential explanation for this result is that it is unlikely that participants where at the same stages of retrieval at the start of each retrieval cue. We note that these results are exploratory and need to be replicated in order to better understand the observed effects.

A) Picture Task
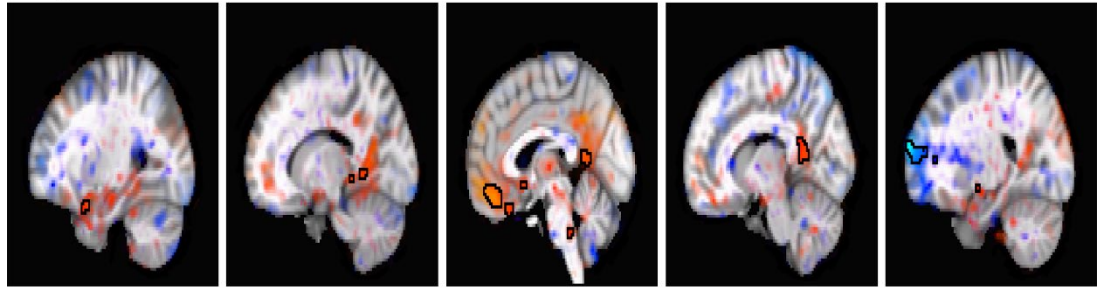
B) Video Task
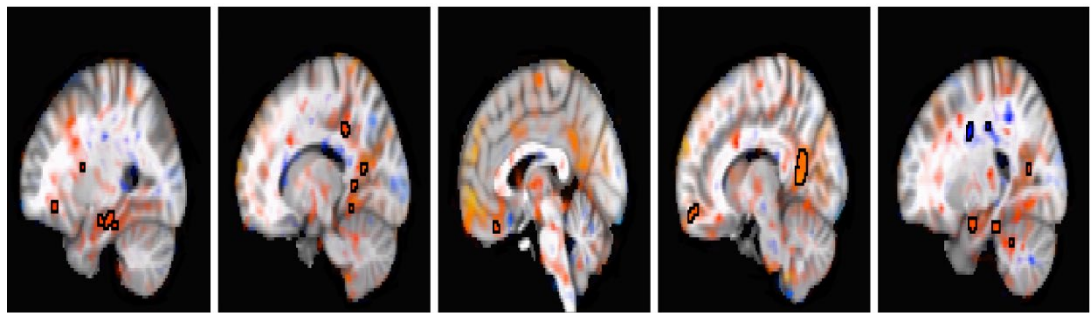
Supplementary Figure 4-1 *Univariate maps of training effects*. Brain map shows contrast between trained and untrained pictures (A) and video onsets (B). Warm colours represent higher activations for the trained pictures or videos. Beta values are mapped to colour hue and t-statistics are mapped to transparency. Higher opacity indicates higher t-statistic. Voxels enclosed within black lines are significant at p < 0.001 uncorrected.

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Chapter 5: An investigation into amodal representations of occupational stereotypes

5.1 Abstract

Knowing that someone is a pilot can already start shaping our perception of them. Social stereotypes can have large influence on our perceptions and opinions about others. Here we ran a pilot experiment to investigate the brain systems that support occupational stereotypes. We were interested in brain areas that could cross-modally distinguish across different exemplars of occupations. We employed two separate tasks that presented information about four occupations in either word or picture format. In the word task participants made subjective judgments about different occupations (e.g. is the typical nurse wealthy). In the picture task participants were presented with pictures of different individuals sharing the same occupation. We performed classification analysis within each task and across tasks aiming to distinguish between the four target occupations used in the current experiment. Within the word task we observed above chance classification in a set of regions including the medial prefrontal cortex (mPFC), angular gyrus (AG), and precuneus. Within the picture task we observed above chance classification mainly in early visual cortices. We did not observe any significant cross-modal classification across occupations. We offer some speculations on these null results.

5.2 Introduction

Social categories have a substantial influence on the processing of information about other people. For instance, knowing someone is a pilot affects whether we expect them to be a well-organized, tidy person. Social knowledge in the form of person "schemas" or "prototypes" can have an important influence in our formation of impressions and is closely linked to prejudice (Amodio, 2014). Interestingly, there has not been much research on how such social categories are represented in the brain. This is in contrast to the increasing literature examining representations of specific person identities (Anzellotti, 2017; Ramon & Gobbini, 2018; Wagner et al., 2018; Wang et al., 2017). In the present study we used multivariate pattern analysis (MVPA) to examine how abstract social categories are represented in the brain.

Social categories and stereotypes are cognitive representations of a number of features shared by larger groups of people. Categorization can occur based on demographic identifications, beliefs, typical overt behaviours, personality traits and occupations. Social categories can help us assign personality traits (e.g. nurses are caring), social status, and associate behaviours and physical attributes to groups of people (e.g. pilots fly planes and wear white shirts). As such, categories represent a conglomeration of features, which can help us predict future behaviour of a specific person. Indeed, social categories have been shown to play an important part in how we form impressions of other people (Bodenhausen et al., 1999; Brewer, 1996; Fiske & Neuberg, 1990; Hamilton & Sherman, 1996; Kunda & Thagard, 1996) and have even been suggested to be better facilitators of social processing than personality traits (Andersen et al., 1990).

For instance, Andersen and colleagues (1990), presented participants with sentences describing a type of person performing a mundane task. The person could be described with either a social category or with a personality trait (e.g. The politician/ The extrovert type opened the drawer). Participants had to judge the likelihood that the labelled person would perform this action. Participants remembered sentences better and judged them more quickly when a social category label was used rather than a personality trait.

Andersen et al., (1990) argued that social categories are more accessible and semantically rich. Personality traits have been argued to be only one of the many elements represented by social categories (Macrae et al., 1994). As such, social categories are an interesting semantic concept since they represent a mixture of features and refer to general characteristics shared by groups of people, yet are also highly informative about typical behaviours and easily imaginable (Andersen & Klatzky, 1987; Andersen et al., 1990). Thus, it is interesting to examine whether these person "schemas" are represented in brain regions often associated with semantic knowledge and general schematic processing.

Our prior social knowledge is thought to allow us to categorise our experiences and structure and reduce the dimensions of the incoming flow of information (Cohen, 1981; Kunda, 1999; Macrae et al., 1994). Social categories also affect how we remember information (Bodenhausen, 1988; Bodenhausen & Wyer, 1985; Cohen, 1981; Klatzky et al., 1982). For instance, Klatzky et al., (1982) showed that recognition was better for faces that were stereotypical examples of occupational labels. In a seminal study Cohen (1981) presented participants with a video clip showing the daily activities of a woman. Some participants were told the woman was a librarian and other participants were told the woman was a waitress. Participants exhibited better memory for features consistent with the provided social category (e.g. waitress). In a second experiment, Cohen (1981) also showed that providing the stereotype label before watching the clip was associated with better memory for both the consistent and inconsistent memory compared to when participants were presented with the social label after watching the clip (see also Bransford & Johnson, 1972; Dooling & Lachman, 1971). The provision of a social category label before watching the videos potentially guided participants' attention to specific features of the video and allowed them to reduce the dimensions of incoming information, semantically elaborate on specific details and structure them, leading to more efficient encoding (Cohen, 1981).

Although the wide behavioural effects of social categories on how we form impressions of others, still little is known on how these concepts are represented in the brain. Recently there has been a few studies trying to

address similar questions (see Amodio, 2014). Van der Cruyssen and colleagues (2014) compared univariate activity when participants were reading sentences describing behaviours performed by either a member of a social category or an individual person with the same trait. They found extended activations in mentalizing areas such as the medial prefrontal cortex (mPFC), anterior temporal lobe (ATL), bilateral angular gyrus (AG) and posterior cingulate cortex (PCC) when participants were reading sentences describing people belonging to social categories versus when processing descriptions of individual traits (see also Contreras et al., 2011; Contreras et al., 2013). These brain areas have often been associated with social cognition and particularly theory of mind processes and mentalizing about other individuals (Frith & Frith, 2006; Van Overwalle et al., 2009; Wagner et al., 2018).

Studies that require participants to make judgments about social identity (Volz et al., 2009), ingroup loyalty (Baumgartner, Götte, Gügler, & Fehr, 2012) and social interaction (Lahnakoski et al., 2012) have often found involvement of the mentalizing network. However, it should be noted that previous studies have relied on univariate activity and have contrasted activations for social categories with other types of knowledge, such as semantic knowledge (Contreras et al., 2011), personality traits (Contreras et al., 2013; Van der Cruyssen et al., 2014), or knowledge about places (Fairhall & Caramazza, 2013b). The areas observed with such a contrast could be partly driven by general category differences and may not be necessarily informative about which brain regions represent information specific for distinguishing different types of social categories. For instance, since social categories are more easily visualised compared to personality traits (Andersen & Klatzky, 1987), some of the observed differences observed by Contreras et al., (2013) and Van der Cruyssen et al., (2014) could be due to general differences in concreteness across social and personality categories rather be due to representations of information that can distinguish between different examples of the same category (e.g. nurses vs pilots).

To address these issues, we examined which brain areas are used to distinguish between different social categories (e.g. pilots vs. nurses). We presented participants with two tasks using four occupation social categories.

We chose occupational social categories since they are widely known and have been shown to be important social schemas (see Feldman, 1972; Goldstein et al., 1984; Oakhill et al., 2005). In the first task, participants read words referring to specific occupations (e.g. nurse) and made simple semantic judgments about them. The use of word stimuli is one way to disentangle stimulus-driven perceptual factors from semantic factors, since the orthographic and phonological features of words are not related to the actual concepts that they represent. However, even with the use of words, it is still possible that the observed representations are modality (e.g. words) specific. To account for this, we used a second task, in which we presented participants with pictures of individuals in the same occupations (e.g. nurses). This was done in order to enable cross-modal multivoxel pattern analyses (Kaplan et al., 2015; Nastase et al., 2016). In this analysis technique data from one modality (e.g. words) is used to train a classifier to distinguish between stimuli, and the classifier's discrimination performance is tested on data from a different modality (e.g. pictures).

This technique has been used in multiple experiments examining representations of semantic memory (e.g. Bruffaerts et al., 2013; Correia et al., 2013; Devereux et al., 2013; Fairhall et al., 2014; Fairhall & Caramazza, 2013a) or in experiments using naturalistic stimuli (Baldassano et al., 2017, Baldassano et al., 2018; Zadbood et al., 2017). For instance, Fairhall and Caramazza (2013a) presented participants with pictures and names of objects and asked them to rate their typicality. They found significant cross-modal classification across different semantic categories in AG, ATL, PCC, posterior middle temporal gyrus and dorsomedial prefrontal cortex. Cross-modal classification is a stringent way to test for amodal semantic representations, which are a central assumption of many semantic memory theories (Fairhall & Caramazza, 2013a; see Nastase & Haxby, 2017 for review). The main idea being that a word ("nurse") will activate a similar semantic representation that would also be activated when seeing a picture of a nurse.

We used both words and pictures referring to the social categories in order to investigate where information about the categories is represented in a modality-independent way. We also included pictures that were either

congruent or incongruent with the stereotypical gender of the profession (e.g. female and male nurses). This was done to potentially examine whether the spatial patterns of activity elicited by words (e.g. nurse) are more similar to patterns of activity elicited by gender congruent pictures of nurses (female nurses). We expected that regions from the mentalizing network would be involved in representing these social categories. It is worth mentioning that some of the regions involved in mentalizing are also commonly observed in semantic memory tasks. We focused our analysis within the ATL, AG, mPFC and PCC, since these regions have been previously shown to be processing information about social categories (Contreras et al., 2011, 2013; Van der Cruyssen et al., 2014) and have been commonly shown to be involved in semantic memory (Binder & Desai, 2011; Binder et al., 2009; Fairhall & Caramazza, 2013a, 2013b; Murphy et al., 2017; Price et al., 2015).

WORD TASK

| NURSE WEALTHY YES <- -> NO | + | 98 ODD <- -> EVEN | + | SOLDIER WORKS IN A TEAM YES <- -> NO |
| 3.5s | 800ms | 12s | 600ms | 3.5s |

PICTURE TASK

| 1.3s | 200ms | 1.3s | 1s | 98 ODD <- -> EVEN |
| | 12s | | | 12s |

8 PICTURES IN BLOCK
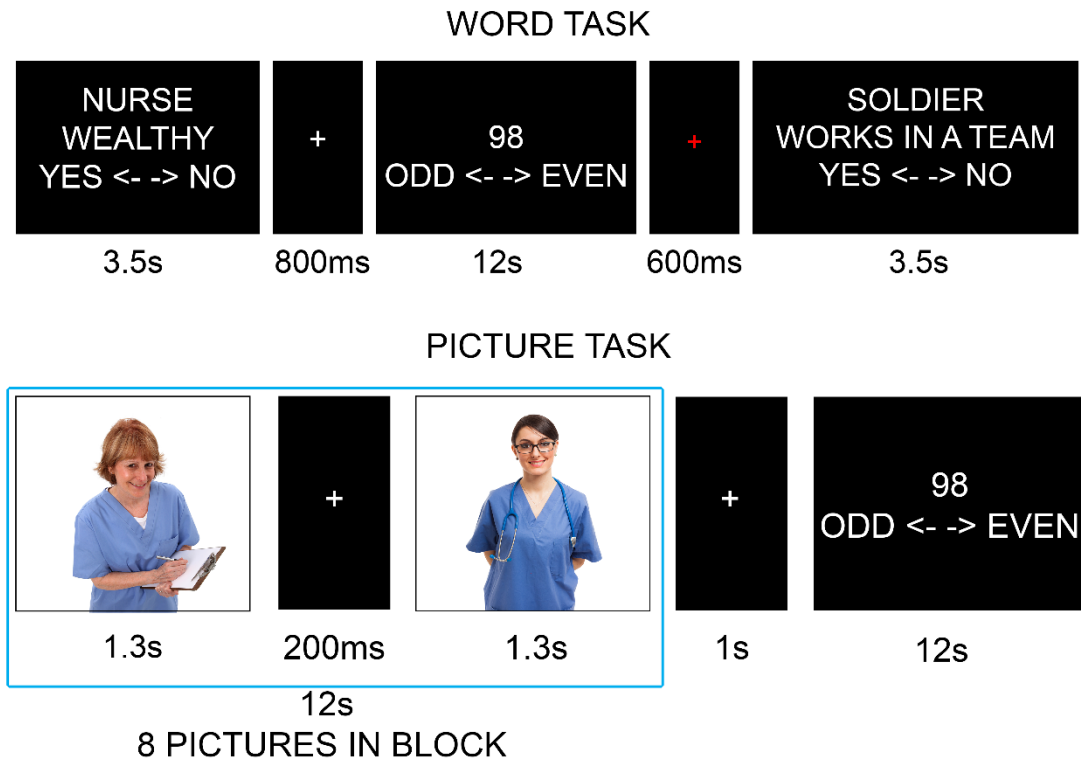
Figure 5-1 *Schematic of study design.* Participants completed two tasks. Initially they were presented with words describing occupations and were asked to make simple semantic judgments (e.g. is the typical nurse wealthy). After each judgment participants made odd-even number judgement. In the picture task participants 8 pictures in a series and their task was to press a button if they detected a picture incongruent with the rest of the pictures in the block. In-between each picture block participants again made odd-even number judgements.

5.3 Methods

5.3.1 Participants

Twenty-four right-handed fluent English speakers between the ages 19-32 (23.26 ± 3.9) were included in the experiment. Due to a technical issue one participant's data were lost and were not included in the final analysis and an additional participant was excluded because they fell asleep, leaving 22 people for all analyses. The Brighton and Sussex Medical School Research Governance and Ethics Committee (RGEC) provided ethical approval for the project. All participants provided informed consent and were paid £20 compensation for their time.

5.3.2 Stimuli

We chose stimuli referring to four widely known occupations (soldier, boxer, nurse, ballet dancer). Based on reported gender perception roles (Misersky et al., 2014) we selected 4 professions – 2 perceived to be male dominated and 2 perceived to be female dominated. We used 288 colour pictures each of a different individual for the 4 different professions, 32 of these pictures were used for the oddball task. 256 pictures were divided equally across the 4 professions (nurse, boxer, ballet dancer, & soldier) and the pictures were equally of male and female professionals. Therefore, there were 64 pictures for each profession and half of them 32 were male with the other half being female. This resulted in 8 sets of 8 pictures that were included in the analyses. An additional set of 32 pictures separated into 4 blocks of 8 pictures was used for the odd-ball task. The inclusion of stimuli that were incongruent with the stereotypical gender of the occupations (male nurse) was done to potentially examine whether words elicited patterns more similar to the pictures of individuals in gender congruent occupations. All pictures were 2100x1500 pixels and represented an individual in prototypical clothing for their profession presented on a white background. All images were taken from Shutterstock (https://www.shutterstock.com/home) and where appropriate the background was removed using Adobe Photoshop.

5.3.3 Procedure

Participants were first screened to assess whether it would be safe for them to go inside an MRI scanner. There were 2 counterbalancing lists in which the order of the presentation for both the word task and the picture task was reversed. Additionally, in the picture task the location of the oddball varied across lists.

The experiment consisted of 10 functional runs each approximately 4 minutes. It has been suggested that MVPA analyses can benefit from brief functional runs (Coutanche & Thompson-Schill, 2012). There were two tasks for the experiment. Participants completed simple "yes/no" judgments on the 4 professions during the word task. Participants were presented with an occupation name (e.g. nurse) below it an adjective (e.g. wealthy) and were asked to make a yes or no judgment on the combination. Most judgments were subjective, although some combinations of occupation and adjectives were considered common knowledge (e.g. nurse – knows first aid; boxer – physically active). Participants were instructed to respond about the typical profession description rather than think of a particular example of the occupation category (see Figure 5-1). Each conjunction of occupation name and adjective was presented as white text on black background for 3.5 seconds followed by an 800 milliseconds fixation. Participants made an odd/even judgement in-between the occupations questions, which served as an active baseline task (Stark & Squire, 2001). An active baseline task was chosen in order to prevent participants from thinking about the social categories during the 'rest' periods. Five numbers randomly chosen from the range 1-98 were each presented for 1.8 seconds with a 600 milliseconds white fixation in between the numbers. There was a red fixation cross presented for 600 milliseconds to signal the upcoming occupation judgment. Therefore, the word fMRI runs implemented a slow event related design with a space of 13.2 seconds in between presentations of the occupation judgments.

In the last 4 runs participants completed an oddball picture detection task. Participants saw blocks of pictures followed by blocks of odd/even judgment, which again acted as an active baseline task. A block consisted of 8

pictures. Each picture was presented for 1.3 seconds with a 200 milliseconds gap in-between. Therefore, the duration of a single block was 12 seconds. After each block of pictures, a white fixation cross was presented for 1 second. The odd/even judgment task (as described above) was also 12 seconds and followed the presentation of the pictures. A red fixation cross, presented for 1 second, signalled the upcoming picture block. Participants were instructed to pay attention to each individual picture and press a button whenever they detect a mismatch between the occupations. For instance, a picture of a soldier presented in a block of nurses would be a target that requires a response. Only 11% of blocks included an oddball and they were not included in the main analyses. Outside the scanner participants completed a practice session to familiarise themselves with the tasks.

Outside of the scanner participants rated the gender prevalence for the 4 different professions. A visual analogue scale from 0 to 100 was used and participants were asked to guess what proportion of the people in that profession were male.

5.3.4 MRI acquisition

Images were acquired on a 3T Siemens Prisma scanner with a 32-channel head-coil. To minimise head movement, we used soft cushions that were inserted into the head coil. Gradient-echo EPI sequence with a multiband factor of 8 with the following parameters (TR = 0.8 seconds; TE = 33.1ms; 52 degree flip angle; FOV = 208x180mm; 72 slices with sliced thickness of 2mm and isotropic 2mm voxels) was used. SpinEcho images with the same parameters were acquired in both the Anterior to Posterior and Posterior to Anterior direction and were used to estimate a field map of the distortions using a method similar to Andresson (2003) using FSL command-line utilities. Using a 3D MPRAGE sequence (TR = 2.4 seconds; TE = 2.14 seconds; 8 degree flip angle; FOV = 224x224mm and 0.8mm isotropic voxels) we acquired a high-resolution structural T1-weighted image.

5.3.5 Image pre-processing

Images were analysed and pre-processed using SPM 12 (Wellcome Department of Imaging Neuroscience, London, UK) and FSL command-line utilities. Images were initially motion corrected to the mean image. Field maps were estimated and applied to the motion realigned images using FSL functions (Smith et al., 2004), which allowed us to correct for image distortions (Andersson et al., 2001). The T1-weigthed anatomical image was coregistered to the mean functional image and segmented into different tissue types (grey matter, white matter, cerebrospinal fluid) using SPM 12 default tissue probability maps. Deformation fields were estimated from the segmented images and used to normalise the functional images to MNI space. A minimal smoothing kernel of 3mm FWHM was applied to the data.

5.3.6 Data analysis

Data were analysed with SPM 12, the CosMoMVPA toolbox (Oosterhof, Connolly, & Haxby, 2016) and custom scripts in MATLAB (Version 2017b, The MathWorks, Inc., Natick, MA, USA). Analyses were conducted on MNI normalised images. Searchlight analyses were run within a grey matter mask. Each individual's grey matter tissue probability map estimated during the segmentation analysis step was normalized to MNI space. These grey matter probability masks were averaged and then thresholded at 0.3 to select voxels within grey matter for the group. To visualise our results, we used the Bspmview (www.bobspunt.com/bspmview) toolbox. The toolbox implements MNI coordinates from the Anatomical Automatic Labelling 2 toolbox for SPM 12. To ensure participants were awake and paying attention in the word judgment task we also examined responses for the odd-even task and also for word trials with occupation and adjective combinations, that were considered to be with commonly known answers. For instance, we included participants that consistently responded with yes for trials: (nurse-knows first aid; boxer is physically active; soldier is physically active). One participant was not consistently responding to the occupation questions or responding to the odd-even task, from which we judged he/she had fallen asleep and did not include them into further analysis, leaving 22 participants for all fMRI analyses.

5.3.7 GLM analysis

Each run was modelled separately. In the word task each of the occupations was modelled with a separate regressor (4 regressors per run; 1 per occupation in a single run). An occupation regressor combined the 4 trials of different judgments made for the occupation in each run. The odd/even task was left unmodelled and acted as implicit baseline. This meant that beta estimates for word judgment task reflected the comparison between the word-judgment trials with the odd-even task. In the picture task each picture block was modelled with a separate regressor. In each run there were 2 regressors per occupation (one male and one female). The oddball picture blocks were included as regressors of no interest. The models for both tasks included the 6 motion parameters, mean session effects and a high pass filter with a cut-off of 1/128 Hz.

5.3.8 Multivoxel pattern analysis (MVPA)

We first carried out classification analyses separately within each task (modality) to examine whether BOLD patterns can be significantly distinguished between the different professions. We ran whole brain searchlight analysis using a searchlight sphere of radius of 4 voxels (mean 235 voxels). For all the searchlight analyses we used support vector machine classifier as implemented in LIBSVM with a linear kernel and a fixed cost parameter ($c = 1$). For each searchlight the multivoxel patterns (*t*-statistics) for each occupation from each run were extracted and vectorized in order to compute classification accuracy. For the within modality classification both training and test data sets were from the same modality. For instance, for the word task we used a leave-one-run out cross-validation, where a classifier is trained on 5 of the word task runs and tested on the left out 6th word task run. This is repeated 6 times, so that each word task run is used as a test set. The average accuracy over the six cross-validation folds is assigned to the center voxel of the searchlight. This process is repeated separately for each searchlight. Each voxel in the resulting map represents a cross-validated accuracy (Etzel et al., 2013). Similarly, for the picture task within modality classification we used again a leave-one-run-out

cross-validation. Each classifier was trained on 3 runs and tested on the left out 4th run.

For the cross-modal classification we first trained a classifier on all word runs and tested it on all picture task runs. We also ran a second analysis in which we trained a classifier on all picture runs and tested in on the word runs. Because the pictures referred to the same 4 professions as the word task these analyses were well suited to examine which brain regions might show amodal semantic representations. To correct for multiple comparisons at the whole brain level we used the threshold-free cluster enhancement (Smith & Nichols, 2009) with 10000 permutations as implemented in CosMoMVPA.

5.3.9 ROI definition

Apart from whole brain searchlight we also examined classification performance in 7 regions of interest (see Figure 5-2). Regions of interest were defined as 8mm spheres around the peak voxels reported in Van der Cruyssen et al., (2014). The regions spanned parts of the mentalizing network and included dorso-medial prefrontal cortex (DMPFC), ventromedial prefrontal cortex (VMPFC), left medial anterior temporal pole (mATL) and left anterior temporal pole (ATL), posterior cingulate cortex (PCC), left and right angular gyrus (AG). Van der Cruyssen et al., (2014) observed higher activations in these regions when participants were processing social categories vs personality traits (Contreras et al., 2013). A grid search was implemented over the cost parameter C for the ROI analyses. Significance was examined with a one sample permutation t-test.

ROIs
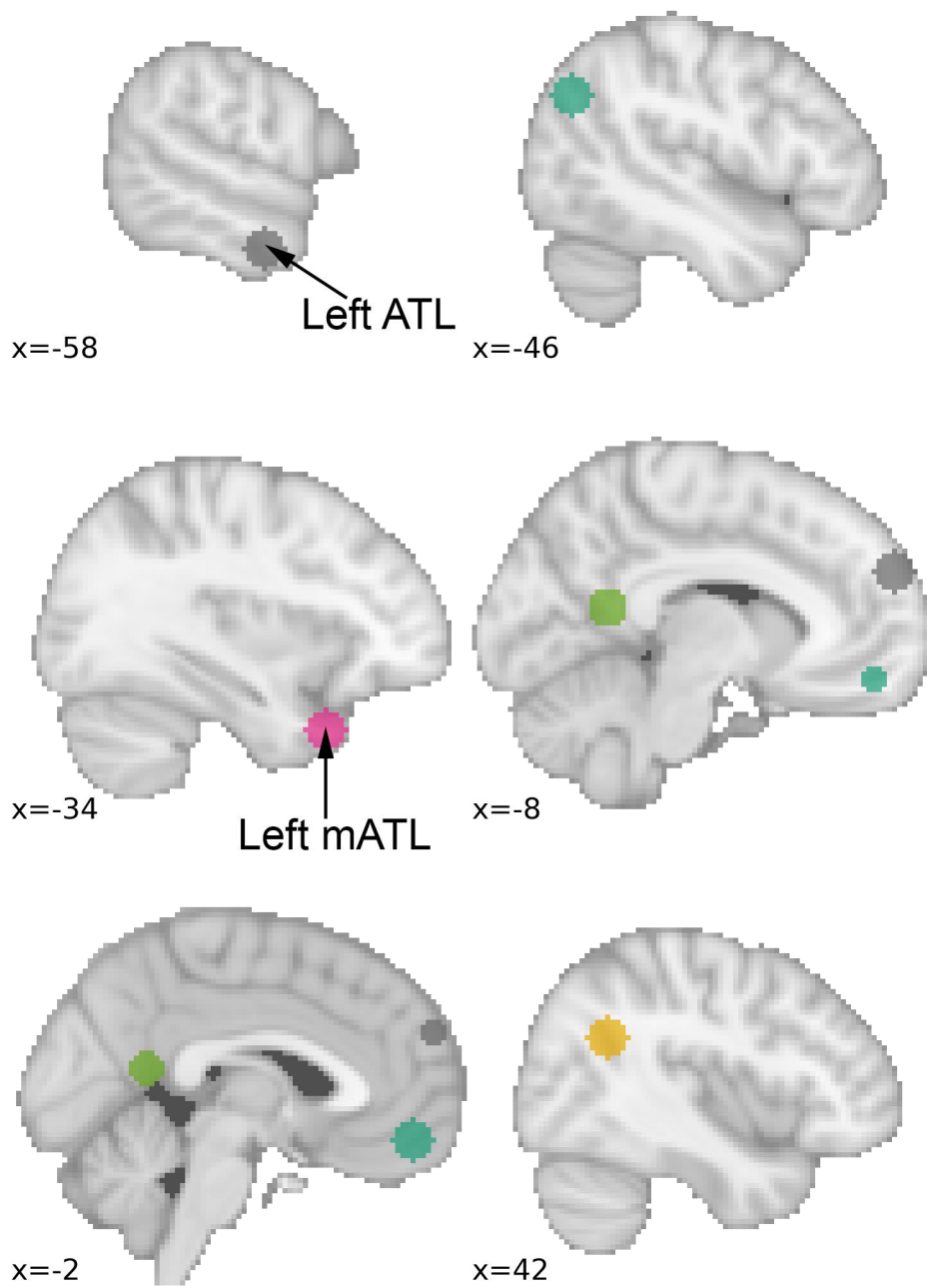
Figure 5-2 *ROI definition.* Seven regions of interest were defined as 8mm spheres around peak voxels reported in (Van der Cruyssen et al., 2014).

5.4 Results

5.4.1 Behavioural

Participants demonstrated high accuracy for the odd-even task with mean performance of 0.95 (± 0.06) during the word task and 0.96 (± 0.04) during the picture task. In their ratings of occupation gender prevalence, participants exhibited similar stereotypes to what has been previously reported (see Misersky et al., 2014). On average 72.13% (± 8.36) of boxers and 73.72% (± 11.98) were judged to be male and 68.9% (± 11.88) of nurses and 71.59% (± 10.42) of ballet dancers were judged to be female.

5.4.2 Within task Classification

5.4.2.1 Words

We initially ran searchlight classification analyses using cross-validation to examine which brain regions could distinguish between the four occupations using only the word task. We observed significant classification in a number of areas overlapping the mentalizing network (see Figure 5-3). We observed significant classification within anterior temporal lobe (ATL), middle temporal gyrus (MTG), medial prefrontal cortex (mPFC), inferior frontal gyrus (IFG), precuneus, angular gyrus (AG). However, we also observed significant classification in early visual cortex.

5.4.2.2 Pictures

The searchlight analysis within the picture task showed classification in early visual cortex, probably reflecting low-level visual differences across pictures of different occupations. For instance, pictures of nurses were often presented in white or blue uniforms whereas soldiers were often in green uniforms. Apart from visual cortex classification we also observed significant classification in supramarginal gyrus, angular gyrus, middle temporal gyrus and left inferior frontal gyrus (see Figure 5-4).

5.4.3 Cross classification

5.4.3.1 Test Pictures Train Words

In order to investigate which brain regions might represent amodal representations of social categories we initially ran searchlight analyses where a classifier trained on all runs from the word task was used to predict stimuli from the picture task. If the classifier had learned representations that are independent of task and stimulus presentation, we would expect to observe above chance classification. We did not observe any regions that showed higher than chance classification when trained on the word task.

5.4.3.2 Test Words Train Pictures

We also ran a searchlight analysis that examined classification accuracy on the word task when trained on the picture task. We did not observe any regions that showed significant above chance classification for words when trained on pictures. Indeed, in both cross-classification analyses we observed small patches in early visual cortex that showed below chance classification (see 5.6 Supplementary Materials). This might suggest that the information learned to distinguish between occupations in the visual cortex from one task is anti-correlated with the information learned from the other task (see also Jamalabadi et al., 2016).

We did not examine whether patterns of activity elicited by the word task were more similar to the gender congruent versus the gender incongruent picture, since we did not observe any general cross-modal classification between the word and picture tasks.

5.4.4 ROI analyses

Apart from whole brain searchlights we also ran the within and across modality classifications in a predefined set of regions (see Figure 5-2). We examined classification in regions previously associated with processing information about social categories (Contreras et al., 2013; Van der Cruyssen et al., 2014). During the word task we observed significant classification of occupations in large set of regions from the mentalizing network, including dorsal and ventral medial prefrontal cortex (DMPFC and VMPFC), left anterior

temporal lobe (ATL), bilateral angular gyrus (AG). During the picture task the DMPFC, VMPFC and left AG showed significant classification across occupations. None of our ROIs showed significant cross classification (see Figure 5-5).
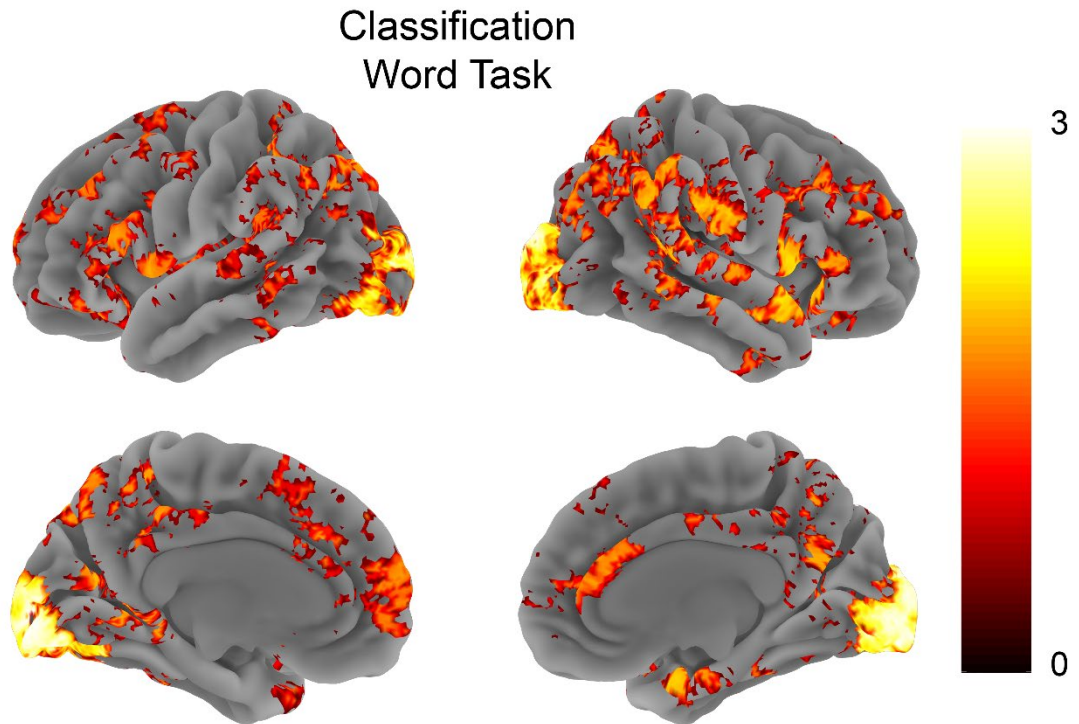
Figure 5-3 *Word task searchlight.* Brain map shows regions with significantly higher than chance classification of different occupations from the word task. Map is thresholded at z-TFCE score of 1.65 corresponding to p < 0.05 one-tailed corrected for multiple comparisons.
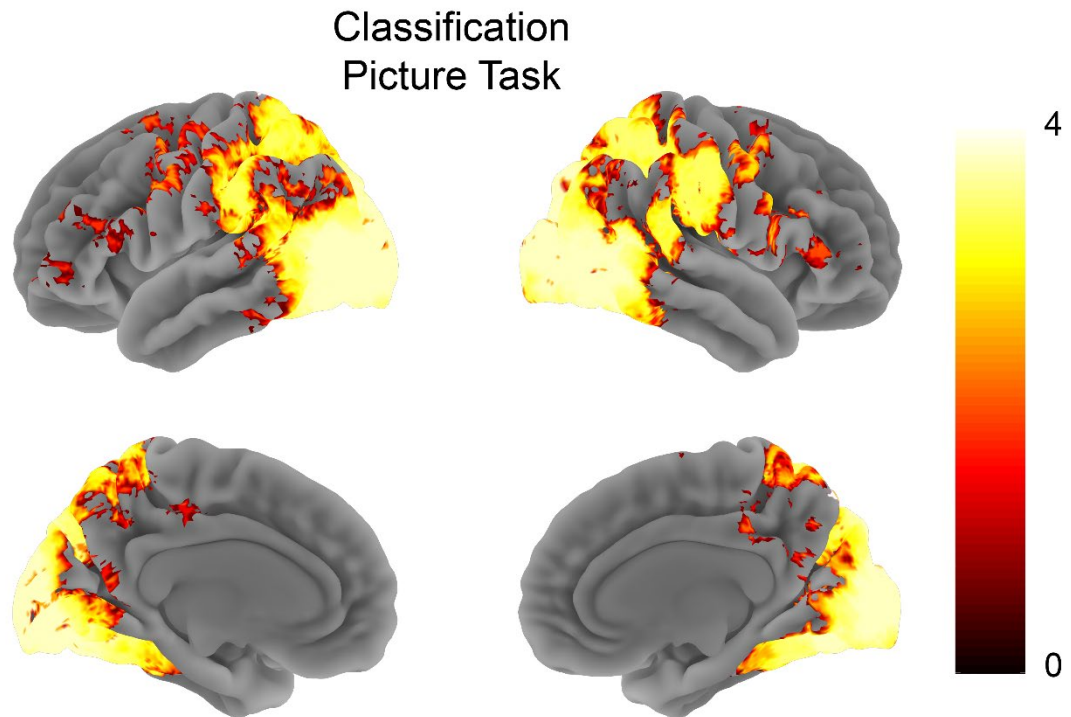
Figure 5-4 *Picture task searchlight.* Brain map shows regions with significantly higher than chance classification of occupations in the picture task. Map is thresholded at z-TFCE score of 1.65 corresponding to p < 0.05 one-tailed corrected for multiple comparisons.
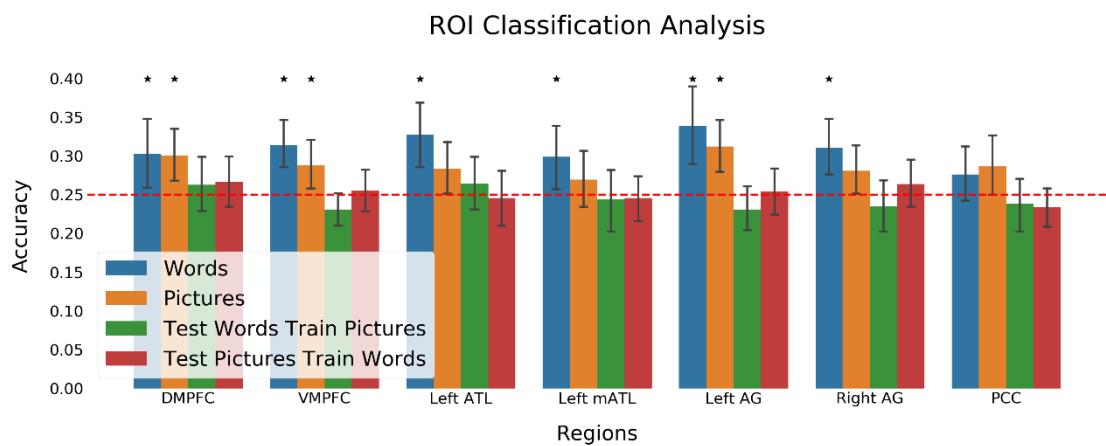
Figure 5-5 *Classification within ROIs.* The plot shows classification accuracy for each of the 7 regions for all 4 classification analyses. The words and picture labels show classification within modality and the other two labels represent the cross-classification analyses. Plot shows mean accuracy across people with bootstrapped confidence intervals. The red dotted line represents chance performance. Asterisks indicate significantly above chance classification.

5.5 Discussion

In this study we were interested in examining the neural representations of social categories. Specifically, we investigated whether we could observe across modality cross-classification for different types of occupational stereotypes. We presented participants with two separate tasks. In the first task participants saw words referring to four occupations and made simple semantic judgements about them (e.g. if the typical nurse is wealthy). In the second task participants saw a series of pictures referring to the same occupations seen in the word task. Participants had to perform an odd-ball task and detect a picture that represented a different occupation than the rest of the pictures in the series. Within the word task we observed significant classification between social categories in a set of regions overlapping with the mentalizing network. We also observed significant classification across social categories in the picture task in prefrontal cortex regions. However, we did not observe any regions that showed significant cross-modal classification.

Our findings of significant classification in the mentalizing network agree with previous studies that have examined the processing of social categories. Previous research has often contrasted more broader semantic categories (e.g. people vs places; social categories vs personality traits) in order to investigate the neurobiology of social knowledge (Contreras et al., 2011, 2013; Fairhall & Caramazza, 2013b; Van der Cruyssen et al., 2014). Fairhall & Caramazza (2013b), for instance, observed higher involvement in ATL, TPJ, DMPFC, and posterior middle temporal gyrus when participants were processing information about kinds of people compared to kinds of places. Similarly, Van Der Cruyssen et al., (2014) observed higher activation in DMPFC, VMPFC, ATL, PCC and bilateral AG when participants were making judgments about social categories as opposed to personality traits.

Here, we extend these findings to show that these regions can distinguish between different types of social categories (e.g. nurses vs soldiers). This supports previous suggestions that these regions represent social knowledge. Interestingly, these regions are often also associated with a vast range of cognitive functions such as semantic memory, episodic memory, and

imagery (e.g. Spreng et al., 2009). Recent studies have also found that MPFC and AG are associated with processing of more abstract generic knowledge, often termed schematic knowledge (see Gilboa & Marlatte, 2017; Wagner et al., 2015; see also Chapter 3 and 4). Social categories have been argued to potentially act as person specific schemas (Cohen, 1981). Future studies will be needed to better understand whether different types of schematic knowledge rely on the same regions and neural mechanisms.

Although we observed significant classification in the mentalizing network during the word task, significant above chance classification during the picture task was mainly constrained to the visual and parietal cortex. The DMPFC and VMPFC seemed to also distinguish different occupations during the picture task, however, since they did not show significant cross-classification this suggests that different patterns were responsible for distinguishing between occupations in the word and picture tasks.

It is difficult to make concrete conclusions based on null results, however, we offer some speculations on the lack of observed effects. It is possible that the picture task did not encourage participants to semantically elaborate on the different social categories. Although participants had to detect a mismatch between occupations in a series of pictures, it is possible the task was performed mainly on a perceptual differentiation between the pictures and did not require participants to actively think about features describing these occupations. Furthermore, the picture task utilised a blocked fMRI design, whereas a slow-event related design was used in the word task. This might have reduced the overlap between the word and picture tasks and might be a potential explanation for the lack of observed effects. Indeed, other studies have shown that attention can modulate which features are classifiable from fMRI data in previous studies (Cukur et al., 2013; Nastase et al., 2017). Our results are not directly in contrast to previous behavioural studies that have argued for more automatic activation of social knowledge (e.g. Oakhill et al., 2005), but imply that these representations may not be easily captured with fMRI.

However, we note that it is possible that our design was simply underpowered to detect cross-modal classification effect. Although we used a similar number of stimuli to previous research (e.g. Fairhall et al., 2014), our classification task was inherently harder since we were trying to distinguish between different examples from the same semantic category (occupations) rather than distinguish broader categories (living vs non-living)(but see Correia et al., 2013). Power calculations in fMRI, especially for MVPA, have been notoriously difficult. However, our results can act as starting point for future studies in estimating required sample sizes using newly developed tools for calculating fMRI power (Durnez et al., 2016; Ellis et al., 2019; Hill et al., 2017; Mumford, 2012).

5.6 Supplementary Materials

Test Pictures Train Words
Classification
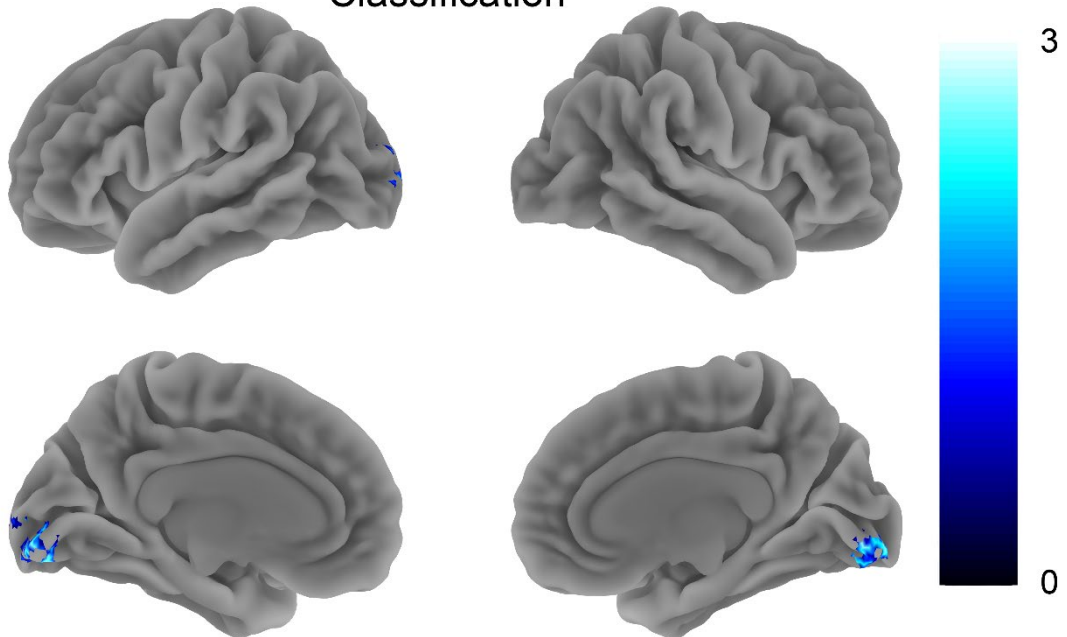
Supplementary Figure 5-1 *Train Pictures Test words.* Brain map showing cross modality classification. Classifier was trained on the picture task and tested on the word task.

Test Words Train Pictures
Classification
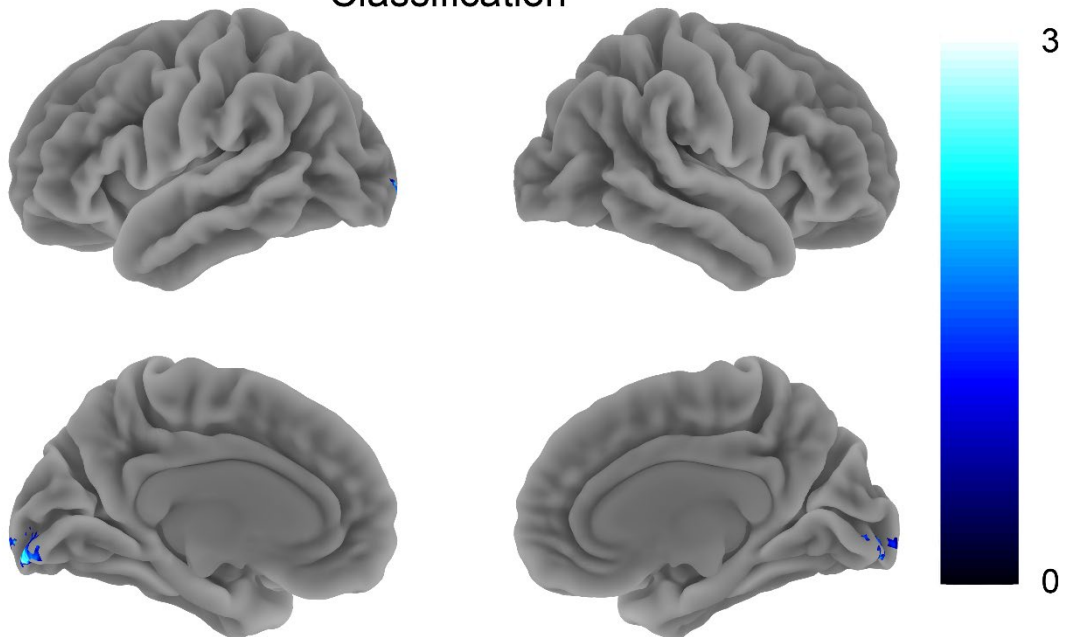
Supplementary Figure 5-2 *Train Words Test Pictures.* Map showing results of Cross modality classification. Classifier was trained to distinguish the social categories based on the word task and tested on the picture task.

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Chapter 6: Processing of complex events in older adults with mild cognitive impairment

6.1 Abstract

Mild cognitive impairment (MCI) syndrome is associated with problems of learning new information and is a major risk factor for later development of Alzheimer's disease. Video stimuli can be a useful tool in examining memory processes in people with MCI, since they more closely mimic the complexity of everyday events. To understand a complex event one can often rely on his prior knowledge of similar situations, but one must also continuously integrate multimodal information over time and sustain attention for relatively prolonged periods. Here we examined whether MCI is associated with problems in encoding of naturalistic events. Participants with MCI, subjective memory impairments or healthy older adults were scanned whilst they watched short clips inside an MRI scanner. Participants' memory for the clips was tested outside of the scanner. Individuals with MCI remembered less details about the clips from both the subjectively impaired and healthy control groups. We used recently developed analysis technique (inter-subject correlation) to examine whether MCI patients as a group would show less reliable BOLD responses to the clips when compared to the other groups. MCI individuals showed less coherent responses in posterior medial cortex, ventromedial cortex, and anterior temporal poles, when compared to the other groups. Our results suggest that MCI patients have problems encoding adaptively naturalistic stimuli.

6.2 Introduction

As we age, our cognitive functions decline. Older adults often experience decreased processing speed, problems with attentional control, multi-tasking and episodic memory. Memory complaints often include word-finding difficulties, problems learning new information, and problems recalling recent events (Balota et al., 2000; Gilewski et al., 1990; West et al., 1992). Deficits in memory are particularly exacerbated in older adults who develop a Mild Cognitive Impairment (MCI) syndrome or Alzheimer's Disease (AD) (Petersen, 2000). MCI is often characterised by decline in episodic memory that is steeper than the decline observed in healthy older adults. Yet patients with MCI are not completely unable to learn new information. MCI is a major risk factor for later development of AD (Flicker et al., 1991; Petersen, 2000; Wolf et al., 1998). MCI patients may even exhibit some subtle difficulties with everyday tasks, and it is possible that part of this is due to their memory problems (Flicker et al., 1991; Jekel et al., 2015; Kluger et al., 1997; Royall et al., 2007). A lot of everyday tasks, such as cooking, navigating in one's environment and even following a television programme rely to some extend on episodic memory (Tulving, 1983; Zacks, 2006). Indeed, problems remembering what just happened can lead to problems orienting oneself in the present moment and keeping track of unfolding information that is inherent in everyday cognition (Zacks et al., 2006). However, it is still unclear how MCI patients process complex events that resemble those encountered during day-to-day activities. Furthermore, it is not clear whether the observed memory deficits in MCI patients are due to problems in the encoding, consolidation, and/or retrieval stage of episodic memory. Here we used naturalistic stimuli to examine whether MCI patients would exhibit difficulties encoding video clips. We hypothesised the commonly observed memory deficits in MCI patients are partly due to maladaptive encoding. Below we discuss the rationale for the study.

With the increase in the ageing population, and the importance of age as a risk factor for neurological conditions associated with cognitive decline or dementia, there is a need to better understand the cognitive and brain systems affected by MCI. This might lead to both the identification of diagnostic

biomarkers as well as the development of behavioural strategies to manage cognitive decline. It is particularly important to examine how such patients process everyday information. Whereas typically laboratory studies have relied on simple stimuli (e.g. individual words or pictures), memory for everyday events is often more complicated. Complex events are structured, contain more rich associations and involve information extending in time. In order to comprehend such events, one must often interpret them with reference to prior knowledge of similar situations. Given the complexity of everyday comprehension it is important to better understand how MCI affects processing of more naturalistic situations, as this can guide development of future interventions.

Video stimuli are a useful tool to examine everyday cognition, because they provide an ecologically valid way to examine participants' encoding. They contain social and emotional information, which may make them more easily memorisable, when compared to more simple stimuli. Indeed, it has been argued that healthy older adults have difficulties engaging and remembering arbitrary information devoid of social meaning (Hess, 2005). Furthermore, to understand the situation described in a video we often rely on our prior experience with similar situations. Such 'schematic' or 'script' knowledge can aid participants' memory by providing a structure to help organise the incoming information. Importantly, such prior knowledge may be well preserved in old age (Umanath & Marsh, 2014). Healthy older adults exhibit better memory on tests involving structured and better contextualised materials (R.T. Zacks et al., 2000). Schemas, scripts and expertise tend to benefit older adults' memory performance (Hess, 1990; Morrow et al., 1992). However, it remains an open question whether similar benefits will be observed in MCI patients. Some studies have suggested that MCI patients might have deficits in their script knowledge of everyday actions (Jekel et al., 2015; Jorm & Jacomb, 1989; Roll et al., 2019; Royall et al., 2007; West et al., 1992). Therefore, it is possible MCI patients might not necessarily be able to benefit from the structure provided by the more complex stimuli.

In addition it should be noted that to comprehend naturalistic stimuli participants must also maintain prolonged attention (Naci et al., 2014), track the

unfolding sequences of actions happening in the videos and switch between retrieving and encoding the clips to memory (Hasson et al., 2015). Comprehending complex events is associated with various cognitive processes such as memory and executive functioning (Cannizzaro et al., 2013; Graesser et al., 1997; Mar, 2004). This can make naturalistic stimuli particularly useful for examining MCI patients who suffer from memory problems and often show deficits in attentional control (Albert et al., 2001; Belleville et al., 2007; Gordon et al., 2015; Rapp et al., 2005; Sarazin et al., 2007; Saunders & Summers, 2010) or can show problems in discourse comprehension (Drummond et al., 2015; see also Fraser et al., 2019).

Only a few studies have used naturalistic stimuli to examine how MCI patients process events. Johnson, Storandt, and Balota (2003) used complex narrative texts to examine memory performance in older adults, and individuals with mild dementia syndrome. Patients with mild impairment retrieved fewer details from the narrative texts at both immediate and short delay tests. Zacks et al., (2006) examined how healthy older adults and mildly demented patients processed movies of everyday activities. They found that mildly demented patients showed deficits in identifying the boundaries between transitions in the movies when compared to healthy older adults and younger adults (see also Bailey et al., 2013). Furthermore, patients with mild dementia showed problems remembering what events happened and their temporal order. Memory deficits for the videos were associated with impaired semantic knowledge for the events, supporting the notion that we rely on prior knowledge to understand complex events (Kurby & Zacks, 2008; Zacks & Sargent, 2010; Zacks et al., 2007).

It is unclear what are the brain areas that might be affected by MCI in processing of complex events. The hippocampus undeniably plays a major role in supporting memory processes (Marr, 1971; McClelland et al., 1995; Schapiro et al., 2017) with focal hippocampal lesions leading to severe memory impairments (Kolb & Whishaw, 2009). AD and to lesser extend MCI are associated with atrophy in the hippocampus and extending medial temporal lobes (see for review Chandra et al., 2019; Du et al., 2004; Pennanen et al., 2004). Interestingly, however, focal hippocampal damage does not impair

completely the patient's ability to understand ongoing everyday activities and to follow conversations whose contents exceed the typical short-term memory capacity for unrelated items of information (Baddeley & Wilson, 2002; Chen et al., 2016; Keven et al., 2018; Squire et al., 2004). This suggests that other brain regions might be representing the complex unfolding sequences of actions occurring in everyday events.

Areas overlapping with the default mode network (DMN), may be particularly important for the integration of information over minutes necessary for everyday comprehension (Hasson et al., 2015). Evidence for this comes from studies that have scrambled the temporal structure of video or auditory narratives at different time-scales and showed that the responses in medial prefrontal cortex (mPFC), posterior middle cortex (PMC), angular gyrus, inferior frontal gyrus and other higher cortical areas are dependent on prior narrative information being intact (Hasson et al., 2008; Honey et al., 2012; Lerner et al., 2011). Further support that these regions represent ongoing events, comes from studies that show shared patterns of activity in these areas in participants experiencing or remembering the same events (Chen et al., 2017; Nguyen et al., 2019; Raykov et al., 2018; Saalasti et al., 2019; Yeshurun et al., 2017; Zadbood et al., 2017). The PMC has been consistently implicated in the perception and retrieval of life-like events (Bird et al., 2015; Oedekoven et al., 2017; see also Chapter 4). Baldassano et al., (2017) showed that changes in patterns of activity in PMC closely matched transitions between events in an ongoing movie as identified by participants. A recent study showed that representations in PMC were shared across healthy participants and a patient with extensive hippocampal damage watching the same movie, further supporting that PMC might be particularly important for the representation of ongoing events (Oedekoven et al., 2019; Zuo et al., 2019).

In the current experiment we examined whether processing of life-like events would be different in patients with MCI impairment. Participants were presented with short clips in the scanner and were later asked to recall them. We relied on inter-subject correlations (ISC) to investigate whether fMRI responses in MCI group were less reliable, which might indicate that patients were not encoding the stimuli adaptively. ISC is particularly well suited for the

analysis of naturalistic stimuli and has been shown to be a useful method to identify group differences in processing of movies (e.g. Geerligs & Campbell, 2018). We hypothesised that MCI patients would exhibit lower ISCs in DMN regions, since they often have difficulties retrieving narratives and have been shown to have deficits in attentional tasks. Indeed, mild dementia has been also linked with problems identifying transitions between events (Zacks et al., 2006).
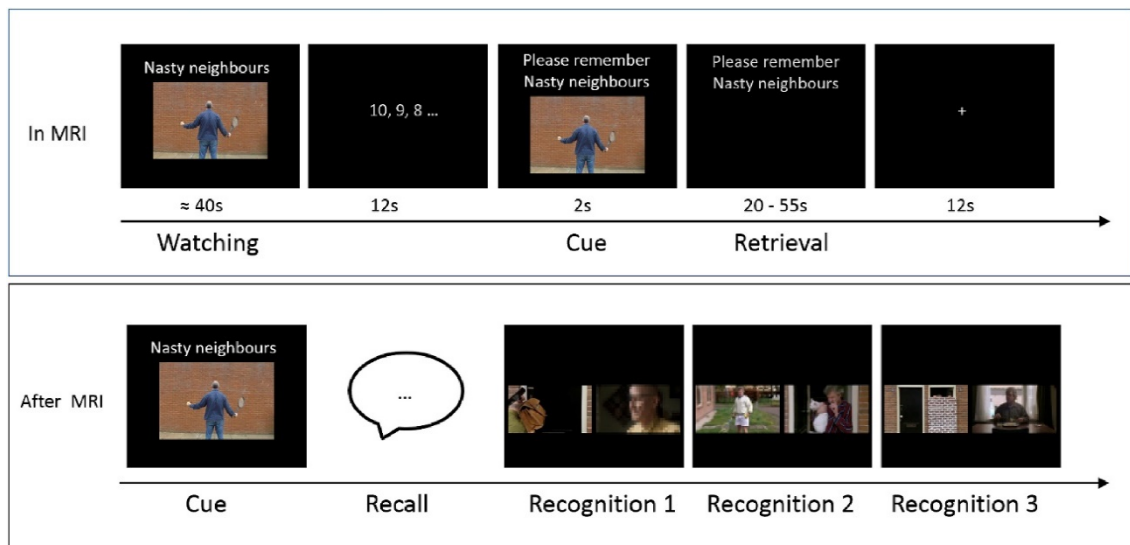
Figure 6-1. *Schema of Study design.* Participants watched a video and after 12s were cued to silently retrieve the video. The title and a screen shot of the video were used as the initial cue. The title of the video remained on the screen throughout the whole recall period (20-55s). There were 8 **videos** in total. After scanning, participants were asked to describe all 8 videos and to answer a forced-choice recognition test.

6.3 Methods

6.3.1 Participants

Ninety-four patients were referred from the Memory Assessment Service (MAS) clinics through Sussex Partnership NHS Trust in Sussex, UK. We relied on a prospective design where we included all participants referred to the MAS clinic that met our inclusion criteria. These criteria were: (1) referral from the MAS clinic for a structural scan, (2) a score of 82 or above on the Addenbrooke's Cognitive Examination (ACE-R/III) score above 82 (Mioshi et al., 2006), (3) unimpaired or mildly impaired score on the Bristol Activities of Daily Living Scale (BADL; Bucks et al., 1996), (4) willingness and possibility to be scanned for 20 minutes whilst performing a video task. There were 4 patients with a diagnosis of AD, 36 patients with diagnosis of MCI, 5 patients with a diagnosis of depression, 10 patients with a diagnosis of underlying vascular dementia diagnosis and 33 patients who were found to be neurologically healthy. In the current study we focused only on the patients with MCI diagnosis and those found to be neurologically healthy. The neurologically healthy participants will be referred to from further on as participants with subjective memory impairment, since were not found to have clinically significant memory impairments but were referred to the MAS clinic based on subjective memory problems. 16 of the MCI (mean age 77 ± 7.3; mean years of education 12) patients and 13 of the subjective memory impairment group (mean age 71 ± 6.8; mean years of education 12) were excluded from any further fMRI analyses due to large motion artefacts. For included participants, we also report scores on the Test of Premorbid function (TOPF), which is used as an approximation of premorbid IQ (Wechsler, 2009). This meant we had 20 MCI patients (mean age 72 ± 9.11; education: 14 ± 2.5; TOPF: 105 ± 11.76) and 20 neurologically healthy participants with subjective memory complaints (mean age 62 ± 9.14; education 14 ± 2.86; TOPF: 101.9 ± 11.44). We recruited additionally 20 healthy controls independently of the Memory Assessment service, of whom 2 were not included in further MRI analyses due to large motion artefacts. Therefore, we had a third group of 18 control participants (mean age 73 ± 7.4; education: 14 ± 2.92; TOPF: 108.5 ± 9.1). The participants with subjective memory impairment were significantly younger than both the

MCI and control group (ps < 0.001). MCI patients had lower ACE scores compared to the subjectively impaired patients (Welch's $t_{30.58}$ = 2.04; p = 0.006). The MCI group was not significantly older than the combined ages of the subjectively impaired and control groups (t_{55} = 1.87, p = 0.066).

6.3.2 Stimuli

Eight short clips taken from www.youtube.com and www.nsi-canada.ca/film-festival/ were used in the experiment. Videos lasted on average 43s (range 40-46s) and were presented without sound. Clips described short narratives involving interaction between two (7 clips) or more characters (1 clip). Half of the clips presented situations happening inside a building and in the other half the videos took place outside. Two videos included change in location. The task was programmed in Cogent 2000 toolbox (www.vislab.ucl.ac.uk/cogent_2000) using Matlab (Version 2013b, The Mathworks, Inc., Natick, MA, USA).

6.3.3 Procedure

Participants took approximately 2 and a half hours to complete the study protocol. Before scanning, participants completed a practice task in which they were familiarised with the study protocol.

Inside the scanner participants watched and recalled 8 short clips. Clips were presented on a black background with the clip title appearing above the clip. This is referred to as the watching phase from now on. After each video participants saw a countdown of grey numbers lasting 12s, followed by the retrieval phase of the preceding clip. Participants saw a screenshot of the initial scene of the preceding video clip for 2s indicating the start of the retrieval phase. Above the screenshot participants saw the instruction "Please remember [Title of video]" in white font. After 2s, the cue disappeared the instructions faded to grey font. The retrieval phase was partially self-paced with participants being able to press a button to continue to the next trial after 20s had passed. If participants did not press a button, the retrieval ended automatically after 55s. After each retrieval, participants were presented with a white fixation cross for 12s. Throughout the experiment, participants watched

and then silently retrieved each video before having to remember the next video (see Figure 6-1).

Outside of the scanner participants sat in a quiet room and recalled aloud the 8 videos they saw in the scanner. Each video was cued with the title and a screenshot of the first scene. Participants were asked to describe what happened in the video and were encouraged to elaborate if they provided very few details. Participants' descriptions were audiotaped. After attempting to recall each video, they also completed a forced-choice recognition memory test during which they had to choose which of two screenshots came from a video that they watched. The lure screenshots were taken from the same videos but featured scenes that were not shown to participants. There were three trials for each video and the maximum score for the recognition test was 24.

6.3.4 Memory Scoring

Audio descriptions of the movie were transcribed verbatim and were scored for the amount of independent details. Scores for each video were averaged which resulted in a single number for each participant representing memory performance. Participants received a score of 0, 0.5 or 1 for each detail. The 0 score indicated the detail was not recalled at all, 0.5 indicated a partially correct recall (e.g. "someone", "picks up something") and 1 indicated the detail was fully correct (e.g. "a man", "picks up bricks"). Details visible in the screenshot were not included in the scoring procedure. There was no maximum amount of details to be recalled per video. Our procedure closely mimicked the widely used scoring of prose recall tests (e.g. Rivermead Behavioural Memory Test (Wilson et al., 1999)). All video descriptions were scored by an experienced researcher, Christiane Oedekoven.

6.3.5 MRI acquisition

All images were acquired on a 1.5 T Siemens Avanto Scanner using a 32-channel head coil. BOLD sensitive T2* weighted images were acquired with a gradient-echo EPI sequence with the following parameters (TR = 2.62; TE = 42ms; voxel size = 3 x 3 x 3.6 mm, FOV = 192 mm, 35 ascending 3mm thick slices with a 0.6 mm gap). For the patient sample anatomical images were acquired during their clinical MRI scan. Due to clinical protocols, 70 patients

were scanned with a 3D-T1 weighted MP-RAGE sequence (TR = 2.4s, TE=3.5ms, voxel size = 1.3 x 1.3 x 1.2 mm, FOV = 240mm). 22 patients were scanned with a different T1-weighed MP-RAGE sequence (TR = 1.16s, TE = 4.24ms, voxel size = 0.9 x 0.9 x 0.9 mm, FOV = 230mm).

6.3.6   Image pre-processing

All EPI images were pre-processed using SPM 12 (Wellcome Department of Imaging Neuroscience, London, UK). Functional images were motion corrected to the mean functional image for the run. The anatomical image of each subject was co-registered to the mean realigned functional image and was segmented into grey, white and CSF maps. The resulting white and CSF tissue probability maps were thresholded at 0.99 and the average signal from the resulting masks plus the six motion parameters were regressed out from the functional images to reduce the effect of motion and temporal drift. Functional images were normalised to MNI space and were smoothed with an 8mm FWHM kernel.

6.3.7   Data analysis

Data were analysed with SPM 12, the CoSMoMVPA toolbox (Oosterhof et al., 2016) and custom MATLAB scripts (Nastase et al., 2019). Libraries in Python were used for visualization of behavioural and supplementary results. Group cluster corrected significance was performed with command-line functions in FSL (Nichols & Holmes, 2002; Winkler et al., 2014). All images were normalised into MNI space and smoothed with 8mm FWHM kernel before further analyses. Segmentation of the high-resolution structural image provided us with grey, white and CSF tissue probability maps. The average signal in white and grey matter was extracted and was regressed out with the 6 motion parameters from the fMRI images before computing the inter-subject correlations. A threshold of 0.99 was used for the white and CSF maps to ensure signal from only non-grey matter voxels was included. The grey matter masks for all subjects were averaged and smoothed with 8mm to create a group level grey matter mask. Voxels with average probability higher than 0.3 of being grey matter were included into the further analysis (Nastase et al., 2019). We used the Bspmview toolbox (www.bobspunt.com/bspmview) to

visualise our data. Anatomical Automatic Labelling 2 toolbox for SPM 12 was used for the description of results. Unless otherwise stated all images were whole brain cluster corrected at FWE p < 0.05 at voxel threshold of p < 0.001.

6.3.8   Inter-subject correlation (ISC) analysis

The ISC analysis allowed us to examine the dynamic processing of the videos by the three groups. Specifically, it allowed us to test whether the MCI group exhibited less coherent signal (lower ISCs) when compared to participants not diagnosed with MCI. ISC measures whether there is shared temporal signal between participants. The ISCs is sensitive to the stimuli-locked signal (shared across participants) and lower ISCs might suggest less reliable processing in participants (Nastase et al., 2019). Previous research has shown that worse comprehension of a complex event is associated with lower synchronization across participants in DMN regions (Ames et al., 2015; Lerner et al., 2011; see for review Nastase et al., 2019). Similarly, here we hypothesised that we might observe lower synchronization within the MCI group because they might be experiencing difficulties attending and comprehending the video stimuli.

To compute the ISCs, we initially extracted the time-course from each individual video, removed the first 2 TRs (5.24 sec), and z-scored each video time-course to account for transient onset effects (Nastase et al., 2019). All z-scored video time-courses were concatenated, resulting in a single time-course per participant per voxel containing the signal from all videos. The ISCs were computed voxel-wise. We examined whether ISCs within each group differed based on diagnosis. Specifically, we compared whether individuals with MCI were less similar to each other than individuals that were with subjective memory problems or a control group. To do this for each subject we computed his correlation with the average of the other subjects that shared the same diagnosis with him/her. This was repeated for each subject resulting in a single ISC map for each subject. For instance, if subjects from 1-20 are all diagnosed with MCI and subjects 40-58 are all controls, the ISC map for subject 1 is represents its correlation with the average of the 2-20 subjects, who also have been diagnosed with MCI. On the other hand, the ISC map for subject 40 was

computed by correlating the time-course of subject 40 with the average time-course of subjects 41-58. Fisher's transformation was applied to each subject's ISC map before examining group level results.

It is important to note that the resulting 58 ISCs maps were not necessarily independent. This is because there is some shared information between maps that is inherent in the computation. To illustrate this if we have 20 subjects in a group, the ISC for subject 1 would be the correlation between subject 1 and the average time-course of subjects 2, 3-20. The correlation between subject 2 and the average 1, 3-20 would be the resulting ISC for subject 2. The data from subjects 3-20 is shared across the ISCs maps between subject 1 and 2 showing that their values are not independent. There are n-2 shared elements between any pair of subjects from a group of size n. Because of this we relied on non-parametric tests to compute the cluster-corrected significance. We performed a group-wise permutation, where the group labels (diagnosis) for subjects were randomly permuted at each iteration. 5000 permutations were run (per analysis) to obtain the permuted null distribution. The observed data was compared to the null distribution to obtain p-values. Images were cluster corrected at FWE at $p < 0.05$ and voxel height-defining threshold of $p < 0.001$. See 6.6 Supplementary materials at end of this chapter for ISCs within each diagnosis group.

6.4 Results

6.4.1 Behavioural results

A between groups Welch ANOVA ($F_{2,35.62}$ = 10; p < 0.001) followed by Games-Howell post-hoc tests showed that participants diagnosed with MCI showed lower average memory (8.53 ± 4.85) for the videos when compared to the controls (14.26 ± 2.83; t = 4.5; p < 0.001) and participants with subjective memory complaints, but no diagnosis of MCI (13.13 ± 4.32; t = 3.2; p = 0.008). There was no significant difference between the controls and subjects with subjective memory problems (t = -0.96; p = 0.603)(see Figure 6-2).
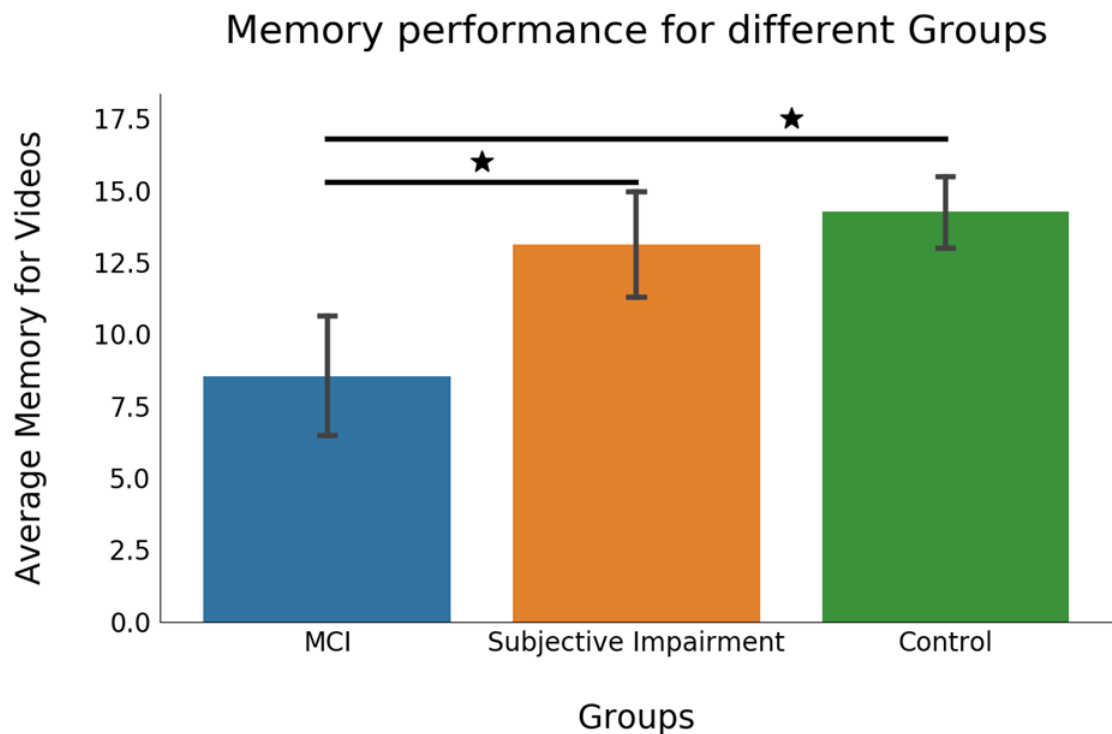
Figure 6-2 *Memory Performance*. The plot shows the average video memory performance for each for the three groups. There were 20 MCI, 18 Controls and 20 participants with subjective memory impairments. Means and confidence intervals are shown. The horizontal lines and star indicate a significant difference between groups at p < 0.01.

6.4.2 fMRI results

6.4.3 ISCs

Initially we contrasted the healthy control group to the MCI patient group. We observed lower ISCs in the MCI group in a set of areas including the right inferior frontal gyrus (IFG), right temporal pole (ATL), posterior medial cortex (PMC), precentral gyrus and superior frontal gyrus (SFG) (see Figure 6-3).
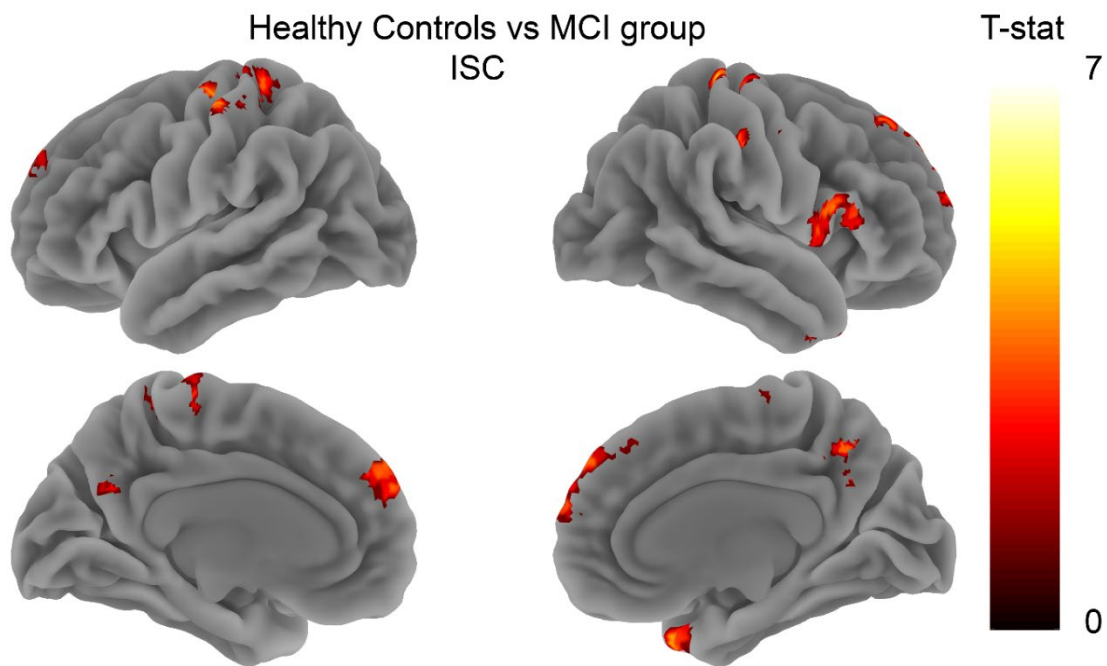
Figure 6-3 *Controls vs MCI group*. Map shows areas where the healthy controls showed significantly higher ISC values when compared to the MCI group. This indicates lower coherence across participants in the MCI group. Map is thresholded at p <0.001 with FWE cluster size correction through permutation testing.

We also observed less synchronized signal in the MCI group when compared to the subjective impairment group (see Figure 6-4). The MCI group exhibited lower ISC values in parts of the posterior medial cortex (PMC), ventromedial prefrontal cortex (vmPFC), SFG, right IFG, left middle frontal gyrus, and in the cuneus cortex.

When comparing the healthy control group versus the subjective memory impairment group, we observed higher synchronization in superior frontal gyrus for the healthy control group (see Figure 6-5). This result was surprising since both the healthy control group and the subjective memory impairment group

performed better on the video memory test when compared to the MCI group. Video memory accuracy however did not differ between the healthy control group and the subjective impairment group. Although the subjective memory group showed more variance on the video memory test compared to the control group, this effect did not reach significance (Levene's test F_1 = 2.74; p = 0.1). Given previous literature (Geerligs & Campbell, 2018) we might have expected that the subjective memory impairment group would show higher ISC values simply because they were younger. Since our main interest was effects in contrasts including the MCI group and the surprising nature of this finding, we do not discuss it further.

Provided there were not large differences in both behavioural and fMRI results across the subjective memory group and the healthy control group, we performed a contrast between both these groups and the MCI group. This was done to increase our statistical power to detect lower synchronization within the MCI group. Therefore, we compared the average ISC values across both the subjective impairment group and the control groups to the MCI group (see Figure 6-6). The group comparison of ISCs showed that participants that did not have a diagnosis of MCI were more similar to each other when compared to the group with MCI in a range of regions. We observed more idiosyncratic signal in the MCI group in ventral medial prefrontal cortex (vmPFC), precuneus, right inferior frontal gyrus (IFG), right anterior temporal pole (ATL), postcentral gyrus, superior frontal gyrus (SFG).
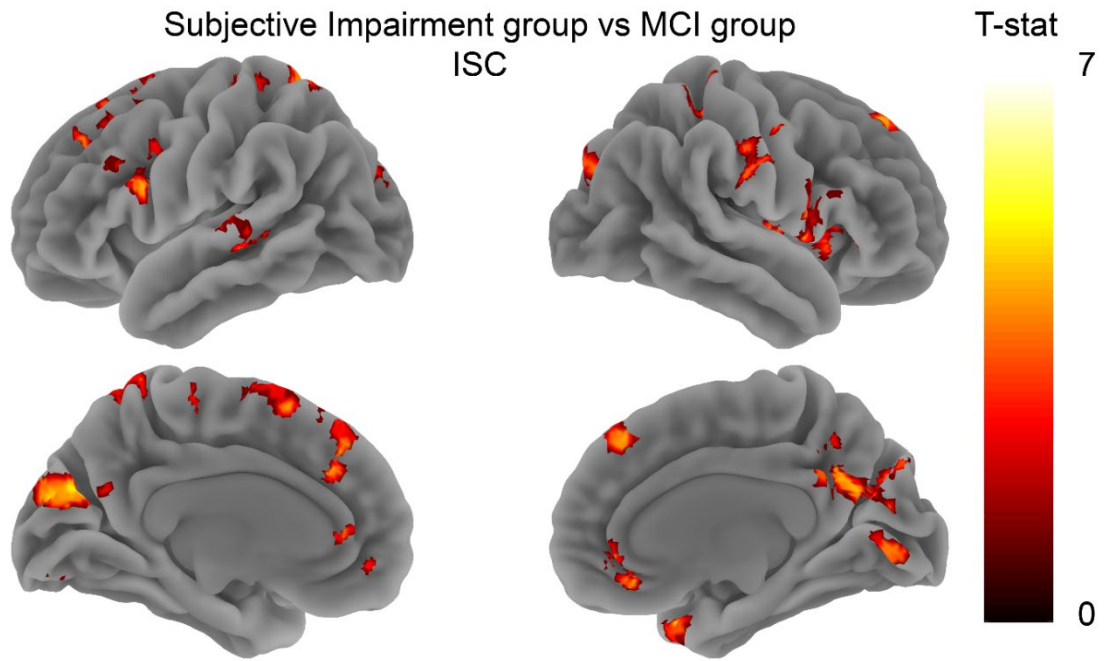
Figure 6-4 *Subjective impairment group vs MCI group.* Map shows areas where the subjective impairment group showed significantly higher ISC values when compared to the MCI group. Map is thresholded at p <0.001 with FWE cluster size correction through permutation testing.
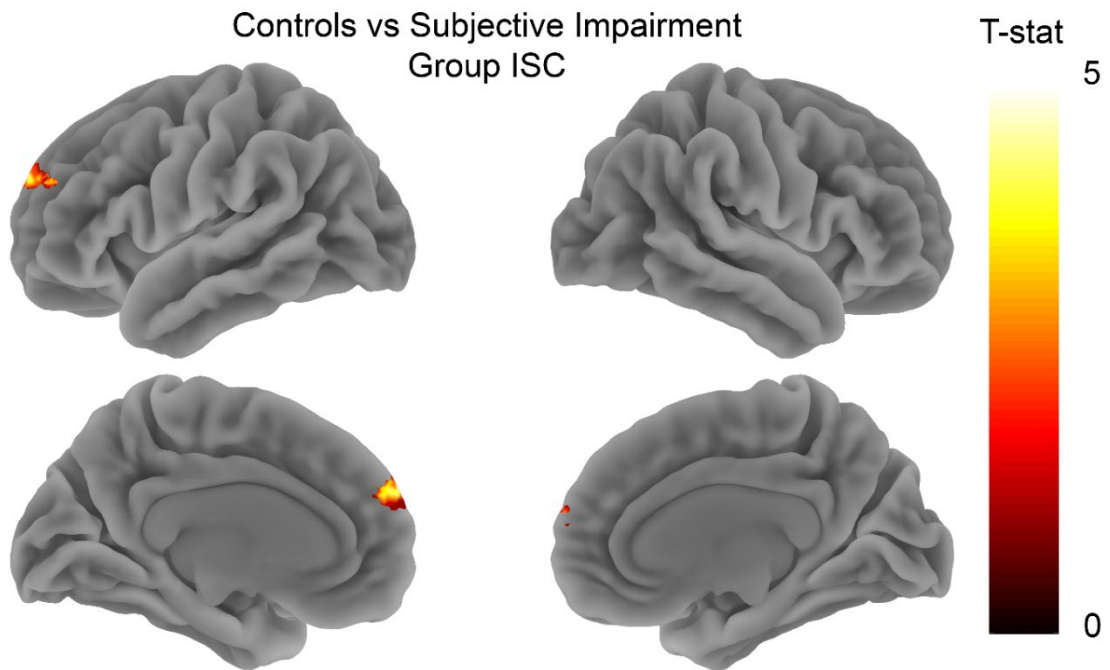
Figure 6-5 *Controls vs Subjective impairment group*. Map shows areas where healthy controls showed significantly higher ISC values when compared to the subjectively impaired group. Map is thresholded at p <0.001 with FWE cluster size correction through permutation testing.
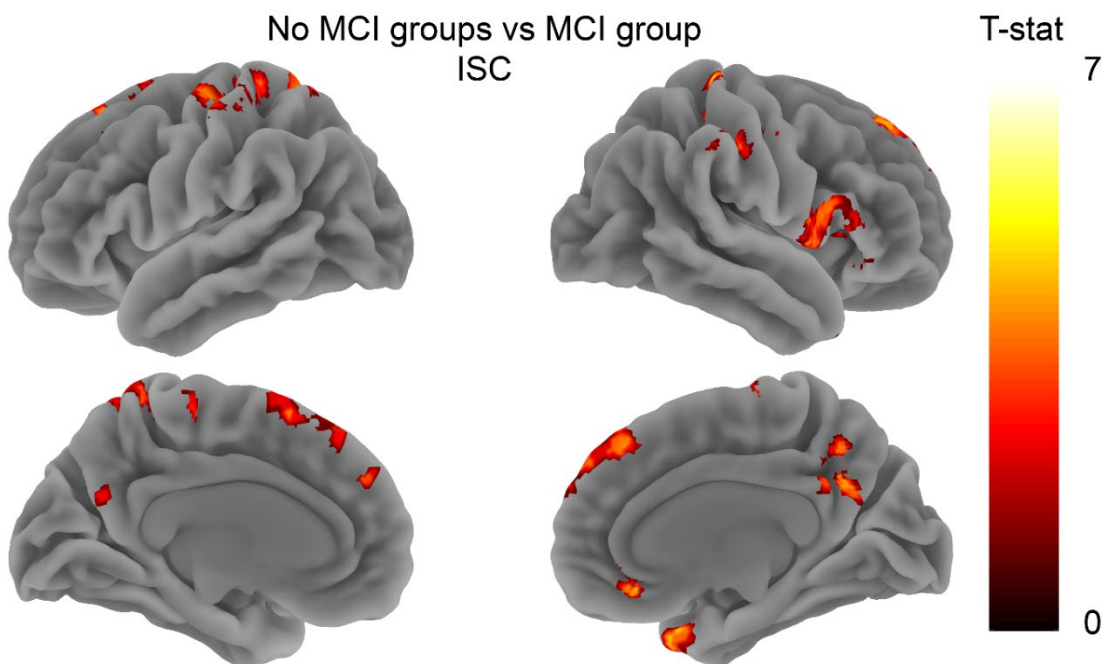
Figure 6-6 *No MCI groups vs MCI group*. Map shows areas where groups without MCI showed significantly higher ISC values when compared to the MCI group. Map is thresholded at p <0.001 with FWE cluster size correction through permutation testing.

6.5 Discussion

In the present study we examined whether MCI patients show less reliable processing of naturalistic stimuli. We had three groups of participants. One group was healthy controls, another group were participants with subjective memory impairment and another group were diagnosed with MCI. We presented participants with short video clips and used ISCs to examine similarity between participants with the same diagnosis. We observed that MCI patients showed less consistent processing in posterior medial cortex (PMC), vmPFC, SFG, right IFG and ATL, when compared to controls and participants with subjective memory impairment. MCI patients also remembered fewer details from the clips, suggesting that the observed lower consistency within the MCI group is indicative of maladaptive encoding. Our results extend previous behavioural experiments showing difficulties in processing naturalistic stimuli in individuals with MCI.

Here we observed that MCI patients showed reduced memory performance for the video clips and exhibited lower temporal similarity whilst encoding them. These results suggest that the MCI patients did not encode the clips adaptively. As outlined earlier, ISC is an analysis technique that is sensitive to stimulus-locked shared signal across participants. For instance, if a stimulus drives BOLD responses similarly across participants one would observe high ISC values. On the other hand, if the response in a brain area during the same stimuli is idiosyncratic across participants one will observe lower ISCs. Therefore, the reduced ISCs for MCI patients suggests that they processed the clips less consistently when compared to healthy older adults, and individuals with subjective memory impairments. Differences in MCI patients were observed in frontal and parietal regions that have previously been shown to be important in representing and encoding complex events (Baldassano et al., 2017; Bird et al., 2015; Chen et al., 2017; Honey, Thesen, et al., 2012; Oedekoven et al., 2019, 2017; Zadbood et al., 2017; Zuo et al., 2019). Our results provide further support in the role DMN regions play in the adaptive encoding of everyday activities. Below we discuss some of the potential explanations of our results.

Previous behavioural research has shown the MCI patients have problems processing naturalistic stimuli. Johnson et al., (2003) showed that patients with mild dementia had less detailed memories for narrative texts. Furthermore, Zacks et al., (2006) showed that participants with mild dementia have problems identifying transitions between events. Participants were shown videos of everyday actions and asked to press a button when they identified a meaningful boundary between events. For instance, when watching someone changing old bed sheets most participants would identify the removal of old sheets as separate from fitting in the new sheets. Mildly demented individuals differed from healthy older adults in how consistently they identified the boundaries and also showed much lower memory for the actual videos and order of presented events. The observed idiosyncrasy in segmentation of events was partly related to semantic knowledge of typical events.

It is possible that in the current study the observed synchrony across participants without MCI in DMN regions was partly driven by the reliable identification of boundaries between events (Baldassano et al., 2017; Zacks et al., 2001). Therefore, one speculation is that the less consistent BOLD activity we observed in the MCI group was because they did not appropriately identify event transitions. However, we did not collect any behavioural data on how participants segmented the stimuli.

One potential explanation for our results of increased idiosyncratic processing in MCI patients is that they had problems adaptively activating schema knowledge whilst they were encoding the clips. This is in-line with the observed lower ISCs in vmPFC. MPFC and particularly vmPFC have been consistently associated with representations of complex events and schematic processing (Ghosh & Gilboa, 2014; Gilboa & Marlatte, 2017). In a recent study Baldassano et al. (2018) presented young adults with clips taken from different shows and movies broadly falling into one of two schemas (airports or restaurant clips). They found that spatial patterns of activity were more similar across clips taken from the same schema, providing strong evidence that medial prefrontal regions are involved in processing generic schematic information about complex events (see also Chapter 3 and Chapter 4). Schema knowledge about events can help participants structure, segment and predict

incoming information more efficiently (Rumelhart, 1977; Schank & Abelson, 1977; Zacks et al., 2007, Zacks et al., 2006). One potential explanation for the reduced synchronization in vmPFC for MCI patients is that if they did not rely as much on prior script knowledge this could have affected how they segmented and comprehended the clips, leading to more idiosyncratic processing. MCI patients often have problems with everyday tasks and a recent study did find that mild impairment was associated with deficits in knowledge of everyday tasks (Jekel et al., 2015; Jorm & Jacomb, 1989; Roll et al., 2019; Royall et al., 2007; West et al., 1992).

It is important to note that one potential contributor to the worse performance exhibited by MCI patients is deficits in attentional control. Understanding everyday events involves interpreting them with reference to prior knowledge of similar events, but also maintaining information of the actions and narrative as it unfolds over time. Attentional deficits are quite common in MCI patients and indeed can be predictive of later development of AD. Using a range of neuropsychological tasks, Saunders et al., (2010) found deficits in simple, divided and sustained attention in patients with MCI impairment. Not paying attention to the same elements of the clips would decrease synchronization across participants and will lead to worse memory for the clips. ISCs have been shown to be affected by differences in attention, prior knowledge and interpretation of complex narratives, suggesting that problems with schematic processing and attentional deficits are not mutually exclusive explanations (Ames et al., 2015; Ki et al., 2016; Nguyen et al., 2019; Raykov et al., 2018; Regev et al., 2018; Yeshurun et al., 2017). Indeed, multiple cognitive processes contribute to narrative comprehension and it has been suggested that that the lines between different stages of memory (e.g. encoding/retrieval) are blurred in event cognition (see Ben-Yakov & Henson, 2018; Graesser et al., 1997; Hasson et al., 2015; Xue, 2018; Zacks & Ferstl 2016; Zacks et al., 2007, Zacks et al., 2006).

MCI patients exhibited differential processing in PMC, SFG and ATL. These results suggest that these regions are important for adaptive encoding of complex events. Recent studies in young adults have started to shed light on the brain areas that support processing of complex events. MPFC, PMC, and

other areas often associated with the default mode network (DMN) have been shown to be associated with integration of information over long time-scales. For instance, scrambling narratives at the paragraph level mostly disrupted processing in PMC, mPFC and AG (Honey, Thesen, et al., 2012; Lerner et al., 2011). Furthermore, Baldassano et al., (2017) showed that transitions across movie events were closely matched by changes in PMC patterns. Interestingly, patterns of PMC activity have been shown to be similar between encoding and retrieving the same events (Bird et al., 2015; Chen et al., 2017; Oedekoven et al., 2017; see also Chapter 4). Furthermore, reinstatement effects in PMC and ATL positively correlated with behavioural memory performance. Recently it has been argued that DMN regions and particularly PMC are involved in representing event models. These models are abstracted from modality and represent the what, where, who of complex events. Further evidence for this viewpoint comes from studies that have shown that spatial patterns of fMRI activity are similar across participants experiencing the same events regardless of modality (Chen et al., 2017; Honey, Thompson, et al., 2012; Regev et al., 2013; Zadbood et al., 2017). It is possible that the MCI patients held less detailed representations of the events, which is supported by the lower ISCs and poorer memory for the clips.

A possible limitation to the current study was that the participants with subjective memory problems were significantly younger than the MCI group. Age has been associated with deficits in cognitive control. Recently, older age was also associated with decreased ISCs whilst watching the movie (Geerligs & Campbell, 2018). We did not observe lower ISC in the control group when compared to the subjective memory impairment group, despite the age differences. Furthermore, we observed differences between the control group and the MCI group, who were both the same age. An important consideration with ISC analysis is whether the differences are due to group differences in noise level. To control for this we regressed out the 6 motion parameters and average WM and CSF signal before computing the ISCs. Our results are similar to previous research that has shown differentiation within the DMN network in MCI and early ADs when compared to healthy older adults (for review Chandra et al., 2019). For instance, Machulda et al. (2009) observed

hypoactivation in a set of frontal and parietal regions including precuneus and posterior medial cortex in MCI patients during encoding of complex visual scenes (see also Hampstead et al., 2011; Hampstead et al., 2019). Future studies with naturalistic stimuli directly controlling prior knowledge will be helpful to better differentiate the contributions of script knowledge and general attentional mechanisms in event cognition in MCI.

In conclusion our results showed that MCI patients had lower memory for the videos and showed idiosyncratic activity in PMC, vmPFC, ATL and SFG, which was suggesting of maladaptive encoding. Our results are in line with previous behavioural findings and further suggest that these regions are particularly important for representations of complex events. We note that future work will be needed to better understand the impact attentional control plays on the comprehension of everyday narratives.

6.6 Supplementary Materials
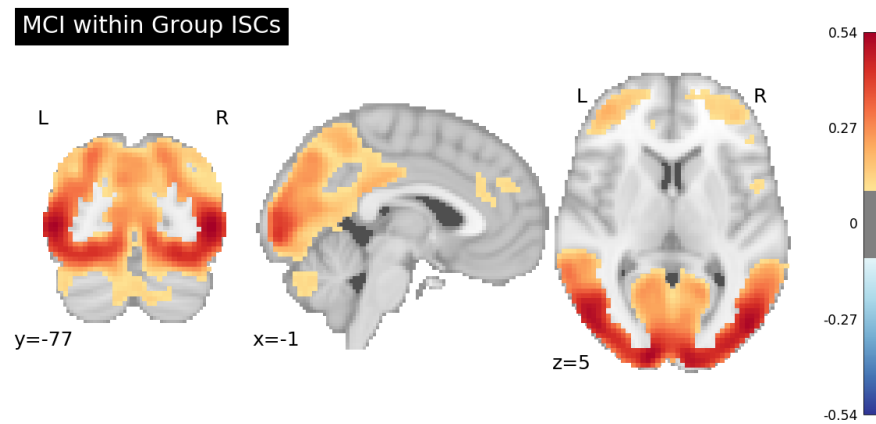
Supplementary Figure 6-1 *ISC map for MCI group*. Map shows brain areas showing significant synchronization across people diagnosed with MCI. Map shows voxels that were significant at the voxel level after applying FDR correction at p < 0.05. Colours represent to correlation values.
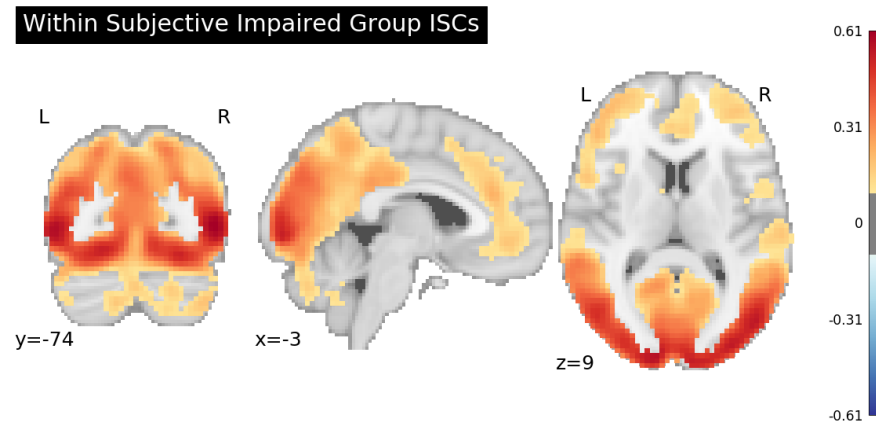
Supplementary Figure 6-2 *ISC map for Subjectively impaired group*. Map shows brain areas showing significant synchronization across people who attended the memory clinic but were diagnosed to be neurologically healthy. Map shows voxels that were significant at the voxel level after applying FDR correction at p < 0.05. Colours represent to correlation values.
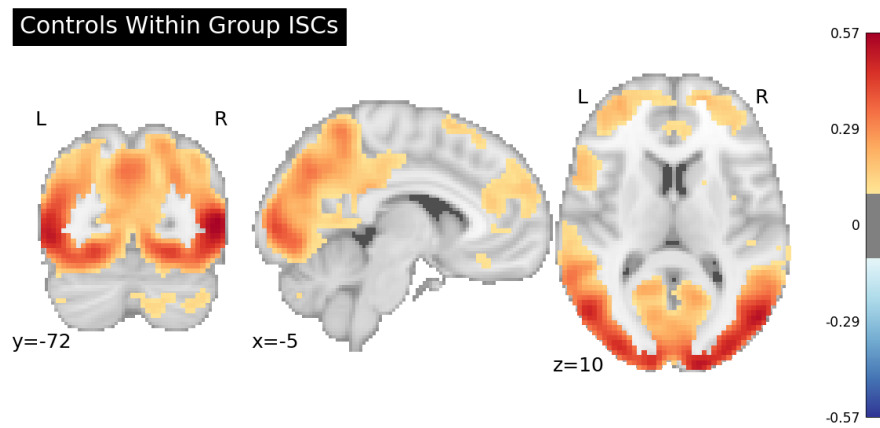
Supplementary Figure 6-3 *ISC map for Controls.* Map shows brain areas showing significant synchronization across healthy older adults. Map shows voxels that were significant at the voxel level after applying FDR correction at $p < 0.05$. Colours represent to correlation values.

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Chapter 7: General Discussion

The present research examined the effects of different types of prior knowledge on event cognition. Functional magnetic resonance (fMRI) data was collected to investigate how the brain utilises prior knowledge to affect processing of new information. One of the aims of the current thesis was to examine whether there are specialised brain areas that are involved in processing all types of prior knowledge. Most previous research using naturalistic stimuli has focused on prior knowledge that is learned in a single episode and relates to a single situation. Furthermore, in previous studies the provision of prior knowledge was often associated with completely different levels of comprehension. In Chapter 2 I examined the effects of a more subtle manipulation of situation specific prior knowledge. This experiment allowed me to investigate how we integrate incoming sensory information with prior knowledge of a narrative topic. In a separate experiment I focused on schematic prior knowledge, which was learned over multiple episodes and was relevant for several events. This experiment allowed me to examine how schematic knowledge about people can affect processing of both picture and video stimuli. In Chapter 5 I examined which brain areas might be particularly important for representing amodal knowledge about person stereotypes. Chapter 6 examines event cognition in individuals with mild cognitive impairment (MCI). In the current chapter I provide a brief summary and discussion of the main results. I also note some methodological limitations and discuss directions for future research.

Chapter 2 focused on the effects of providing narrative context on processing continuation videos. Participants watched first half videos with either coherent or incoherent audio. Therefore, when watching the second half videos, they either had or did not have knowledge of the previous narrative. This type of situation specific prior knowledge was associated with better memory for the second half clips and resulted in more similar brain activity across participants sharing the same knowledge. Specifically, regions often associated with semantic processing and discourse comprehension seemed to

be affected by the provision of narrative context. The paradigm was particularly helpful in allowing me to investigate how we integrate narrative information in order to construct a more detailed event model of the situation. Unlike previous studies of prior knowledge that prevented individuals from constructing an event model at all, in the current study participants were provided with some general information about the situation even in the condition where they did not know the topic of conversation. As such my manipulation probably affected how participants interpreted the situation and how detailed was their mental representation of the event. I believe this is particularly helpful as similar paradigms can be useful to understanding how we represent different dimensions of the event models (e.g. location, narrative context, people).

There have been already quite a few studies showing that a large set of regions (particularly in the DMN) are involved in representing different situations or vastly different interpretations of the same story. However, it is still unclear what information is represented by the different brain areas. For instance, some of the differences could be attributed to more general or schematic differences in the situations (e.g. train ride vs a bank robbery). My results suggested that semantic regions may be particularly important for integrating prior narrative information with incoming sensory stimuli in order to build a more coherent event model.

Chapters 3 and 4 aimed to investigate effects of prior schematic knowledge about people. Particularly, participants watched a set of episodes from a TV show over the course of a week and learned how the main characters typically act, where they live, and what is their relationship. Inside the scanner, participants were presented with still pictures and short clips taken from the trained and an untrained show. The results from the picture and video task are presented in separate chapters (3 and 4 respectively).

In the picture task, the contrast of trained versus untrained stimuli was associated with higher BOLD activation in ventromedial prefrontal cortex (vmPFC), hippocampus and retrosplenial cortex (RSC). These results go against some of the predictions made by the SLIMM model (van Kesteren et al., 2012). According to van Kesteren and colleagues (2012) the hippocampus,

should be more involved in the processing of stimuli that are incongruent with prior knowledge. Based on this, we might have expected that the hippocampus would be more activated when processing the untrained stimuli when compared to the trained stimuli. Our results did not support this prediction or the SLIMM proposal that the vmPFC and hippocampus have competing roles during processing of information related to prior knowledge. Indeed, our results suggest that both vmPFC and hippocampus are similarly involved in encoding of new information related to prior knowledge.

It should be noted that the untrained stimuli are not necessarily incongruent with prior knowledge, but potentially fall under the category of new information unrelated to prior knowledge. Nonetheless, the SLIMM model still would not predict higher hippocampal involvement for the trained stimuli. A very important consideration for the SLIMM is that it is often difficult to quantify a stimulus' congruency with prior knowledge and indeed this is potentially task dependent. More research will be needed to better understand the interactions between vmPFC and hippocampus and the factors that influence whether they exhibit complementary or competing roles (Preston & Eichenbaum, 2013; van Kesteren et al., 2012).

Interestingly, in the video task I did not observe any brain areas that showed significant differences between processing the whole duration of the trained and untrained videos. At the face of it, these results demonstrate that responses to simple stimuli may not necessarily generalize to more naturalistic stimuli. The use of naturalistic stimuli was useful as it implied that it is important to consider when and for how long a particular cognitive process is engaged. For instance, when examining the BOLD response to the onset of the videos I observed higher BOLD activity for the trained versus untrained clips in vmPFC, hippocampus and RSC (see Chapter 4 Supplementary Materials). I note that given the exploratory nature of the analysis future work needs to be done to better understand such effects. Nonetheless, the point that naturalistic stimuli may be particularly useful for elucidating at which stage of an event a cognitive process is engaged still holds. This is because by design naturalistic stimuli contain information that unfolds over time.

In both Chapters 3 and 4, I find some evidence that prefrontal regions, particularly vmPFC and mPFC are involved in representing schema information. The use of still pictures, in Chapter 3, was helpful as I could more easily relate the result to previous work done on the topic. Indeed, we were able to examine how univariate brain activity is modulated by the presence of schematic knowledge. Furthermore, I used an analysis technique recently developed to compare between BOLD signals in different brain areas. This was particularly helpful as some theories have proposed that vmPFC and hippocampus have competing roles. However, direct comparison across regions has rarely been done in the neuroimaging literature. My results neatly demonstrate that observing a significant effect in one region, but not in another at pre-set threshold does not necessarily mean there is significant difference in the activations across the regions.

In Chapter 4 I find higher pattern similarity between trained clips when compared to untrained clips in mPFC, angular gyrus (AG) and superior frontal gyrus (SFG). My results further extend previous work by showing that mPFC, AG and SFG are supporting person specific schematic knowledge during event perception.

Based on previous literature and the results in my experiments, in particular Chapters 2 and 4, it is possible to speculate that the posterior medial cortex (PMC) is particularly important for representing the very slowing changing characteristics of the situation, such as the location and gist. For instance, Ames et al. (2015) presented participants with vignettes that were difficult to interpret without the provision of prior context. They found increased synchronization of BOLD activity in vmPFC and PMC across participants sharing the same knowledge. In separate studies similar patterns of activity in PMC have been shown across participants watching, remembering or listening to the same events being described (Bird et al., 2015; Chen et al., 2017; Oedekoven et al., 2017; Zadbood et al., 2017). Having a completely different interpretation of the narrative has also been shown to be associated with differences in BOLD activity in PMC and vmPFC (Yeshurun et al., 2017). Previous manipulations have often either prevented participants from constructing an event model at all or made them construct vastly different event

models and commonly observed differences in PMC and vmPFC (Ames et al., 2015; Nguyen et al., 2019; Saalasti et al., 2019; Yeshurun et al., 2017). The manipulation in Chapter 2 was more subtle as in it provided better context for the situation, but possibly did not change completely the interpretation of the events. Indeed, it is quite likely that participants understood the gist of the situations even in the second half clips. This might explain why I did not observe any modulation of the PMC with the provision of prior narrative knowledge in Chapter 2. PMC has been associated with theory of mind functions and story comprehension (Mar, 2011). Therefore, one speculation is that the PMC might be particularly important for representing the gist of the event. This is consistent with previous suggestions made by Ranganath and Ritchey (2012).

However, I note that this is at the moment a mere speculation and not all data is in agreement with it. First, this interpretation is partly based on null results (in Chapter 2), which could be potentially due to various other reasons (e.g. lack of power). Second, I found evidence of higher reinstatement effects in PMC being correlated with memory accuracy (see Chapter 4). This suggests PMC does represent not only the gist of the event but also some more detailed information about the events. This is further supported from the results in Chapter 6 where I did observe less reliable processing of complex events in PMC in patients with mild cognitive impairment. Although it is possible that they had problems understanding the gist and activating the relevant prior knowledge, it is also possible that the observed memory deficits were more related to lack of more detailed encoding. Future studies will be needed to better understand to what extend PMC represent only the gist of the event.

Chapter 5 examined stereotypical knowledge about professions. This study was partly ran as a pilot to examine whether, I could observe amodal representations of stereotypes and whether they would be present in regions often associated with representing schematic knowledge. Stereotypes can act to help us interpret our social environment and provide structure to the incoming information. As such they might resemble schematic information since both can help us compress the dimensions of the incoming information. Furthermore, whereas the knowledge participants learned in Chapter 3 and 4 was schematic

but still specific to an individual, the stereotype task in Chapter 5 was designed to activate general social knowledge not related to any one individual. I did not find any cross-modal classification effects, which most likely speaks to an underpowered design. However, it is also possible that the picture task was not best suited to activate social stereotypes. This study was mostly informative to show me that it is often not as straightforward to observe multivariate classification effects in fMRI analyses.

In chapter 6 I applied ISC analysis to examine data collected by other researchers. I examined processing of naturalistic stimuli in healthy older adults or individuals with mild cognitive impairment (MCI), I was particularly interested in the MCI group, since they often suffer from memory problems, but also might experience difficulties with everyday activities, sustaining attention and orienting themselves. This suggested that they might have difficulties encoding the video clips, which was supported by the both behavioural and neuroimaging data. It should be noted that it is possible that MCI patients' problems processing the clips might not only be due to problems with attention but might be due to issues with appropriately activating prior knowledge. Indeed, some evidence suggests that MCI patients do have deficits on tasks examining knowledge of everyday task structure. However, it is difficult to distinguish between these two accounts without including further tests. This is partly due to the fact that previous research suggests that how attentional resources are allocated partly depends on participant's prior knowledge of the task being performed (Kim & Rehder, 2011; Kosie & Baldwin, 2019). One possible way of distinguishing between these two accounts in the future would be to include explicit tests of attention and prior knowledge and examine how performance on these tests correlates with performance on more naturalistic tasks. Techniques with better temporal resolution might further add to our understanding on how prior knowledge and attention interact. It is possible that these cognitive processes could be separated at smaller temporal scales than measured with fMRI. For instance, it is possible that prior knowledge aids participants to adequately allocate attention in certain points in the narrative by providing a scaffold of when change in important information might occur. However, more research would be necessary to understand how these processes operate.

An important limitation for the results from Chapter 6 is that not all groups were matched on age. This was partly due to the prospective design, where participants were recruited before knowing their diagnosis. The subjective memory group was younger than both the MCI and control group. Age has been previously associated with decrease in synchronization across participants (Geerligs & Campbell, 2018). However, I did not observe decreased synchronization in the control group, which was on average older, when compared to the subjective memory impairment group. I included the subjectively impaired group as well since it was better matched to the MCI group in other aspects. For instance, anxiety and other personality factors might have been more similar between the subjectively impaired and the MCI groups who were both referred from a memory assessment clinic due to subjective complaints. Another important consideration during the interpretation of the results of this chapter is that MCI is often associated with grey matter deterioration. Therefore, it would be important to also examine brain structural differences between the groups to better understand whether effects here are partly due to reduction in grey matter in the MCI group.

Naturalistic stimuli can be very useful for examining cognition. Indeed, it is important to demonstrate whether results using simpler stimuli generalise to more ecologically valid experiments. Naturalistic designs can be particularly helpful to understand when a particular cognitive process is engaged. They can help us understand whether we maintain a schema for a restaurant for the whole duration of a dinner event, or we simply activate it at the beginning. Additionally, they can help us distinguish which features (location, people, narrative) are most important for memory. However, it should be noted that this inherent complexity of the stimuli comes at a cost. Such designs often require more difficult analysis techniques and it can be more difficult to achieve the same level of experimental control as achieved by more traditional experimental designs. This can sometimes make interpretation of results more difficult. Nonetheless, the inherent complexity of naturalistic stimuli can be particularly fruitful for our understanding of cognition. That is not to say that more traditional experimental studies are superseded, but simply that naturalistic

studies can help us address a different set of questions that might be difficult to investigate with more traditional experiments.

One potential consideration in the work presented in Chapter 2 and 4 is that my prior knowledge manipulations, not only boosted memory performance, but also increased subjective ratings of engagement with the stimuli. In real world situations it might be common for prior knowledge to also boost one's engagement with video stimuli. Future work will be useful to better distinguish evaluation processes from prior knowledge effects (Liu et al., 2016). Furthermore, it is often difficult to distinguish prior knowledge effects from successful memory recollection effects. It often is the case that similar brain regions are involved in episodic memory and prior knowledge effects and it is possible that recollection does play an important role in prior knowledge effects. The tasks I used often did not explicitly require recollection. However, it is still possible that recollection did affect the results.

Nonetheless, there are several reasons I think that an episodic memory account is not complete. The IFG and AG regions observed in Chapter 2, and AG region observed in Chapter 4 have been strongly associated with semantic memory and indeed damage to these regions lead to deficits in semantic processing (DeLeon et al., 2007; Robson et al., 2017; Schwartz et al., 2011). MPFC has often been associated with schema processing and has been suggested to represent abstract level schematic information (Gilboa & Moscovitch, 2017; Robin & Moscovitch, 2017). Furthermore, recent views have started to suggest that some of the previously observed episodic memory effects in regions overlapping in with the DMN might be actually representing semantic concept knowledge rather than retrieval itself (Renoult et al., 2019). The spatial pattern similarity effects we observed in Chapter 4 are very similar to tasks that exhibited no demands on episodic recollection (Baldassano et al., 2018). The design and analysis in Chapter 4 suggest that in order to observe such effects each training video should have acted as a memory cue to the same episodic information. However, it is the case that often it is very difficult to exhibit direct control over participants cognitive process, so I cannot completely discount effects of episodic recollection. Further studies will be needed to

better understand how retrieval and prior knowledge effects interact and how they can be distinguished.

I note that an important limitation in the use of naturalistic stimuli inside a scanner is the factor of time consideration. For practical reasons, it is often difficult to scan participants for extended periods of time. This limits the number of stimuli that can be used in an experiment. In my experiments I have tried to use different video clips in order to achieve some generalization across clips. In Chapter 4 I examined how participants processed clips that were taken from either a familiar or an unfamiliar TV show. However, due to time constraints I could not investigate how more gradual differences in schema knowledge will affect processing. Particularly interesting would have been to be able to include clips that contained information that is directly incongruent with participants schema knowledge (see Greve et al., 2019; van Kesteren et al., 2012).

Another limitation that should be mentioned, is not specific to naturalistic fMRI designs, but is important to reiterate. The BOLD signal is not a direct measure of neuronal activity. Indeed, research is still unveiling what exactly is the relationship between the measured BOLD signal and neuronal activity in different brain areas (Hall et al., 2016). A further consideration is the low temporal resolution allowed by the BOLD signal, which can complicate some of the inferences about cognitive processes (Ghuman & Martin, 2019). No technique is perfect, and converging evidence from multiple methods is often needed to make very strong claims about cognitive processing in the brain. Electroencephalography (EEG) and electrocorticography (ECoG) are two methods that might be particularly useful for examining the timing of schematic processes. Furthermore, such methods might be useful to investigate the dynamic connectivity between brain regions during naturalistic processing.

In the current thesis I have examined the effects of situation specific and schematic prior knowledge. Both types of prior knowledge were associated with memory benefits. Different brain areas were observed across experiments further supporting the importance of better dissociating between these different types of prior knowledge. The current paradigms could be adapted to further examine how the content of the prior knowledge can affect neural

representations. The use of naturalistic stimuli allowed me to examine how we integrate the incoming information with our prior knowledge to build coherent event models. Open questions are to what extent are the effects currently observed due to representations of semantic information rather than because of the cognitive and evaluative processes that are associated with prior knowledge. For instance, it is possible that stimuli that are related to prior knowledge are associated with more evaluative processes or trigger episodic recall. Furthermore, it should be noted that more research needs to be done to understand how we update our event models and indeed how such updating is affected by prior knowledge. Taken together the findings from my thesis add further to the growing literature on the effects of prior knowledge on event cognition.

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