The function of medial prefrontal cortex in mental imagery and autobiographical memory

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Submitted for PhD in Cognitive Neuroscience

2016

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Declaration:

I, Wen-Jing Lin, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Experiment 2 in Chapter 3 was reported in the paper by Lin, W.-J., Horner, A. J., Bisby, J. A., & Burgess, N. (2015). Medial Prefrontal Cortex: Adding Value to Imagined Scenarios. Journal of Cognitive Neuroscience, 27(10), 1957–1967. http://doi.org/10.1162/jocn_a_00836

Experiment 3 in Chapter 4 was reported in the paper by from Lin, W.-J., Horner, A. J., & Burgess, N. (2016). Ventromedial prefrontal cortex, adding value to autobiographical memories. Scientific Reports, 6, 28630. http://doi.org/10.1038/srep28630

Signed: 林雯菁

Date: 8/Feb/2017

Acknowledgements

Firstly, I would like to express my sincere gratitude to my primary supervisor Professor Neil Burgess for the continuous support of my study and research, for his extraordinary patience, generous, and knowledge.

My sincere thanks also go to Dr. Aidan Horner for his enormous help in my research and the writing up process. I would also like to thank my viva examiners, Dr. Sam Gilbert and Dr. Jon Simons for their helpful comments and suggestions. I appreciate the financial support from Taiwanese government that funded my PhD study. I would also like to thank Dr. James Bisby, and Dr. John King who provided me much useful advice.

I thank all the labmates in Space and Memory Group at UCL and my officemates. Also, I thank my friends and families for their support and understanding. I am also thankful to my participants, for participating my experiments and for willing to share their stories with me.

最後，感謝宇瞻。

Abstract

The medial prefrontal cortex (mPFC) is consistently implicated in the network supporting autobiographical memory and episodic simulation, but its functional contribution to these cognitive abilities remains unclear. Given its involvement in value processing in decision-making processes, mPFC might be important in contributing in a similar way during memory and imagery. Two fMRI experiments were carried out in order to examine if the mPFC plays a role in representing the subjective value of elements in autobiographical memory and, separately, in mental imagery. In Experiment 1, a paradigm was designed in which participants imagined scenarios involving details about spatial context, a physiological state of need (e.g. thirst), and two items which could be congruent (e.g. drink) or incongruent (e.g. food) with the imagined state. Results confirmed that the imagined-value paradigm is able to manipulate the participants' subjective values of imagined items. Therefore, the same paradigm was performed while the participants were in the scanner in Experiment 2. The fMRI signal in the mPFC reflected the modulation of an item's subjective value by the imagined physiological state, suggesting that the mPFC selectively tracks subjective value during mental imagery. In Experiment 3, the participants recalled autobiographical episodes and items (liked and disliked items) from each episode in the scanner. The blood oxygen level dependent (BOLD) signal in the ventromedial prefrontal cortex (vmPFC) was parametrically modulated by the affective values of the items in the participants' memories when they were recalling and evaluating these items. An unrelated modulation by the participants' familiarity with the items was also observed. During the retrieval of

an event, the BOLD signal in the same region was modulated by the personal significance and emotional intensity of the memory, which was correlated with the values of the items within them. These results support the idea that vmPFC processes self-relevant information and suggest that it is involved in representing the personal emotional values of the elements comprising autobiographical memories. In conclusion, the experiments in this thesis provided evidence to support the hypothesis that mPFC represents the subjective values of elements in our mental imagery and autobiographical memories.

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1.1. Autobiographical memory recall and episodic imagery

Autobiographical memories are memories regarding events that have occurred in our real life (Conway, 1992; Conway & Pleydell-pearce, 2000). Autobiographical memories consists of both episodic memory and semantic memory (Levine et al., 2004). For example, to recall the experience of your first job interview is an autobiographical memory recall. You can not only recall the facts of this event but can also vividly re-experience most, if not all, of what happened within that event. You might be able to recall the setting of the waiting room, as well as the feelings of nervousness and anxiety while waiting for the interview. You might recall which pair of shoes you wore and also re-experience the pain on your heels from the shoe rubbing. Autobiographical memories, especially those significant ones, play a major role in defining and shaping who we are.

Episodic imagery, or mental imagery, is the ability to mentally construct a situation or scenario which differs from the current one. The content of mental imagery is constructed from multimodal such as visual, auditory, odour, haptics, emotions and so on. For example, to imagine oneself finally arrive the top of Mount Everest on a sunny day after 40-days of climbing. The imagined scene may involve the great scenery view from Mount Everest, physical tiredness and muscle soreness from climbing, happiness, and excitement because of the accomplishment.

Memory retrieval is a reconstructive process (Bartlett, 1932), and so is autobiographical memory recall. In addition to involving the complex details of the scene from an event, the concept of self and self-relevant processes are also thought to be incorporated in our autobiographical memories (e.g., Gilboa, 2004; St. Jacques, 2012). Such self-relevant processes are often evident during episodic retrieval (e.g., Brian Levine, 2004), imagination or ‘episodic simulation’ (e.g., Benoit & Schacter, 2015; i.e. to mentally simulate oneself in a situation which is different from the current one, or to simulate an alternative situation to what really happened in the past, or to picture a circumstance in the future). To create such detailed and complex scenes in our mind, it is proposed that one must (1) construct pieces of information into a meaningful narrative (Schacter & Addis, 2007), (2) visualise or construct the complex scene (Bird & Burgess, 2008; Byrne, Becker, & Burgess, 2007; Hassabis et al., 2009; Hassabis, Kumaran, & Maguire, 2007; Mullally & Maguire, 2014) and (3) project oneself into the scenario via mental time travel (Buckner & Carroll, 2007; Tulving, 2002).

1.1.1. Neural mechanisms of autobiographical memory retrieval and episodic imagery

Considering that there are many commonalities between autobiographical memory recall and episodic imagery, it is not surprising that patients with impaired memory also demonstrate difficulties during mental imagery (Addis, Wong, & Schacter, 2008; Bertossi, Aleo, Braghittoni, & Ciaramelli, 2016; Bertossi, Tesini, Cappelli, & Ciaramelli, 2016; Hassabis, Kumaran, Vann, & Maguire, 2007; Klein, Loftus, & Kihlstrom, 2002; Tulving, 1985). For example, when imagining novel experiences, patients with hippocampal lesions generated fewer details and less coherent contents than controls did (Hassabis, Kumaran, Vann, et al., 2007). Patients with mPFC lesions had impairments in both memory recall and future imagination (Bertossi, Aleo, et al., 2016; Bertossi, Tesini, et al., 2016).

Neuroimaging studies have also shown that autobiographical memory retrieval and episodic imagination recruit a similar brain network, or so called “core network” (Buckner & Carroll, 2007). The core network (see Figure 1) includes the hippocampus, parahippocampal gyrus, retrosplenial cortex, posterior parietal cortices (PPC), and medial prefrontal cortex (mPFC) (e.g., Addis, Wong, & Schacter, 2007; Szpunar, Watson, & McDermott, 2007; for a review, see Schacter, Addis, & Buckner, 2009; for meta-analysis, see Benoit & Schacter, 2015). Given the broad range of regions identified by such studies, understanding how each of these areas function and interact with each other is critical to the field of memory.

Among these brain regions, the medial temporal lobe has a well-known essential role in memory encoding and retrieval (reviewed in Eichenbaum, Yonelinas, & Ranganath, 2007). In general, the hippocampus is critical to memory encoding, consolidation and recollection. The potential functional roles of the hippocampal, parahippocampal and retrosplenial and medial parietal cortices in generating visual imagery for spatial scenes have been proposed and simulated in some detail (e.g., Bird & Burgess, 2008; Byrne et al., 2007).

Meanwhile, although there are still ongoing debates about the function of posterior parietal cortex (PPC) in autobiographical memory retrieval, there are multiple theories regarding its potential function. For example, based on the classical accounts of PPC function in attention processing, one hypothesis suggests that the superior PPC mediates top-down attention when attention is necessary for memory retrieval and the inferior PPC mediates bottom-up attention when attention is captured by memory contents (for reviews, see Cabeza, Ciaramelli, Olson, & Moscovitch, 2008; Ciaramelli, Grady, Levine, Ween, & Moscovitch, 2010; Yazar, Bergström, & Simons, 2012). An alternative hypothesis tries to address this issue from the perspective of memory dual-process, i.e. familiarity- and recollection-related recognition judgment (e.g., Montaldi, Spencer, Roberts, & Mayes, 2006; Vilberg & Rugg, 2007). Some other researchers propose that the function of inferior parietal cortex is relevant to maintain or represent retrieved information, like a temporary information buffer (Vilberg & Rugg, 2008; Wagner, Shannon, Kahn, & Buckner, 2005). Which is similar to the working memory buffer proposed by Baddeley (Baddeley, 2000).

Finally, although studies have consistently shown that both autobiographical memory recall and episodic imagery recruit the medial prefrontal cortex (mPFC), the functional role of mPFC in autobiographical memory recall and episodic imagery is not clear yet. Regarding the function of mPFC in autobiographical memory, there is not much relevant literature at the moment. In one study, Speer and colleagues (2014) found that activity of mPFC and striatum was enhanced by retrieval of positive emotional autobiographical memories. They, therefore, hypothesised that the involvement of mPFC in autobiographical memory retrieval is because these memories are valuable (see also D'Argembeau, 2013). In another study, Bonnici and Maguire (2012) demonstrated that vmPFC contains both recent (two weeks old) and remote (10 years old) autobiographical memories. However, the remote memories are more strongly represented in vmPFC and other neocortical regions. In short, there is little agreement on what role mPFC plays in mental imagery and autobiographical memory retrieval.

The involve of mPFC beyond autobiographical memory retrieval. Memory encoding, confabulation, and fear extinction all recruit regions within mPFC (Milad et al., 2005; Milad & Quirk, 2002; Schnider, 2003; Simons & Spiers, 2003). For instances, in a trait adjective judgement study, mPFC activity was found to be greater for subsequently remembered words than that for subsequently forgotten words and also greater for self-descriptive traits (Macrae, Moran, Heatherton, Banfield, & Kelley, 2004). Patients with mPFC lesions may manifest spontaneous confabulation (for a review, see Schnider, 2003). These may provide insight into the role of mPFC in autobiographical memory retrieval and episodic imagery.

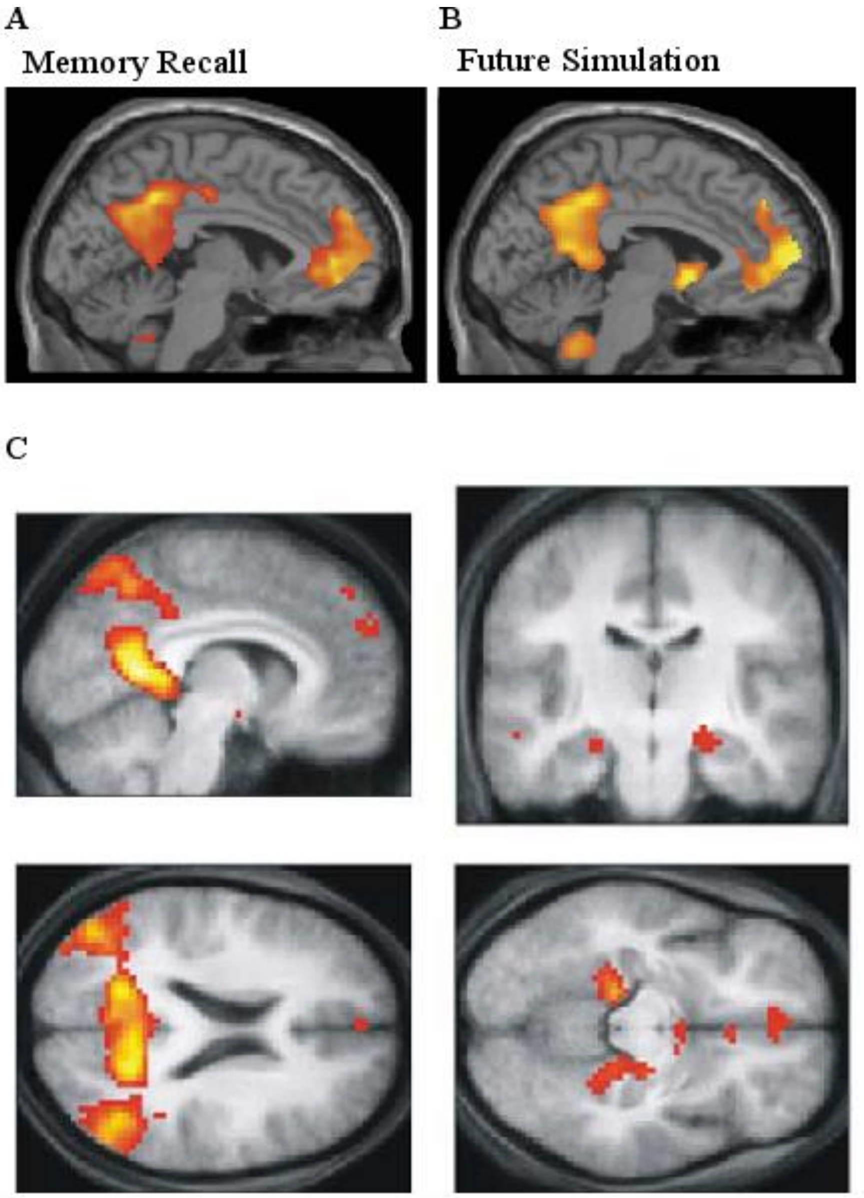


Figure 1. The core network

Illustration of the core autobiographical memory network demonstrating the similarity in regions between (A) memory recall and (B) future simulation (taken from Buckner and Carrot, 2007) and (C) the overlap of activity between episodic memory recall, recalling a previously imagined fictitious scene, and imaging a novel fictitious scene. Regions in this core network, included hippocampi, parahippocampal gyrus, retrosplenial, posterior parietal cortices, middle temporal cortices, and medial prefrontal cortex (taken from Hassabis, Kumaran, & Maguire, 2007).

1.1.2. Hypotheses regarding the overlap of AM and mental imagery

As mentioned above, mental imagery and autobiographical memory retrieval recruit similar brain regions, so-called the core network (Schacter et al., 2009). Several hypotheses which have been proposed aimed to explain why both of these two cognitive functions rely on the core network. In this section, I will briefly introduce three relevant hypotheses or theories, i.e., the constructive episodic simulation hypothesis, the scene construction theory, and self-projection hypothesis.

1.1.2.1. Scene construction theory

According to scene construction theory, episodic memory recall, mental imagery, future simulation, and spatial navigation all require an ability to generate, maintain, and visualise a reasonable and spatially-coherent scene (Bird & Burgess, 2008; Hassabis et al., 2009; Hassabis, Kumaran, & Maguire, 2007; Mullally & Maguire, 2014). And hippocampus is the key region to construct these complex scenes (Maguire & Mullally, 2013).

A former London taxi driver with bilateral hippocampal lesions became unable to navigate from one location to another efficiently after limbic encephalitis. This patient reported that he cannot picture the route beforehand during navigation and the authors believe this implies that hippocampus is critical to scene construction (Maguire, Nannery, & Spiers, 2006). Another evidence supporting scene construction theory is the phoneme of boundary extension. Boundary extension was described by Intraub and Richardson (1989, as cited in Mullally & Maguire, 2014) in healthy people. After viewing a picture of a scene, people implicitly extend the boundary of the scene and representation of the scene contains more details than the actual picture. If the same picture is shown to people after a delay, they would believe the second picture is closer up than the first one. Boundary extension has only been observed when the picture contains background scene but not when the picture presents a background isolated object. Boundary extension requires intact scene construction (Mullally & Maguire, 2014). Patients with hippocampal damage showed smaller boundary extension effect than healthy controls (Chadwick, Mullally, & Maguire, 2013; Mullally, Intraub, & Maguire, 2012). These results hence support the scene construction theory.

Also, the computational elements of ‘scene-construction’ are consistent with the neural firing patterns found in medial temporal and parietal regions (Burgess, Becker, King, & O’Keefe, 2001; Byrne et al., 2007). However, this theory focuses on hippocampal and posterior cortical areas and does not explain the involvement of prefrontal regions within the core network.

1.1.2.2. Self-projection hypothesis

The term ‘mental time travel’ refers to the ability to immerse oneself in scenarios which are different from the currently experiencing one- an ability which might be absent in most other animals (Tulving, 2002; although see Clayton & Dickinson, 1998; Clayton, Bussey, & Dickinson, 2003). To vividly recall a past experience is hence a mental time travel to the past. The direction in which an individual engages in mental time travel is not simply by reminiscing on the past but by also visualising future events. According to Tulving (2002), humans are able to perform mental time travel because they have three critical abilities.

Humans have the sense of subjective time; they are able to differentiate when recalling the past, experiencing the physical world or simulating the future; and they have the sense of self. In other words, humans are able to project themselves into various time points, i.e., self-projection.

Self-projection may not only contribute to mental time travel, but also to Theory of Mind and spatial navigation because these abilities all engage similar brain networks, or, the core network (Buckner & Carroll, 2007). In other words, humans are able to project themselves into other times, spaces, and agents (Okuda, 2007). According to the self-projection hypothesis, the MTL, prefrontal and parietal areas of the core network collaborate together to make self-projection possible (Buckner & Carroll, 2007; Szpunar et al., 2007). However, some have suggested that such self-projection is mainly supported by the frontal and parietal areas of the core network, without the MTL (e.g., Nyberg, Kim, Habib, Levine, & Tulving, 2010). Both views therefore agree that the prefrontal region of the core network is essential to self-projection.

In a recent study, Bertossi et al. (2016) demonstrated that patients with ventromedial Prefrontal cortex (vmPFC) lesions have difficulty in recalling memories and imagining future events. Compared to healthy controls, patients in Bertossi et al. (2016) created fewer and less vivid details when imagining future scenarios. The authors suggested that this confirms the involvement of vmPFC in constructive processes. Interestingly, these patients did not only demonstrate deficits in imagining self-related scenarios but also showed deficits when imagining scenarios relating to others (in this case, others were family members or the president of the Italian Republic). This implies that the self-projection hypothesis itself is not enough to explain the function of mPFC because to picture a future event happening to a close other or a distant other do not involve self-projection but mPFC patients still have deficits in these domains.

1.1.2.3. Constructive episodic simulation hypothesis

According to the constructive episodic simulation hypothesis, the reason why episodic counterfactual thinking or episodic mental imagery recruit similar brain networks as autobiographical memory recall does is because mental imagery contains two critical parts: (1) to retrieve or access to memory contents, and (2) to integrate the retrieved information into a meaningful story/narrative (Schacter et al., 2012; Schacter & Addis, 2007).

Memory retrieval is a reconstructive process (e.g., Bartlett, 1932; Ranganath, 2010; Schacter, Kenneth, & Koutstaal, 1998; Suddendorf & Corballis, 2007). When encoding, we do not memorise information bit by bit; when recalling, we do not simply replay the encoded contents. Otherwise, we would not be able to observe the phenomena of false recognition or memory confabulation (e.g., Schacter et al., 1998).

To recall an episode, people need to access to memory, to pick up relevant details and to assemble all the elements into a meaningful story. Schacter and Addis (2007) argue that the episodic memory system makes these steps possible because it is highly adaptive. It is critical for an individual to mentally simulate plausible situations so he/she is able to prepare or plan ahead before the events happen in the real world. The process of episodic memory recall is very similar to that in episodic simulation and this similarity caused the overlapping of neural networks in episodic memory retrieval and mental imagery (Schacter & Addis, 2007).

Although episodic simulation and episodic memory retrieval recruit similar brain network, there are also observable differences in brain networks. The constructive episodic simulation hypothesis also focuses on the subtle differences between simulation and memory recall (Schacter et al., 2012) and it suggests that there are two distinct subsystems within the core network (Addis, Pan, Vu, Laiser, & Schacter, 2009)- one for imagining and the other one for remembering. The one for imagining includes anterior hippocampus, medial prefrontal cortex and inferior frontal gyrus while the one for autobiographical memory recall includes hippocampus, parahippocampal gyrus, and visual cortex.

In general, neuroimaging studies have shown that, several regions show greater activity during episodic simulation than during episodic recall (for a meta-analysis, see Benoit & Schacter, 2015), including mPFC, dlPFC, posterior cingulate gyrus, posterior inferior parietal lobe, and MTL (Figure 2). The constructive episodic simulation hypothesis explained these differences in two ways. First, episodic simulation may demand higher cognitive control than episodic memory recall does. Unlike the contents of episodic memory, the contents of episodic simulation have not yet happened hence there is usually more than one way to develop the imagined contents. To carefully select theoretically plausible contents for imagined scenarios and to exclude unwanted outputs may require higher cognitive control demands. This could be able to explain why episodic simulation activates dlPFC to a greater degree than episodic memory recall. Second, in order to acquire adequate information to complete a plausibly imagined scenario, it is necessary to retrieve multiple memories. This could be the reason why the MTL activity is higher in episodic simulation than episodic memory recall.

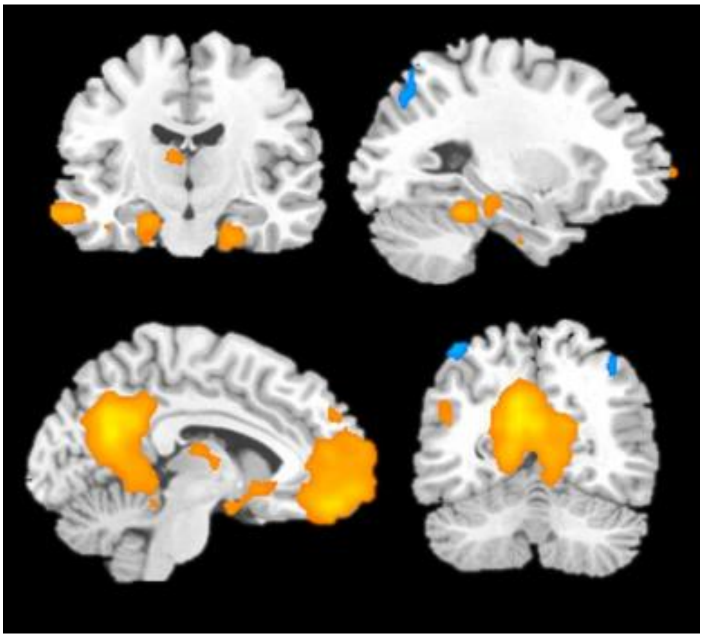


Figure 2. EPISODIC SIMULATION VS. MEMORY RECALL

Brain regions showing greater activity during episodic simulation versus memory recall (warm colours), and vice versa (cool colours) (figure taken from Schacter et al., 2012).

1.1.2.4. Summary

In this section, three theories have been introduced and briefly discussed. All these three hypotheses attempt to explain why autobiographical memory and episodic imagery recruit similar neural networks. They all assume that some similar components are included in both cognitive processes and the similarities contribute to the overlapping of neural networks recruitment. Scene construction theory suggests that both autobiographical memory recall and episodic imagery involve the process of generating and visualising complex spatial scenes, while the self-projection hypothesis suggests that to project oneself into certain time-points or locations is the common component between autobiographical memory recall and episodic imagery. Finally, constructive episodic simulation hypothesis focuses on the function of MTL and suggests that both cognitive processes require us to recall a memory and reconstruct it into a coherent story. These hypotheses may not be mutually exclusive. Instead, they focus on different perspectives and all these perspectives are logically reasonable. For example, it seems plausible that, in line with a constructive episodic simulation hypothesis, both memory retrieval and episodic simulation are constructive processes in nature. To generate a plausible imagined scenario, one has to retrieve information from multiple stored memories and combine all the information together and turn it into a complete and comprehensive scene. However, this process also involves self-concept representation or self-related processing because 'self' is a fundamental component of autobiographical memory and episodic imagining.

1.2. Anatomy of mPFC

In this section, I will introduce the anatomy of human mPFC and its connections with other cortical and subcortical areas. Figure 3-A depicts the architectonic subdivisions of the human medial prefrontal cortex.

There are several ways to divide mPFC into subdivisions (Lemogne, Delaveau, Freton, Guionnet, & Fossati, 2012). Some have divided mPFC into two main parts: the dorsal (i.e., dorsomedial PFC, dmPFC) and ventral subregions (ventromedial PFC, vmPFC); whereas others use three parts: dorsal, ventral, and orbital subregions (medial Orbitofrontal Cortex, or mOFC, Figure 3-B) (e.g., Barbey, Krueger, & Grafman, 2009); or dorsal, central, and ventral subregions.

There seems to be no general agreement on the boundaries of each subdivision. The region defined by researchers varied between lesion studies and neuroimaging studies and even varied within same study field (e.g., Zald & Andreotti, 2010). For example, in some studies, the upper boundary of vmPFC extends to the genu of corpus callosum and the lower boundary to the gyrus rectus. While in some other studies, researchers have used the z coordinates along the MNI space to define the dmPFC and the vmPFC (e.g., dmPFC are regions which have z> 10 while vmPFC are those have z<10). This inconsistency makes the review difficult. A cluster of voxels could belong to the dmPFC in one study but the very same region could fall into the vmPFC in another study. Also, in some studies, the term vmPFC actually indicate the medial orbital frontal cortex (mOFC), and vice versa.

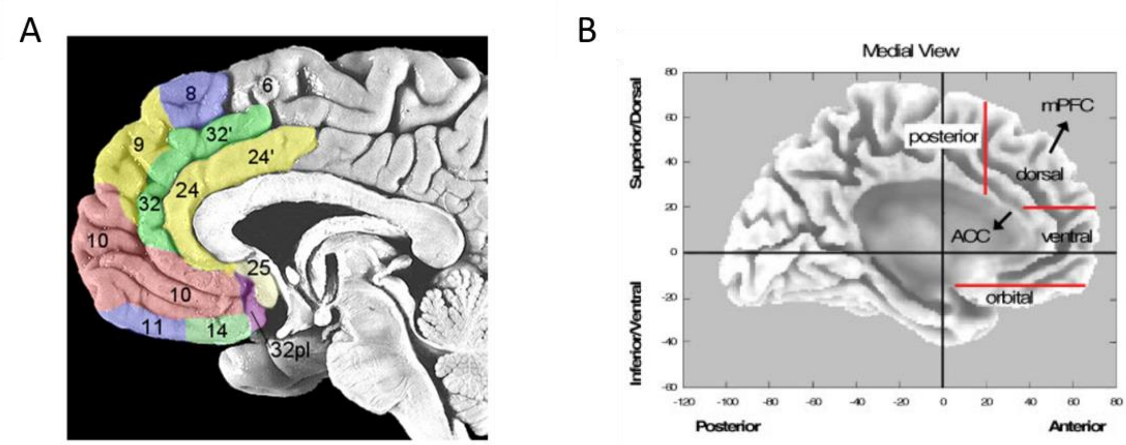


Figure 3. HUMAN PREFRONTAL CORTEX

(A) Cytoarchitectonic maps of the human medial prefrontal cortex, numbers refer to Brodmann areas. Taken from Ridderinkhof et al. (2004). (B) The parcellation of mPFC. Note, this is only one of many different parcellation schemes. Taken from Van Overwalle et al. (2009).

The network within mPFC is complex (Öngür & Price, 2000), because every subdivision has its connection with other subdivisions. Each subdivision (see Figure 4)., especially the vmPFC, receives abundant afferents from and has plenteous efferents to other brain regions, including cortical, subcortical, and brainstem regions (Berendse, Graaf, & Groenewegen, 1992) The large amount of inputs and outputs may be one of the reasons why mPFC is involved in so many cognitive tasks, including memory, decision making, and self-related processing.

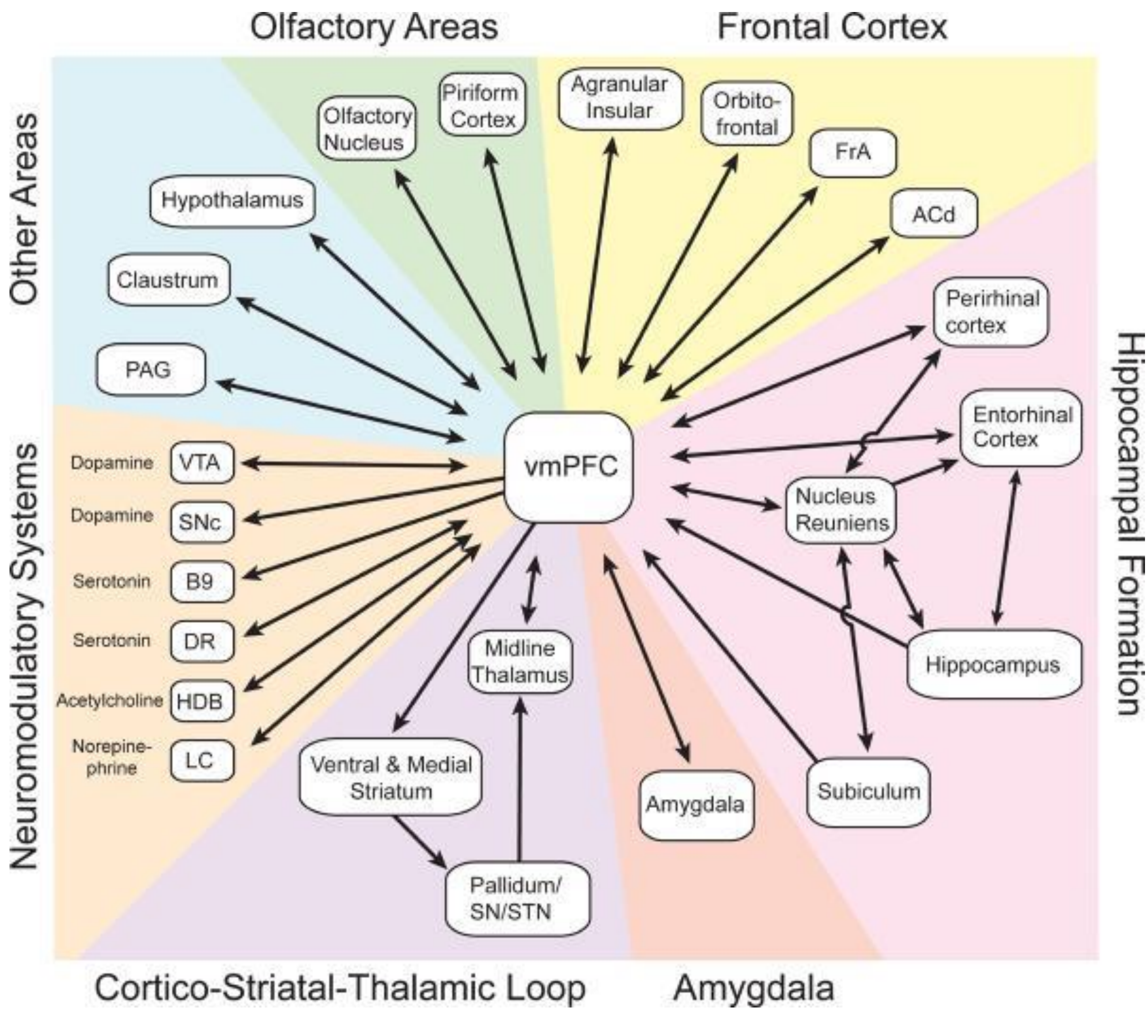


Figure 4. Anatomical connections of vmPFC.

Arrows represent directionality. Figures taken from Euston et al. (2012) shows that the ventromedial prefrontal cortex receives inputs and provide outputs to multiple brain cortices and subcortices. Abbreviations: ACd, dorsal anterior cingulate cortex; B9, B9 serotonin cells; DR, dorsal raphe; FrA, frontal association cortex; HDB, horizontal limb of the diagonal band of Broca; LC, locus coeruleus; PAG, periaqueductal gray; SN, substatia nigra, STN; subthalamic nucleus, VTA, ventral tegmental area.

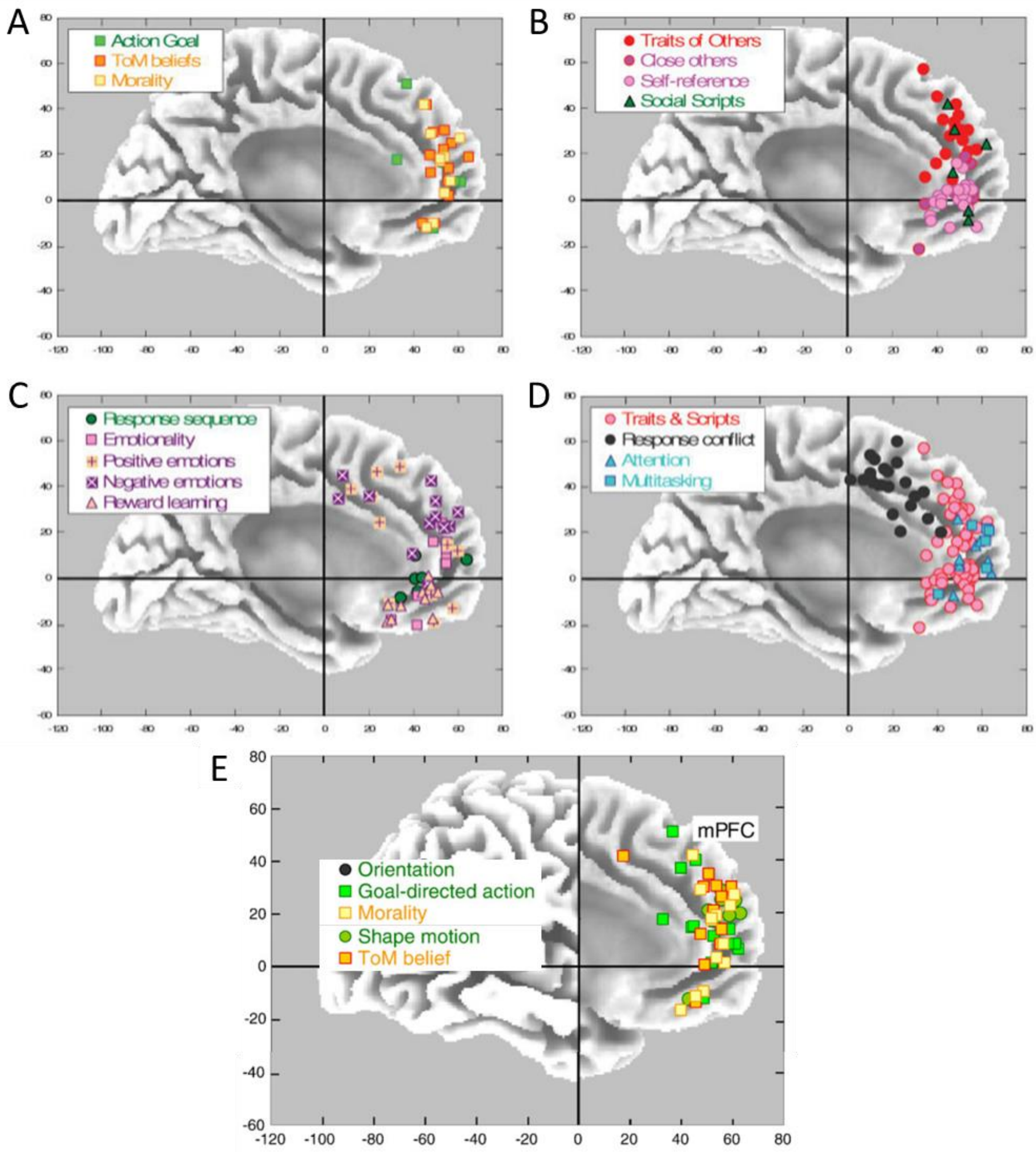


Figure 5. Functions of human mPFC.

Figure adapted from Van Overwalle& Baetens (2009) and Van Overwalle (2009).

1.3. mPFC in different cognitive tasks

Autobiographical memory and episodic imagery are not the only two processes that mPFC is often shown to be involved in. Studies have found that mPFC also plays a functional role in several other cognitive processes, such as decision-making, self-related processing, mind wandering, and theory of mind (for reviews, see Buckner & Carroll, 2007; Schacter & Addis, 2007). Figure 5 shows that a wide range of processes all recruit mPFC. Among these process, two of them are directly relevant to the specific hypothesis investigated in this thesis, i.e., decision-making and self-related processing. Therefore, I introduce these two processes and the potential functional roles of mPFC in these tasks, below.

1.3.1. mPFC in Decision-making

People begin to make decisions at the very moment that they wake up in the morning, and they keep making decisions until the time they fall asleep. In fact, we all have to make many decisions every day. For example, which shirt should I wear today, the white one, the pink one or the blue one? What about shoes? What to have for lunch later, chicken sandwich or salad? Should I go to the gym today after work, or should I go home directly, or should I go to the pub with friends? Should I drink beer, wine, lager, or cider? Most of these are ordinary trivial decisions, whilst others can be important and critical. For example, should I take a job offer or turn it down? Should I buy this car or a different one? Should I have surgery or should I not?

The process of decision-making is complicated, even when needing to choose between two simple options. Figure 6 is part of the framework often identified by studies investigating decision-making, as proposed by Rangel et al. (2008). The assumption of this framework is that decisions are made after comparing the value of each available option. After the identification of available options, the value of each option is computed. The outside world context, the physiological and emotional states of the individual are all taken into account during this value computation stage. The individual must then decide which option to choose, and this is based on comparing the internal and external value of all options. After executing the chosen action and receiving the outcome, the individual will compare the actual outcome to the expected one and update self's own knowledge about this option, therefore, the individual is able to make a better decision in the future. It is no doubt that to evaluate the value of each option as accurate as possible is a critical part of decision-making process and the mPFC has been reported to be involved in value-relevant representation and processing.

The value of an option computed in the above mentioned valuation process is not invariant across different decision-making situations (e.g., Kable & Glimcher, 2007; Kringelbach, O'Doherty, Rolls, & Andrews, 2003). This is because the value is calculated based on both internal and external states, and both states varies from context to context. For example, hunger level is an internal state. When we compute the value of a chocolate bar, the value of the chocolate bar would be higher after fasting than after having a feast. That is to say, the value computed in this process is a subjective value rather than an absolute value.

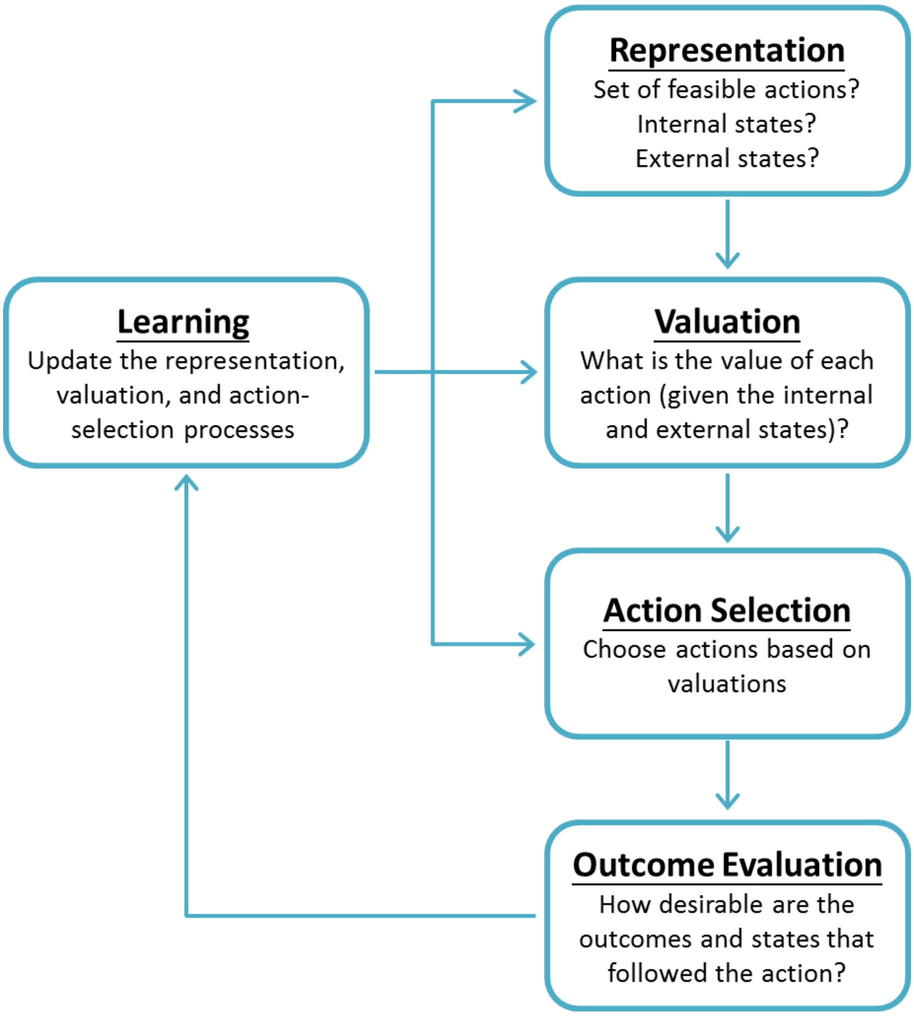


Figure 6. Value based decision-making.

Figure adapted from Rangel et al. (2008) illustrates five steps in the value-based decision-making process. (1) Representation: this first step includes identifying and defining all potential options or actions. (2) Valuation: during this step, the value of each option is calculated based on one or more valuation systems. Valuation systems include the Pavlovian system, Habitual system, and goal-directed system. (3) Action selection: a decision is made based on the value of each option. (4) Outcome evaluation: after carrying out the chosen action, the outcome will be compared to expectation and be recorded for the future. (5) Learning: information gathered from the current experience will be used to update knowledge about each option so the individual is able to make a better choice next time.

The mPFC is consistently engaged in the process of decision making, both in the decision-making phase and the reward-receiving phase (for meta-analyses, see Bartra, McGuire, & Kable, 2013; Clithero & Rangel, 2014). In decision-making studies, one general experimental paradigm is to allow participants choose between two alternative options which would deliver a different amount of rewards within each experimental trial. For instances, to choose between a chocolate bar and an apple, or to choose between receiving £0.50 immediately and receiving £5.00 after a 3-month delay (e.g., Leathers & Olson, 2012). Another paradigm is for participant to decide whether to accept or refuse a proposed offer (e.g., Hare, Camerer, & Rangel, 2009). Studies have examined the duration when participants are making decisions (decision-making phase) or after they receive a reward (reward-receiving phase). A large number of studies have demonstrated that mPFC activity is correlated with the subjective value of chosen option during both decision-making phase and reward-receiving phase (for meta-analyses, see Bartra et al., 2013; Clithero & Rangel, 2014; for a review, see Rushworth, Noonan, Boorman, Walton, & Behrens, 2011).

Nevertheless, there are also studies showing that mPFC activity is not correlated with the value of chosen option but is instead correlated with the value differences between a chosen option and an unchosen option (Basten, Biele, Heekeren, & Fiebach, 2010; Boorman, Behrens, Woolrich, & Rushworth, 2009; FitzGerald, Seymour, & Dolan, 2009; Kim, Adolphs, O'Doherty, & Shimojo, 2007; Nicolle et al., 2012; Sripada, Gonzalez, Phan, & Liberzon, 2011). For example, participants made decisions between two options in a two-armed bandit task (Boorman et al., 2009) within each trial. The vmPFC activity during decision-making phase was correlated with the difference between a chosen value and an unchosen value. Overall, both views do convergent in that they suggest that mPFC plays a role in value representation or value-related processing during decision making.

1.3.1.1. Common value

When making decisions among multiple choices, these choices do not usually come from the same category and they can sometimes be very different from each other. For example, to choose between attending a friend’s birthday party or studying in the library to prepare for an exam. Each option carries diverse attributes with the attributes within one option highly dissimilar to those within other options. Attributes within the ‘attending the party’ option may include friendship, social-interaction while the ‘study’ option includes academic performance, personal achievement.

It has been generally accepted that the value of each attribute is converted into a common value via a common scale so the comparison between options from different categories is possible (Levy & Glimcher, 2012). The mPFC is believed to be critical to this process based on neural imaging studies in human.

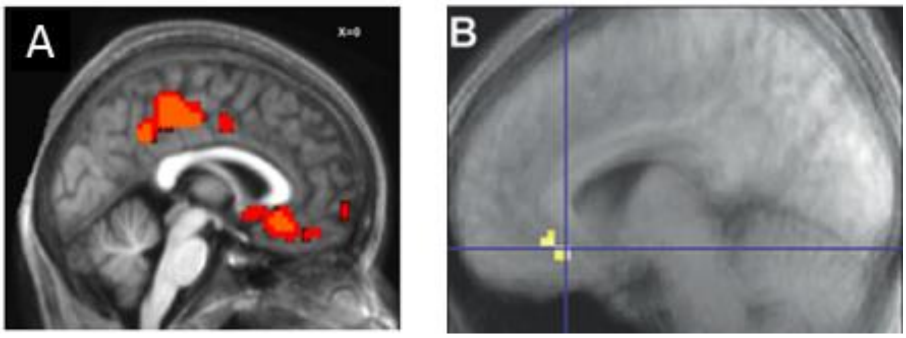


Figure 7. mPFC involves in common value processing.

(A) The figure is taken from FitzGerald et al. (2009) shows the activity of vmPFC and posterior cingulate cortex was modulated by the differences between choices from different categories (i.e., cash and trinkets). (B) Figure taken from Kim et al. (2011) shows overlapping response during juice and money expectation.

Studies have shown that the value of the chosen option or the value differences between available options that modulate activity in mPFC is not constrained by the type of stimuli or by the potentially available options. In other words, the values of items from various categories can modulate activity in mPFC. The mPFC activity is correlated with the subjective value of available options no matter whether the options are common incentives such as food (Barron, Dolan, & Behrens, 2013; Hare et al., 2009), water (Bouret & Richmond, 2010), monetary reward (Kable & Glimcher, 2007; Kanayet, Opfer, & Cunningham, 2014; Ludwig et al., 2015; Peters & Büchel, 2009); or inconsumable goods such as face and artistic painting (Lebreton, Jorge, Michel, Thirion, & Pessiglione, 2009), the amount of voluntary donations to charity (Hare, Camerer, Knoepfle, O’Doherty, & Rangel, 2010), and even physical action (Gläscher, Hampton, & O’Doherty, 2009) or warmth on the hand (Grabenhorst, D’Souza, Parris, Rolls, & Passingham, 2010). Studies have also found that value representations of two or more different kinds of items overlapped within mPFC within the same participants. For example, money and consumer goods (FitzGerald et al., 2009); money and juice (Kim et al., 2011) in Figure 7; money, snacks, and trinkets (Chib, Rangel, Shimojo, & O'Doherty, 2009); face and place attractiveness (Pegors, Kable, Chatterjee, & Epstein, 2014); scoring a goal in a football game and winning monetary reward (Häusler, Becker, Bartling, & Weber, 2015). Together with similar results in monkeys (e.g., Padoa-Schioppa & Assad, 2008), mPFC might play a critical role in common value scale (for a review, see Levy & Glimcher, 2012). That is to say, mPFC encodes or represents values of all items based on a common currency regardless the categories or types of the items.

1.3.1.2. Automatic valuation system

Studies suggest that a valuation process does not occur only when decision making is required. For example, activity in mPFC when participants were passively viewing different items (e.g., books, CDs, lotteries) was predictive of their preferences between two different items during a separate task (Levy & Glimcher, 2011). In other words, the valuation system is still working under the circumstances when no decision has to be explicitly made. Another study has also shown that activities in value-related brain regions, including mPFC, were modulated by participants' preferences even when they were engaging in a preference-irrelevant task (i.e., age estimation), which also implies that this valuation process is automatic (Lebreton et al., 2009).

1.3.2. mPFC in Self-related processing

1.3.2.1. Self-reflection/ self-referential processing

The neural mechanism of self-referential processing is an intriguing topic and it has been suggested that mPFC may play an essential role in self-reflection or self-referential processing. In 2002, Kelley et al. (2002) suggested that self-referential processing is supported by mPFC, based on the results of their fMRI experiment. In Kelley et al. (2002), participants made judgements about trait adjectives (e.g., honest) in three conditions: self (e.g., “Does the adjective describe you?”), other (e.g., “Does the adjective describe current U.S. President George Bush?”), and semantic control. Compared to others-referential judgment, self-referential judgment showed higher activity in vmPFC and posterior cingulate. On the other hand, other-relevant processing engaged a more dorsal subdivision of mPFC. Further studies replicated this result and the changes in vmPFC relating to self was the most consistent finding, therefore, some researchers suggest that vmPFC is the centre for self-referential or self-reflection (for meta-analyses, see Hu et al., 2016; Murray, Schaer, & Debbané, 2012; van der Meer, Costafreda, Aleman, & David, 2010).

Although studies using trait judgments of self or others have consistently shown that self- and other-referential processing reflects changes in ventral and dorsal areas of mPFC, respectively. However, there were some potential confounds in these studies. One potential confounding in trait adjective judgments is that when making self-referential judgments, participants tended to rate positive traits be more fit than negative ones. Moran et al. (2006) showed that the vmPFC still had higher activity when judging self-relevant traits than judging other-relevant traits after controlling the emotional valences, which implies the self- and other-referential differentiation within mPFC was not caused by emotional valence differences.

However, does the self- and other-referential differences observed in mPFC really reflect differences between the self- and other- representation? Other alternative accounts include similarity, intimacy, and familiarity (Wagner, Haxby, & Heatherton, 2012) because judgements relating to self and others can also differ in these domains. Similar other regard to person who are similar to participants themselves in personality, social and political believes, or personal interests while familiar others regard to personal familiar ones, such as friends, and relatives. Note, familiar famous people are not counted as familiar others. In terms of familiarity, a meta-analysis revealed that self-referential processing evoked greater vmPFC activity than personal familiar other-referential processing although they shared multiple common brain regions (Qin & Northoff, 2011). There was one study that attempted to distinguish between the influence of similarity and of familiarity (De Brigard, Nathan Spreng, Mitchell, & Schacter, 2015). More specifically, participants provided 35 memories of decisions made in the past on day 1 (e.g., getting their favourite t-shirt stained because they decided to mix whites with colours in the laundry). On day 2, participants performed a counterfactual simulation task in an MRI scanner. In each trial, participants were instructed to imagine how outcomes would have been better for the target person in an event (e.g., "If only I had separated the whites from the colours when doing laundry that one time"). The target person in each simulation trial could be self, a familiar/similar character, an unfamiliar/similar character, or an unfamiliar/dissimilar character. The results confirmed previous findings, both self and familiar conditions during counterfactual simulation involved mPFC but simulating from an others perspective involved more dorsal and lateral areas in comparison to the self-condition. Interestingly, mPFC activity did not differ between simulating unfamiliar/similar and unfamiliar/dissimilar others which implies that similarity do not modulate mPFC activity.

Some studies have further demonstrated that vmPFC is involved in evaluating similar others (Benoit, Gilbert, Volle, & Burgess, 2010; Jenkins, Macrae, & Mitchell, 2008; Mitchell, Banaji, & Macrae, 2005). For example, Benoit and colleagues (Benoit et al., 2010) found that when the perceived degree of self-friend similarity was high (in this case, similar in personalities), the mPFC activity differences between self- and friend-referential trait judgments became small. But the results of Krienen et al (2010) showed a different pattern when participants were judging preferences of target persons in some certain situations. For example, self/ prefer window seats to aisle seats when flying. The target person could be self, a friend similar to self, a friend dissimilar to self, a stranger similar to self, or a stranger dissimilar. The fMRI results confirmed that mPFC activity was higher while evaluating self and a close others than when evaluating strangers. But similarity did not modulate mPFC activity in this social evaluation task. In short, there are no consistent findings on whether the similarity is able to modulate the mPFC activity and whether it is an account for the self/other-referential processing differences.

1.3.2.2. Assigning value to self-related contents

D’Argembeau (2013) has argued that the function of vmPFC in self-processing is to assign values to self-related contents, but not self-reflection. D’Argembeau made this claim based on several aspects and evidence. For instance, the value of one’s current self is usually higher than the value of self in the past or in the future and studies have shown that vmPFC activity was higher when thinking about present self than when thinking about past or future selves (D’Argembeau, Stawarczyk, Majerus, Collette, Van der Linden, & Salmon, 2010). Furthermore, vmPFC activity can also vary along with importance of self-view when making trait judgements (D’Argembeau et al., 2012) and individual differences in self-reflection also matched the activity differences of vmPFC (D’Argembeau et al., 2014). Both autobiographical memories and episodic simulations contain contents which are self-related. Based on D’Argembeau’s proposal, mPFC would be expected to show higher activity during recalling an item that is relevant to self and has high value compared to recalling a self-related item with a lower value in autobiographical memory. D’Argembeau’s proposal can also explain the results of Bertossi et al. (2016) that vmPFC lesioned patients did not only have impairment in imagining self-related scenarios but also in imagining others-related (i.e., family members and the president of the Italian Republic) scenarios. In general, family members or the president of one’s country could be self-related to some degree. And this may be the reason why vmPFC patients showed deficits in imaging scenarios related to others.

1.3.3. General function of mPFC across tasks

Based on the literature mentioned above, it seems that mPFC is consistently involved during several cognitive functions, including autobiographical memory retrieval, episodic mental simulation, decision-making, and self-related processing. Some believe that there is a general function of mPFC across all different domains and mPFC is recruited in all these tasks because they all rely on this general function of mPFC.

Euston et al (2012) suggested that the function of mPFC in memory and decision making is to learn associations between context or events and required responses which in turn could be used to guide adaptive behaviour. To be specific, the dmPFC receives inputs from sensorimotor regions while the vmPFC receives inputs from subcortical structures and then generate appropriate motor and emotional responses after integrating current inputs and prior experiences.

Another hypothesis regarding the general function of vmPFC (Roy, Shohamy, & Wager, 2012) suggests that it works as a hub to link concepts from different systems and to generate affective meanings to guide adaptive behaviour generation. This claim was made based on the findings that vmPFC activity was found relevant to various domains, and diseases, including visceromotor control, threat regulation, valuation, memory, self-projection, and mood disorders. Roy and colleagues argued that, to think of vmPFC function as a basic concept would be not sufficient to explain its involvement in divergent situations.

1.4. Research questions

In Chapter 1, I first reviewed literature related to the overlap of neural circuits between autobiographical memory retrieval and episodic imagery and briefly introduced the function of each brain region within the core network. Although several hypotheses aim to explain this overlap, none of them focuses on the function of mPFC. I also reviewed the involvement of mPFC in different cognitive functions, including decision-making and self-related processing. Accumulated evidence has suggested that the function of mPFC in decision-making is related to value processing or value representation. Furthermore, some also suggested that the function of mPFC in self-related processing is also value representation. Therefore, it is possible that mPFC involvement during autobiographical memory, and episodic simulation, may reflect a similar role due to representing values of critical elements or components (i.e. items which are important in the event or mental imagery based on subjective perceived importance) of the memory or imagined scenario irrespective of the element type. This hypothesis is similar to the one proposed by D'Argembeau that mPFC assigns value to self-related contents during self-referential processing (D'Argembeau et al., 2012).

Therefore the motivation of this thesis is to answer two main research questions in regard to the function of mPFC in episodic simulation and autobiographical memory retrieval:

1. Does mPFC function reflect representation of the subjective values for imagined components during mental imagining?
2. Does the mPFC represent subjective values during the retrieval of autobiographical memories?

To tackle the first question, a paradigm which is able to manipulate participants' subjective values of imagined items is necessary. The logic behind this is that if the mPFC represents values of imagined objects, then its activity should be higher when people are imagining objects with higher subjective values, and vice versa. To exclude potential confounding, it was essential to make sure the imagined objects with high subjective values were similar to those with low subjective values. Experiment 1 hence aimed to test if it is possible to manipulate the subjective values of objects in mental imagery and the imagined-value paradigm was adopted to this end. After confirming the validity of imagined-value paradigm, this paradigm was carried out in the fMRI scanner to answer the first main research question- does the mPFC represent subjective values of imagined components during mental imagining? If the answer is yes, the BOLD signal of mPFC should be parametrically modulated by the subjective values of imagined items.

The second main research question - does the mPFC represent subjective values during retrieval of autobiographical memory? To answer this question, it was necessary to collect participants' real autobiographical memory. Four different methods were usually used in investigating autobiographical memory and its neuronal mechanism (Cabeza & St. Jacques, 2007; St. Jacques & De Brigard, 2015), including generic cues, pre-scan interview, independent sources, and prospective methods. Figure 8 exemplifies these four methods. In the generic cues method, cues used for eliciting memories are usually common nouns. In each single trial, participants receive a cue word, search a proper relevant memory and then elaborate it while lying in the scanner. In the pre-scan interview method, participants receive cues and provide memories before they are scanned. The scanning happens after a duration of delay. In the individual sources method, cues used are gathered from other sources such as friends, families, or journals. Participants have no chance to know the cue words before the scanning. In the prospective methods, participants take photos or wear digital devices which take photos periodically. These photos can be used as cues during retrieval phase and can also be used to verify recall accuracy.

Each method has its advantages and disadvantages. For instance, the generic cues method can guarantee that when a participant recalls a memory in the MRI scanner, the content of recalling has not been influenced by the experience of recalling the same memory in the previous session like that in the pre-scan interview. However, participants may recall uneven numbers of liked and disliked items in the generic cues method. Or, they may always recall liked items before disliked items, and this could induce potential confounds. The pre-scan interview method can prevent these situations happening since researchers can to collect enough memories and items from each and every category beforehand. However, there is a chance that participants' memories may be contaminated by the experience of recalling these memories during the pre-scan interview phase. The advantage of the independent sources method and the prospective method is that researchers are allowed to verify the authenticity of memories provided by participants. However, it takes longer to prepare and finish data collection for these methods.

The pre-scan interview was adopted in the present study because it provided the chance to control the recall of an equivalent number of high-value objects and low-value objects. Although the generic cues method can guarantee less contamination from recently retrieval experiences, it does not allow for controlling the amount of objects with different subjective values. Apart from the subjective values of objects in the memory, taking ratings in regard to these memories were also necessary to further support the idea that the mPFC is involved in the autobiographical memory for self-relevant values, rather than pure value representations in general.

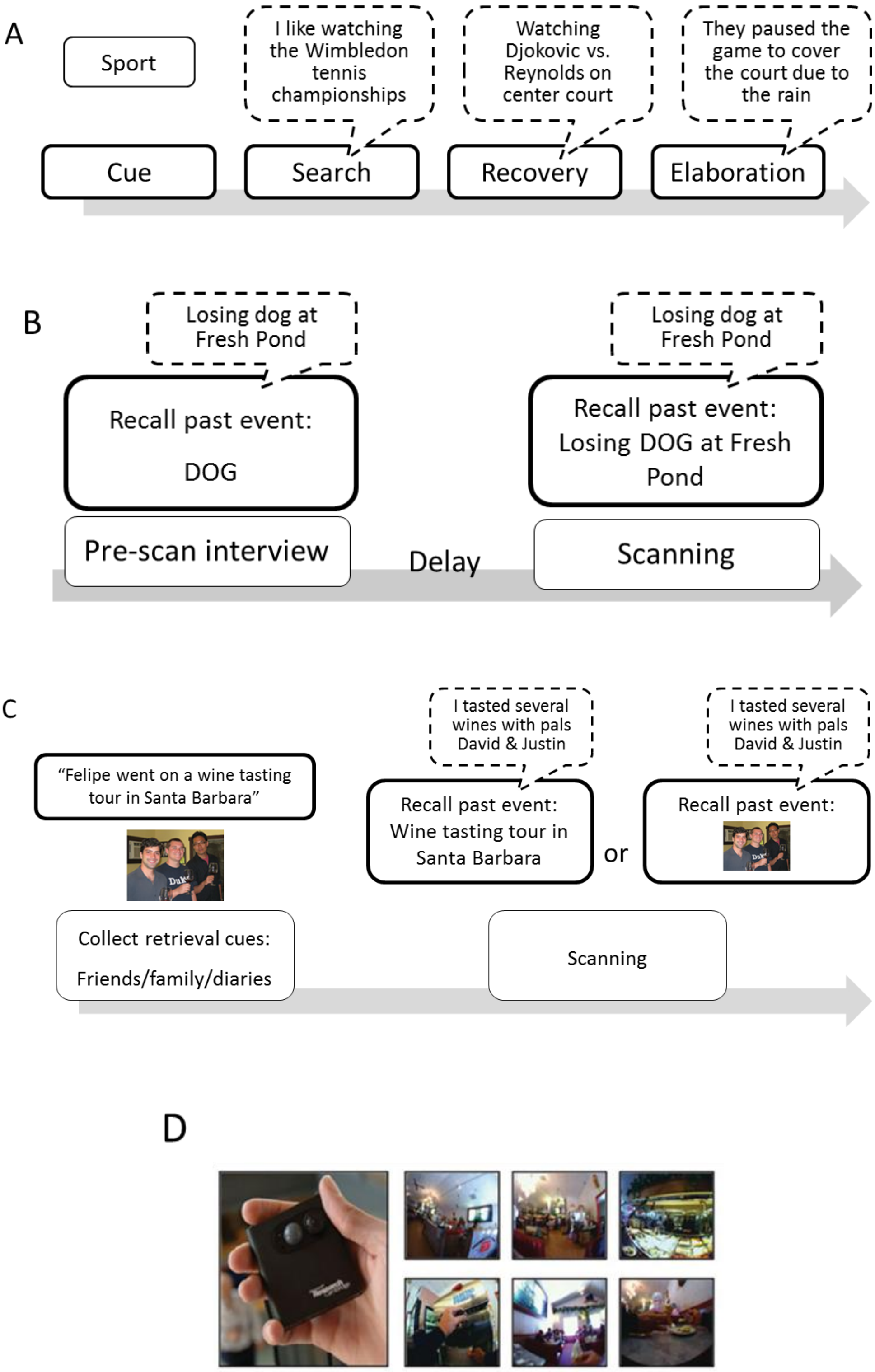


Figure 8. Methods used to investigate autobiographical memory

Figure adopted from St. Jacques and De Brigard, (2015) illustrates four common methods: (A) generic cues; (B) pre-scan interview, (C) independent sources, and (D) prospective methods.

1.5. Overview of the thesis

The three experiments in the present thesis were aimed to tackle the questions raised above. First, Chapter 2 (Experiment 1) designed and tested the validity of an imagined-value paradigm, aimed at modifying participants' motivations and preferences through mental imagery. It demonstrated that people changed their subjective values of common items in response to imagining themselves exposed to a set of physiological states, for example, instructing an individual to imagine themselves in a state of hunger. Following the successful development of this paradigm, an imagined-value experiment was next carried out during fMRI (Chapter 3). Results support the hypothesis that mPFC represents subjective values of imagined components during imaginary scene construction and elaboration. Chapter 4 presents a further experiment to extend the findings on whether mPFC is involved in subjective value representation during autobiographical memory retrieval. More specifically, participants recalled their autobiographical events and also items within each event. The subjective values of items modulated vmPFC activity during item recall and valuation. Finally, Chapter 5 reviews the results of all experiments, discusses the similarities and differences between the two fMRI experiments, the importance and implication of the results, potential application of imagery ability and autobiographical memory recall on the clinical field and makes a summary of the present thesis.

Chapter 2. Experiment 1- Subjective values of imagined items varied in different imagined contexts

*This chapter derives partly from Lin, W.-J., Horner, A. J., Bisby, J. A., & Burgess, N. (2015). Medial Prefrontal Cortex: Adding Value to Imagined Scenarios. Journal of Cognitive Neuroscience, 27(10), 1957–1967. http://doi.org/10.1162/jocn_a_00836

To answer the question of whether mPFC activity is modulated by the subjective values of imagined objects, we first set out to design a paradigm in which we can manipulate the value of key elements within simulated scenarios.

One might be willing to pay £10.00 for a sandwich only when he is starving and has no other choices but not in any other situation. That is to say, people give the same object different values under different circumstances (e.g., physiological states). This seemed to be a potential way to manipulate the value of objects. But if we are to adapt this method to address our hypothesis concerning value in imagined scenarios, then the question for us is: Are we able to manipulate participants' motivation and subjective values of objects via imagination instead of actually depriving them of specific physiological needs (such as food)?

Imagining eating a certain kind of food can make participants eat less of that kind of food later, compared to participants who did not imagine eating this kind of food or imaged eating other kinds of food (Morewedge, Huh, & Vosgerau, 2010). In a behavioural study, Morewedge et al. (2010) required participants to imagine themselves putting 3 coins into a laundry machine and eating 30 M&M's one by one or imagine putting 30 coins plus eating 3 M&M's. After this imagination, participants were allowed to eat any amount of M&M's. It turned out that participants consumed less M&M's if they imagined them eating 30 M&M's compared to those who imagined eating 3 M&M's. In another experiment with a similar method, participants who imaged eating 3 or 30 M&M's or 3 or 30 cheddar cheese cubes and then were later allowed to eat any amount of cheddar cheese cubes. The results showed a significant interaction.

Participants who imagined eating more cheddar cheese cubes actually then ate less than those who had imagined eating less cheddar cheese cubes. In the meanwhile, the amount of actual cheese cube consumption did not differ between two groups of participants who imagined eating M&M's. Another study even demonstrated that the subjective enjoyment of consuming salty food could be decreased if participants were required to rate 60 salty food pictures beforehand, but not if they had to rate 60 sweet food pictures (Larson, Redden, & Elder, 2014). In general, these studies suggest that mental imagery itself is enough to influence our motivation for satisfying our basic needs. Therefore, it is reasonable to speculate that to imagine oneself in a hungry state may cause a person to experience a higher need for food, which in turn raises food's subjective value.

Experiment 1 was a behavioural experiment which aimed for testing if participants' preferences changes according to the imagined states on a behavioural level. A secondary aim of this experiment was to see if the influence of imagined states exists on an implicit level. For these purposes an attention bias task was incorporated into the imagery task.

Studies have shown that visual attention can be biased by pictures of naturally threatening stimuli, e.g., spiders or snakes (Lipp, Derakshan, Waters, & Logies, 2004; Öhman, Flykt, & Esteves, 2001). It can also be biased by food-related words when participants were hungry (Mogg, Bradley, Hyare, & Lee, 1998), and by emotional vocalisations, such as laugh and scream (Van Dessel & Vogt, 2012). Mogg et al. (1998) used a dot probe paradigm to test attention bias on participants who were fasting. In the dot probe paradigm, a word pair- a food-relevant word and a food-irrelevant one- showed up on the screen for 500 ms. A dot probe occupied either the food-relevant or the food-irrelevant location after the word pair disappeared. Participants had to respond to indicate the probe dot location. The results showed that hungry participants responded faster when the probe occupied the same locations as food-relevant words rather than food-irrelevant words. It seems that people's attention can be attracted to the spatial location by their need or motivation. Therefore, it is reasonable to speculate that participants' attention could be biased by their imagined needs in our study.

Participants were requested to picture themselves in a certain context (e.g., classroom) and in a certain physiological state (e.g., hungry), then they encountered two types of objects. One type of objects was able to fulfil their imagined need after consumption (e.g., a burger) and another one was not (e.g., a bed). Participants then rated how strongly they wanted each object. Objects that are potentially able to fulfil imagined needs should trigger higher desire than those that are unable to fulfil imagined needs. Simultaneously, participants should respond quicker when the probe dot was located in the same location as those objects were able to fulfil the imagined needs.

2.1. Materials and Methods

2.1.1. Participants

Fourteen right-handed participants were recruited from the University College London student population. The mean age was 23.07 years (SD = 5.12, range 19- 33) and 10 of them were females. All participants gave written informed consent to participation, in accordance with the local ethics committee (1825/003).

2.1.2. Stimuli and Design

Four different physiological states of need were used: thirst, coldness, hunger and tiredness. A neutral state was used as a baseline condition (instruction for the neutral state: Imagine you are just fine. You are not in any state of need but just in an ordinary condition). Fifteen spatial contexts were used as the context for imagery: beach, kitchen, desert, fields, classroom, aeroplane, forest, office, library, playground, church, ship, swimming pool and football stadium. These were included to make the imagined scenarios more realistic and because, without instruction, participants would be likely to imagine uncontrolled backgrounds to facilitate imagery. Each context was combined with four states of needs (i.e., thirst, coldness, hunger, and tiredness) once, and this made 60 state-context combinations. Each location appeared twice when combined with the neutral state, thus there were 30 trials with the neutral state. All the 90 trials were split into three blocks equally for participants to have two short breaks between blocks. Each block contained an equal number of trials with each state of need and neutral state, i.e., six trials with thirst, six with coldness, six with hunger, six with tiredness, and six with the neutral state. The sequence of these trials within each block was randomly assigned.

Pictures from four categories were used as items, each category contained items which were usually used to satisfy one of the four physiological states of need. The first category contained water, juice, beer and any other beverages used to quench thirst. The second category contained items which were able to be used to help people resist cold weather, such as a fireplace, hot drink, and winter clothes. Another category contained food and the final category had items used for taking a rest or relieving tiredness included bed, couch, bathtub and so on. There were 46 pictures in two of the categories and 44 in the other two categories. Therefore, there were 180 pictures in total. All of these pictures were obtained from FreeDigitalPhotos.net (http://www.freedigitalphotos.net/).

In the imagery task, each trial contained one state-context combination as cue words and also two different pictures. The relationship between the participant's current imagined state and each item picture during a single trial could either be congruent or incongruent. For a congruent item, the type of item presented would meet the participant's current need created by the imagined state. For instance, a food picture would be classified as congruent if the state was hunger but incongruent if the state was tired, cold or thirsty. Note that, 'incongruent' items were irrelevant rather than opposite to the current state of need. Ambiguous items were never used as 'incongruent items' (e.g. hot drink was not used in thirst trials). From the two item pictures, sequentially presented during each trial, either item could be congruent or incongruent with the current state. This provided four possible combinations: congruent-congruent, incongruent-incongruent, congruent-incongruent, and incongruent-congruent. Importantly, all four combinations of items occurred in pseudo-random order across trials, allowing us to identify the effects of an individual items' subjective value, as modulated by its congruency with the imagined state. If the state was neutral, then both pictures in that trial were neutral pictures. In total, there were 60 congruent, 60 incongruent, and also 60 neutral pictures in the 90 trials.

2.2. Procedure

Participants were provided with task instructions first and completed a number of practice trials. Each trial began with a 0.5s fixation cross at the centre of the screen and it was replaced by a pair of state-location cue words (Figure 9). Participants were instructed to build up their imaginary scenario based on the cue words and try to make it as vivid as possible. For instance, to imagine feeling tired in the classroom if the cue pair is “tiredness-classroom”. The cue words were presented for 4 seconds and then a blank screen appeared for 8 seconds, participants had to keep imagining during this period of time. They were allowed to close their eyes if they thought it’s helpful for building up their imagery scenario. Later, a cross fixation appeared simultaneously with a 0.8s beep sound (500Hz). Participants were instructed to open eyes and pay attention to the centre of the screen when they hear the beep sound. Two white frames along with the central fixation appeared after the 0.5s fixation, one frame was located in above the centre and the other one was under the centre. Two pictures, one congruent and one incongruent or two neutral ones, replaced the two frames for another 0.5s before the probe appeared either in the upper or the lower position (the probe appeared in the upper location for 50% trials and in the lower location for 50% trials). The probe was a small white square, and it stayed on the screen until participants pressed a key to indicate the location of the probe. After participants made four subjective judgement ratings, the trial ended with a blank screen (4-6 sec, jittered, based on a uniform distribution). The first two ratings regarded how much participants wanted each item when they met each item within the imagined scenario. The last two were about the vividness of their imagination, state and context separately. All ratings were using a 4-point rating scale (1 for not at all, 4 for very much). Based on the after-task debriefing, none of the participants were aware of the purpose of the attention bias task when they were performing this task. Visual stimuli were presented by MATLAB (MathWorks) and COGENT 2000 toolbox (http://www.vislab.ucl.ac.uk/cogent.php).

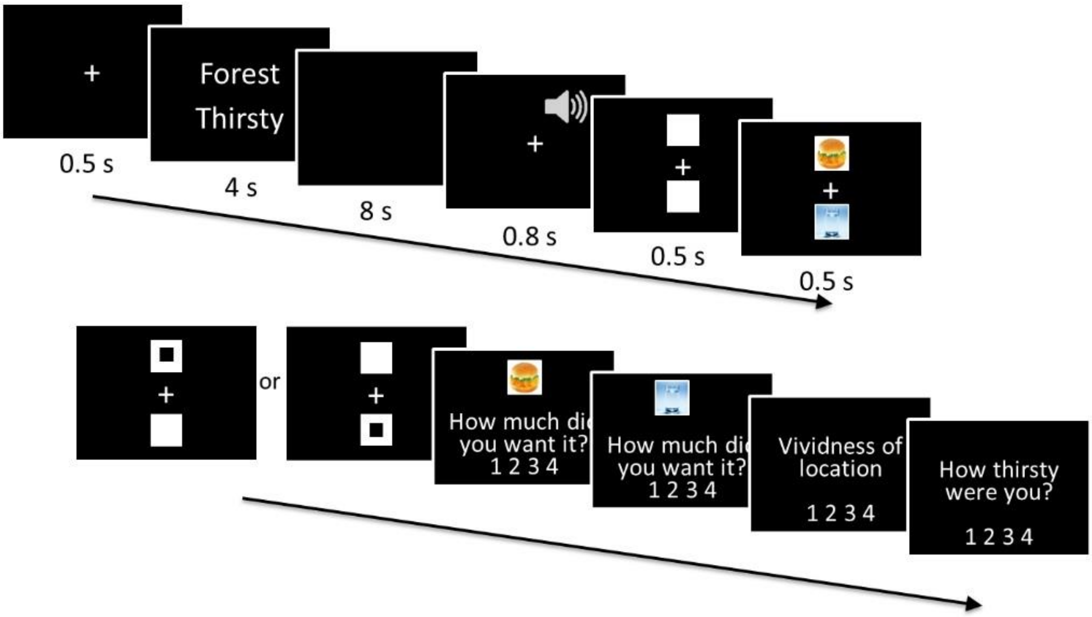


Figure 9. Procedure of Expreiment 1

This task is a combination of imagery and attention bias task.

2.3. Behavioural Results

2.3.1. Probe detection accuracy

A one-way repeated measure ANOVA was carried out with the factor congruency (congruent, incongruent, and neutral) to see if there was any different accurate rate of detecting probe locations after different categories of pictures. The main effect was not significant, $F(2, 26) = 2.07$, $p = 0.147$. The probe detection accuracy after congruent objects was 98% (SD= 0.21), 96% (SD= 0.51) for incongruent and 96% (SD= 0.52) for neutral ones. Participants had high accuracy in detecting the location of probe no matter whether its location was previously occupied by congruent, incongruent, or neutral pictures.

2.3.2. Probe detection RT

Trials with errors were removed from this analysis. Reaction times (RT) slower than 1000 ms or faster than 150 ms, and those more than 2SD above each participant's mean were considered as outliers and discarded from analyses (Mogg et al., 1998; Vogt, De Houwer, Crombez, & Van Damme, 2013). In total, 6.1% of trials were considered outliers. The one-way repeated measure ANOVA did not show significant differences of RT among probes presented after different types of pictures, $F(2, 26) = .40$, $p = .68$. The mean RT was 501 ms for those probes presented after congruent pictures, and 504 ms for incongruent and 495 for neutral pictures. Thus our imagination task did not produce any measurable attention bias.

2.3.3. Object "subjective values"

To examine whether participants' estimation of value (or level of wanting) was modulated by the congruency of pictures with imagined-values, a one-way repeated measure ANOVA was applied with a factor of congruency (congruent, incongruent, and neutral). This analysis revealed a significant main effect of congruency, $F(2, 26) = 46.27$, $p < .001$. The mean rating for congruent pictures (3.44) was significantly higher than incongruent pictures (mean = 2.31, $p < .001$)

and neutral pictures (mean = 2.26, $p < .001$) while there was no difference between incongruent and neutral pictures ($p = 0.71$). This result suggests that participants' preferences varied with the imagined state.

2.4. Discussion

First, the results of Experiment 1 confirmed the validation of the imagined-value paradigm. In other words, to imagine oneself in a certain physiological state can change one's subjective values of imagined objects. This suggests that this paradigm is valid for testing the hypothesis that mPFC activity is modulated by the subjective values of key objects in our imagined scenarios.

Unfortunately, we were unable to detect any significant implicit attentional bias according to subjective value in this experiment. Although a probe-detection task is often used to measure attentional biases, most studies used threat stimuli and appetitive stimuli and it remains unknown whether stimuli from other types of categories rather than these two can induce attentional biases. Four different physiological states of need were used in Experiment 1: hunger, thirst, coldness and tiredness. Stimuli included food, beverages, common things used to keep people warm or feel relaxed. The null results may be due to the fact that the non-food items used were unable to induce an attentional bias. An alternative explanation is that unequal perceptual salience among different pictures dampened the effect. Some pictures were more perceptually salient than others, and they may have attracted participants' attention even when they were served as incongruent pictures. Another possible explanation is that not all attentional biases can be detected by the dot probe paradigm (Öhman et al., 2001).

Some recently published studies also failed to find attention biases in normal controls by using the dot probe paradigm (e.g., Emery & Simons, 2015; Jacoby, Berman, Graziano, & Abramowitz, 2015; Jacoby, Wheaton, & Abramowitz, 2016; Miloff, Savva, & Carlbring, 2015; Werthmann et al., 2015) and the effect obtained from dot probe task was less reliable than that obtained from modified Stroop task (Ataya et al., 2012). It is possible that the dot probe paradigm is not a reliable task to investigate attention bias. So it is too early to conclude whether an implicit influence of state imagination does or does not exist.

Chapter 3. Experiment 2- mPFC activity in the imagined-value paradigm

*This chapter derives partly from Lin, W.-J., Horner, A. J., Bisby, J. A., & Burgess, N. (2015). Medial Prefrontal Cortex: Adding Value to Imagined Scenarios. Journal of Cognitive Neuroscience, 27(10), 1957–1967. http://doi.org/10.1162/jocn_a_00836

As discussed above, mPFC is involved in decision-making processes during decision-making and outcome-receiving phases, due to its roles in reward prediction/expectation and value representation. What if the reward is an imagined reward rather than a real one? Does mPFC still represent the value of the imagined reward? In a study (Bray, Shimojo, & O'Doherty, 2010), researchers found vmPFC was significantly more active in the contrast of real reward and punishment. This exact region also showed significantly higher activity levels in the imagined reward and baseline contrast and they ruled out the possibility that this region only served as a more general function for all kinds of imagery. This implies that mPFC may play similar roles in imagined reward processing and real reward processing. Therefore, it is possible that mPFC plays a role in simulated scenarios similar to its role in autobiographical memory retrieval, i.e., representing the subjective values of key elements in autobiographical memory or simulated scenarios.

Given the association between memory and imagery, it is interesting that imagery can interact with subjective value and can influence our motivation for satisfying basic needs, such as food consumption (Larson et al., 2014; Morewedge et al., 2010), and imagining future scenarios in greater detail correlates with increased choice of those scenarios (Benoit, Gilbert, & Burgess, 2011; Lebreton et al., 2013; Peters & Büchel, 2010). Human memory can be influenced by the value or motivational salience of the to-be-remembered stimuli (Erwin & Ferguson, 1979). For instance, fasting people have enhanced memory for food pictures (Morris & Dolan, 2001). Given the association between memory and imagery, the memory for items could also be modulated by their imagined values.

The aims of this experiment (Experiment 2) were, (1) to examine whether mPFC activity represents the values of elements in imagined scenarios; (2) to examine whether the subsequent memory of objects was influenced by the imagined physiological states of need. The imagined-value paradigm was used again and combined with the fMRI scanner in Experiment 2, based on the results of Experiment 1 which showed that this paradigm was able to modify people's subjective ratings of imagined objects by manipulating their imagined physiological states. A memory recognition task was also carried out after the imagined-value task in order to achieve the second aim of Experiment 2. Participants were asked to imagine themselves in some states of need and saw pictures of objects to imagine, which may or may not fulfil their imagined needs. Based on the results of Experiment 1, imagination should be sufficient to influence people's motivation, so that items which were able to fulfil imagined need should have higher value and should be memorised better than those were not able to fulfil people's imagined need. Furthermore, items which were able to fulfil participants' imagined needs should induce higher mPFC activity than items which were not able to fulfil imagined needs.

The procedure of Experiment 2 slightly differs from the procedure of Experiment 1 because the aim of each experiment was different. First, participants were requested to imagine the assigned physiological states and context but not the items in Experiment 1. In Experiment 2, participants were requested to imagine both the scenario and items to enable collecting the imaging data of imagined items with various values. Second, the duration of scenario imagery in Experiment 2 was jittered for the purpose to reduce the correlation between stimulus presentation and BOLD response. Third, the probe detection task was removed from the Experiment 2 because it was irrelevant to the aims of this experiment.

3.1. Materials and Methods

3.1.1. Participants

Twenty right-handed participants were recruited from University College London student population. One did not finish the task so the data reported here concern the remaining nineteen participants (12 female). The mean age of the remaining participants was 21.7 years (SD = 2.68, range 19-27). All participants gave written informed consent to participate, in accordance with the local ethics committee (1825/003). One participant did not complete the post-scan memory task so the results from the memory analyses are based on eighteen participants.

3.1.2. Stimuli and Design

Four different physiological states of need were used: thirst, coldness, hunger and tiredness. Neutral state (instruction for neutral state: Imagine you are just fine. You are not in any state of need but just in an ordinary condition), was used as a baseline condition. Twelve spatial contexts were used: beach, kitchen, desert, fields, classroom, airplane, forest, office, library, playground, church, and ship. Spatial contexts were included to make the imagined scenarios more realistic and because, without instruction, participants would be likely to imagine uncontrolled backgrounds to facilitate imagery. There were 60 state-context combinations with each appearing only once during the 60 trials of the imagery task.

Pictures from four categories were used as items, each category contained items which were usually used to satisfy one of the four physiological states of need. The first category contained water, juice, beer and other beverages used to quench thirst. The second category contained items which were able to be used to help people resist cold weather, such as fireplace, hot drink, and winter clothes. Another category contained food and the final category contained items used for taking a rest or relieving tiredness included a bed, couch, and bathtub and so on. Items which were unrelated to any of the physiological states were not included as this group of items would be intrinsically different to the congruent or incongruent items in this study. Ambiguous items were never used as ‘incongruent items’ (e.g. hot drink was not used in thirst trials). There were 180 item pictures in total consisting of 45 pictures per category. Among these pictures, 120 appeared in the imagery task and another 60 served as new items during an old-new recognition test. The assignment of pictures to old items and new items was counterbalanced across participants. All pictures were obtained from FreeDigitalPhotos.net (http://www.freedigitalphotos.net/).

In the imagery task, each trial contained one state-context combination presented as cue words and also two item pictures (see Figure 10 for an example of trial presentation order). The relationship between the participant’s current imagined state and each item picture during a single trial could either be congruent or incongruent. For a congruent item, the type of item presented would meet the participant's current need created by the imagined state. For instance, a food picture would be classified as congruent if the state was hunger but incongruent if the state was tired, cold or thirsty. Note, incongruent could be described as 'neutral' rather than 'incongruent' with respect to the current state. From the two item pictures, sequentially presented during each trial, either item could be congruent or incongruent with the current state. This provided four possible combinations: congruent-congruent, incongruent-incongruent, congruent-incongruent, and incongruent-congruent. Importantly, all four combinations of items occurred in pseudo random order across trials, allowing us to identify the effects of an individual items' subjective value, as modulated by its congruency with the imagined state. Among the 120 item pictures presented during the imagery task, twenty-four served as neutral pictures as they occurred in a neutral state. The remaining 96 pictures were equally assigned as congruent or incongruent items.

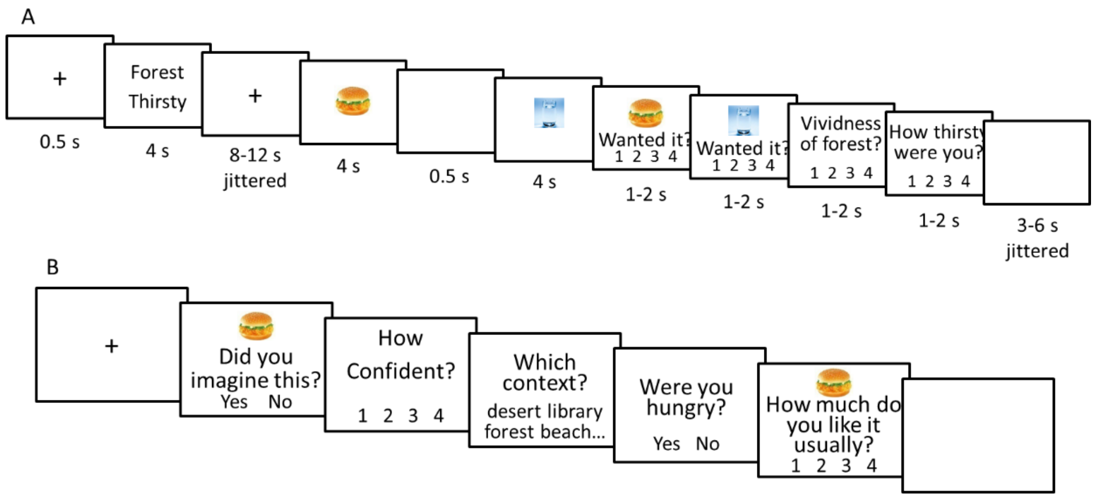


Figure 10. Procedure of the task in Experiment 2

(A) the imagery task and (B) the memory task.

3.2. Procedure

3.2.1. Imagery task

Participants were provided with task instructions prior to scanning and completed a number of practice trials outside of the scanner. The entire imagery task, consisting of 60 imagery trials, was equally divided into two sessions, and scanning lasted for 1 hour in total, including acquisition of a structural scan. See Figure 10A for an illustration of stimulus presentation for the imagery task. Each trial began with a fixation cross at the centre of the screen which was replaced by a pair of state-context cue words after 0.5s. Participants were instructed to vividly imagine the context and state according to the cue words provided. The state-context cue words were presented for 4s and then a fixation cross appeared again (for 8-12s, jittered, based on a uniform distribution), during which the participants were instructed to continue imagining. Next, two pictures were presented sequentially, each for 4 seconds separated by a 0.5s blank screen. Participants were required to incorporate each presented item into their imagined scenario during the trial. Participants were explicitly instructed to not imagine consuming these items to satisfy their imagined state and its associated need. For example, they were required to imagine seeing (but not consuming) a chicken burger in a forest whilst they were thirsty (as in Figure 10A). After a further blank screen (1-4s, jittered, based on a uniform distribution), participants made four simple ratings, one at a time. The first two ratings asked participants to rate how much they had wanted each item when they initially saw it during the trial. The last two separately rated how vividly they had imagined the current state and context. All ratings used a 4-point scale (1 for not at all, 4 for very much). Each trial ended with a final blank screen (3-6s, jittered, based on a uniform distribution). Visual stimuli were presented by MATLAB (MathWorks) and COGENT 2000 toolbox (http://www.vislab.ucl.ac.uk/cogent.php).

3.2.2. Memory task

The memory task took place outside of the scanner after the imagery task was completed. Each trial consisted of a 500ms fixation cross followed by a picture of an item, and participants were required to judge whether the picture had been presented in the imagery task or not (i.e., old/new item recognition judgment) and how confident they were of their answer (Figure 10B shows an illustration of the memory task). If participants answered ‘new’, participants were then asked how much they like that item in their daily lives. If an item was judged ‘old’, two further source memory questions were presented to the participant to test memory for the associated state and context. To test state, one of the state words (hunger, thirst, tired, cold or neutral) was presented and participants judged whether that state was the one they had been asked to imagine when the recognized item picture had appeared in the imagery task. The correct answer was yes for fifty percent of trials, and within these trials, forty percent of the state words were congruent with the tested item, forty percent were incongruent, and twenty percent were neutral. For the context source memory test, all twelve of the contexts were listed to allow participants to select the one which had accompanied the recognized item picture. The trial ended with the daily subjective rating. There were 180 memory trials in total (120 with ‘old’ items and 60 with ‘new’ items). Alternative forced choice was the most efficient way to test memory for the spatial context of an item's presentation, but could not be used to test memory for the physiological state, because a simple strategy of guessing the congruent state would be effective (e.g., choosing 'thirst' when presented with a drink). The congruent state would be correct in 40% of trials, the neutral state would be correct in 20% of trials and the three incongruent states correct in 13% of trials. Instead, we tested participants with yes/no cued recognition of a single state that was chosen to be correct 50% of the time irrespective of its congruence with the item.

3.2.3. fMRI data acquisition and preprocessing

Functional imaging was performed on a 3T scanner (Siemens TIM Trio) during the imagery task. The functional data were acquired with a gradient-echo EPI sequence (TR, 3.36s; TE, 30ms; flip angle, 90°; resolution, 3×3×3 mm; 64×74; 48 slices per volume, slices were tilted 45° up at the front). The total number of volumes in each run varied across participants because of the variation of response time for each rating (the mean number of volumes was 332 per session, range= 304- 380). A high-resolution T1-weighted 3-D structural image (1 mm3) was acquired after two sessions of functional scans. A double-echo FLASH fieldmap sequence was also recorded.

Functional images were processed and analyzed with SPM8 (Wellcome Trust Centre for Neuroimaging, London UK, http://www.fil.ion.ucl.ac.uk/spm/software/spm8/). The first five volumes of each scan were discarded for T1 equilibration. Preprocessing procedures included bias correction, realignment, unwarping, coregistration, slice timing correction, and normalization to the MNI template using the Dartel toolbox. EPI images were smoothed with an isotropic 8mm full-width half-maximum Gaussian kernel. One of the participant's fieldmap scan was not collected so the unwarping procedure was skipped in their data.

3.2.4. Data analysis

The preprocessed functional images were analysed with general lineal models (GLMs). Five GLMs have been estimated for different purposes. All GLMs included 6 movement regressors for each session, estimated during realignment, as well as two further regressors modelling each session. Based on the strong a priori hypothesis about the mPFC, I performed small-volume correction (SVC) within a combined anatomical mask of these regions: bilateral mPFC which included both the dorsal and ventral regions of mPFC (volume ~ 53,493 mm3). This mask was derived from the AAL atlas (Tzourio-Mazoyer et al., 2002), as implemented in the WFU PickAtlas Tool (Maldjian, Laurienti, Kraft, & Burdette, 2003).This mask contained bilateral superior frontal gyrus, medial frontal gyrus, anterior cingulate and cingulate gyrus. Within these small volumes I report effects that survive $p<.05$ FWE correction. For completeness, I also report effects at $p<.001$ uncorrected across the whole brain, however caution is needed in interpretation of these effects.

The first model (GLM1) was a parametric modulation analysis, searching for regions that correlated with the subjective value of an item during states of need. The first-level model contained 7 regressors per session: (1) imagining a state of need, (2) imagining a neutral state, (3) imagining an item in a state of need, (4) a parametric modulator of the item regressor based on the participant's normalised subjective value of each item (i.e., rating in imagery-everyday rating), (5) imagining an item in a neutral state, (6) ITI periods and (7) key-presses. Trial periods were modelled with a boxcar function for the entire length of each period (e.g., the 4s of imaging an item), convolved with the canonical HRF. The second-level analysis was a one-sample t-test on the parameter estimates from the parametric modulator (regressor 4) averaged across the two sessions. For the parametric modulation I used the subjective rating of each item when imagined in the state of need of the current trial minus the subjective rating of the item in the participant’s daily life, given after the scanning session. This calculation allowed us to control for variations in the participants’ baseline preference for the various items. The range of these normalised subjective ratings was from -3 to 3.

The second model (GLM2) was used for comparing imagination of congruent items versus incongruent items (given that the first GLM collapsed across these conditions to maximize power in the parametric modulation analysis), and also for comparing imagining states of needs versus neutral states. This model included seven regressors per session: (1) imagining a state of need, (2) imagining a neutral state, (3) imagining a congruent item in a state of need, (4) imagining an incongruent item in a state of need, (5) imagining an item in a neutral state, (6) ITI periods and (7) key-presses. Parameter estimates for (1) imaging a state of need, (2) imaging a neutral state, (3) imagining a congruent item in a state of need and (4) imagining an incongruent item in a state of need, averaged across the two sessions, were entered into a second-level model. A separate regressor was also included for each individual subject that consisted of a '1' for each condition for that specific participant (i.e., subject effects). A third model (GLM3) aimed to test the subsequent memory effect for imagined items. The model was similar to GLM1, but replaced the subjective value parametric modulator with a modulator based on subsequent memory. The model included 6 regressors per session: (1) imagining a state of need, (2) imagining a neutral state, (3) imagining an item (in either a state of need or neutral state), (4) a parametric modulator of the previous regressor based on subsequent memory for the item, (5) ITI periods and (6) key-presses. Note that the parametric modulator focused on subject value focused on item imagination during a state of need, as we were specifically interested in how states of need modulated subjective value. For the subsequent memory modulator I included all item imagination trials (included during neutral states) to maximize power. Subsequent memory was parameterized as a transformed confidence rating to maximize sensitivity. Participants' 1-4 confidence ratings for old and new items at test were transformed into a measure of successful memory performance by combining ratings for item 'hits' with negative ratings for item 'misses' (e.g. a 'miss' given a confidence rating of 4 would become -4 in the parametric modulator). The second-level analysis was a one-sample t-test on the parameter estimates from the parametric modulator (regressor 4) averaged across the two sessions.

The final two models (GLM4 & GLM5) aimed to test the subsequent memory effect for the state of need (GLM4) and the context (GLM5) in which items were imagined (i.e. two types of source memory). GLM4 contained 7 regressors per session: (1) imagining a state of need, (2) imagining a neutral state, (3) item imagination trials for which the item and state of need are subsequently remembered, (4) item imagination trials for which the item but not the state is remembered, (5) item imagination trials for which the item is not remembered, (6) ITI periods and (7) key-presses. GLM5 was similar to GLM4, but split item imagination trials (regressors 3-5) by according with whether the context (rather than the state) was remembered. Second-level models for each GLM were paired t-test comparing either state or context hits vs misses (regressors 3 and 4) averaged across the two sessions.

Note separate GLMs were built for each analysis of interest. This was due to the overlapping nature of certain regressors. In particular, the categorical congruent vs incongruent contrast correlated with the related, but more sensitive, item-by-item parametric modulation of value by state. Further, the parametric modulators relating to subsequent memory and subjective value were also correlated. Despite the overlapping nature of these regressors of interest, our separate GLMs revealed distinct activation patterns.

3.3. Behavioural Results

3.3.1. The subjective value of items in imagery

If the manipulation of imagined state work, the proportion of high-value congruent items should be high and the proportion of low-value congruent items should be low. In the meanwhile, the proportion of high-value incongruent items should be low, and the proportion of low-value incongruent items should be high. A three-way repeated measure ANOVAs with the situation (two levels: everyday rating and rating during imagery), rating (1-4), and category (congruent, incongruent, and neutral) was carried out to verify if the paradigm work. The dependent measure was the mean proportion of trials receiving the rating specified by the ‘rating’ factor. The three-way interaction was significant ($F(6, 102) = 18.7$, $p < .001$) so further analyses were carried out which revealed that the distributions of ratings differed between categories for ratings during imagery (rating* category $F(6, 102) = 27.4$, $p < .001$), but not for everyday ratings (rating* category $F(6, 102) = .662$, $p = .68$). Thus, it was only when participants imagined being in a specific state of need that the subjective value of the items differed between the “congruent” and “incongruent” conditions. Table 1 shows that a greater proportion of congruent items had positive subjective value (controlling for baseline value, i.e. rating of imagined value – everyday rating) (39.67%), while most incongruent items had negative subjective values (60.25%). This suggests that the participants indeed followed the instruction to imagine the assigned state of need and that those imagined states influenced the subjective value of the item on that trial.

Another two-way repeated measure ANOVA with congruency between state question word and item (congruent and incongruent) and rating (1-4) as within subject variables was carried out to test whether the preceding state question might bias ratings (e.g. ‘hungry’ increasing ratings for food items). There was no significant interaction between congruency and rating ($F(3, 51) = .40$; $p = .75$), suggesting that the everyday ratings were not influenced by the preceding source memory questions.

Table 1 Percentage of subjective values of items during imagery

Percentage of subjective values of items during imagery, according to whether they were imagined in a congruent, incongruent or neutral state of need, controlling for baseline value (value during imagery – everyday value).

	-3	**-2**	**-1**	**0**	**+1**	**+2**	**+3**
Congruent	2.36%	5.20%	17.66%	35.10%	23.27%	11.95%	4.45%
Incongruent	6.63%	18.64%	34.98%	27.31%	8.93%	2.94%	0.58%
Neutral	6.35%	18.03%	30.90%	28.32%	11.43%	4.97%	0.00%

3.3.2. Old-new recognition

A one-way repeated measures ANOVA across congruency (congruent, incongruent, and neutral) was carried out to test for differences in hit rate among different categories of items. The results revealed a significant main effect of congruency, $F(2, 34) = 9.01$, $p < .001$ (see Figure 11A for memory performance). Pairwise comparisons showed that hit rate was higher for congruent items than for incongruent ($t(17) = 5.16$, $p < .001$) and neutral ($t(17) = 3.14$, $p = .006$) items. However, there was no significant difference between incongruent and neutral items ($t(17) = .35$, $p = .73$). This result suggests that participants had better memory for items which were able to fulfil their needs in the imagined state. Participants showed a high correct rejection rate for new items (87%). Table 2 shows confidence ratings across all responses.

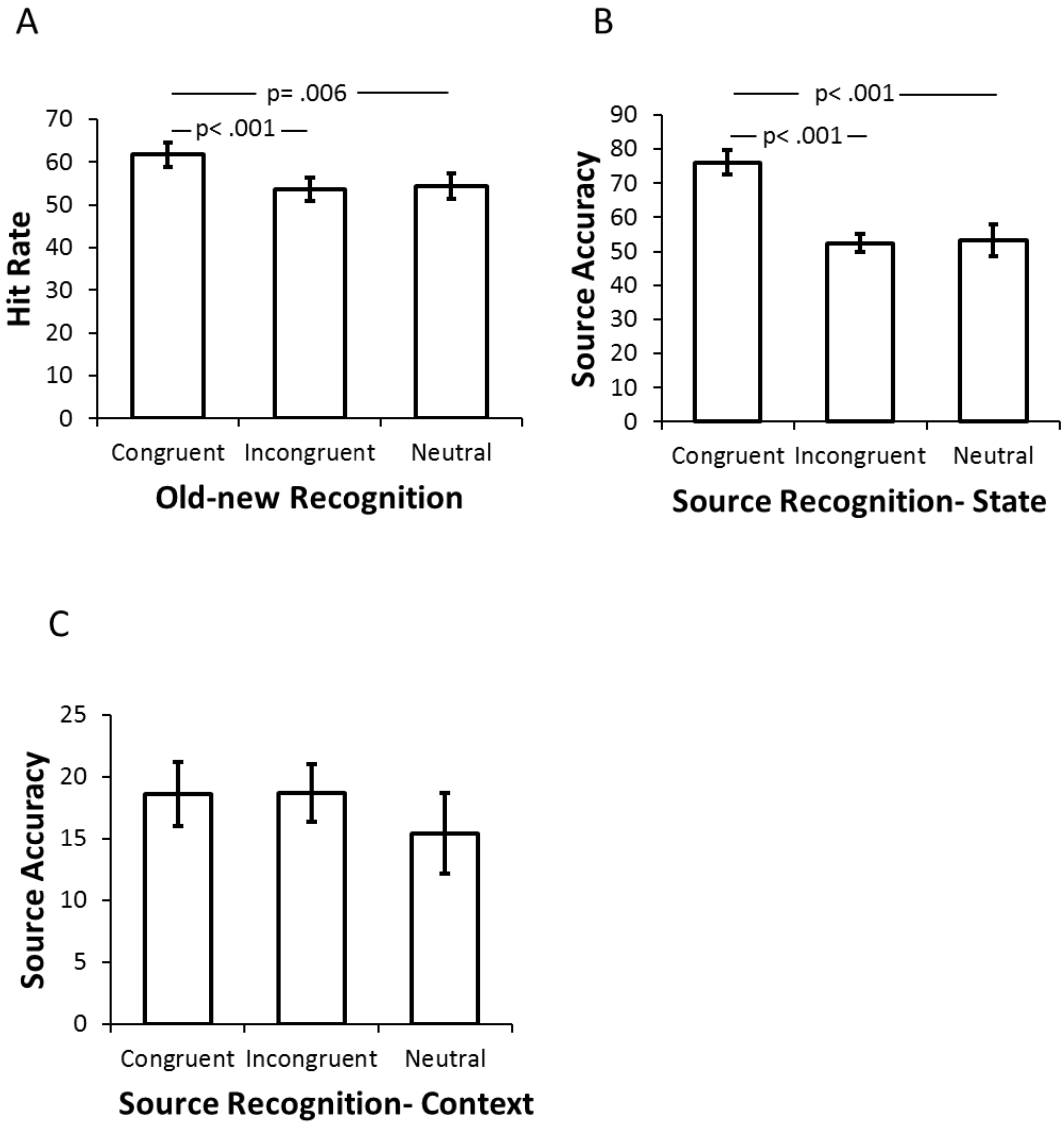


Figure 11. Behavioral results for the memory task

A, Mean values of hit rate in the item recognition memory task. B and C, Mean performance in the source recognition task- for the state of need (B) and the spatial context (C). Error bars represent +/- 1 SEM.

Table 2 Confidence ratings

Percentage of confidence ratings given for the different types of response in the old-new item recognition task.

	Hit	Miss	False Alarm	Correct Rejection
1	3.9%	16.7%	17.0%	10.4%
2	14.1%	19.8%	29.1%	15.3%
3	20.1%	26.8%	29.1%	23.5%
4	61.9%	36.7%	24.8%	50.7%

A two-way repeated measure ANOVA with order of presentation (two levels: first or second), and category (three levels: congruent, incongruent, and neutral) as within-subject factors on the subjective ratings and subsequent memory scores was also carried out to test whether the results varied with the order in which items were presented within a trial. The results shows that the order of presentation during encoding did not affect item memory (order, $F(1,17) = .198$, $p = .660$; category, $F(2,34) = 9.215$, $p = .001$ order*category, $F(2,34) = 1.89$, $p = .167$), and there was a non-significant trend towards lower ratings for the first versus second item (order*category, $F(2, 34) = 1.05$, $p = .36$; order, $F(1, 17) = 3.92$, $p = .064$)).

3.3.3. Source memory

Source memory performance for correctly associating the imagined state with the recognized item was analysed using a similar one-way ANOVA. There was a significant main effect of item congruency ($F(2, 34) = 17.30$, $p < .001$). Pairwise comparisons showed that the conditional state source hit rate (source hits over item hits) for congruent items was significantly higher than for incongruent items ($t(17) = 6.16$, $p < .001$) and neutral items ($t(17) = 5.44$, $p < .001$) while there was no significant difference between the latter two categories ($t(17) = .17$, $p = .864$). See Figure 11B. Although participants showed a response bias towards accepting the state (answering 'yes') when it was congruent (55.6% responses were yes) or neutral (54.2% yes) relative to the item, and 'no' when it was incongruent (41% responses for incongruent items were no), this response bias could not account for the results (the correct proportion of 'yes' responses being 50% in both cases – so that a bias cannot improve source accuracy scores, which are measured as % correct).

Analysis of source memory performance for the imagined spatial context (e.g., 'beach') within the recognized item showed no significant main effect of item congruency ($F(2, 34) = .889$, $p = .42$; see Figure 11C for context source memory performance). It is possible that this reflects the irrelevance of spatial context to the subjective ratings which the participants are required to give on each trial, or that any small effects of congruency on context-source memory were obscured by low levels of performance (chance = 8%) although performance was above chance in each category (congruent: $t(17) = 3.96$, $p = .001$; incongruent: $t(17) = 4.48$, $p < .001$; neutral: $t(17) = 2.14$, $p = .047$).

In general, behavioural results supported the prediction. Subjective values of items support the validity of our imagine-need paradigm. There was also a greater recognition performance for congruent than incongruent items, and better memory for the imagined state of congruent than incongruent items. In other words, there was better memory performance for items when their value was congruent with the imagined state

3.4. fMRI Results

3.4.1. Subjective value of items in imagery (GLM1)

First, the analysis focused on the main prediction of Experiment 2: that the subjective value of items in imagined scenarios would correlate with the BOLD response in the mPFC. To isolate imagined value from differences in the intrinsic values of the items used I calculated the participant's subjective value for the item when imagining it in the current state of need minus their subjective value for the same item in their daily life. This parametric modulator revealed an effect in the mPFC (+9, +57, +12, $Z = 3.98$; $p<.05$ FWE SVC). See Figure 12. Therefore the results provide evidence that mPFC represents the values of elements in imagined scenarios, controlling for variations in their intrinsic value in other situations.

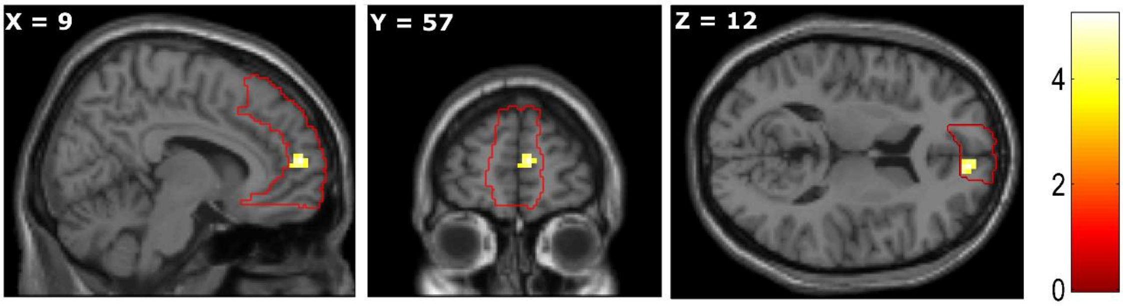


Figure 12. mPFC during object imagination

The activation of mPFC during imagination of an object during a state of need varied according to the extent to which the subjective value of item was modulated by the imagined state of need. All peaks significant at $p < .001$, uncorrected. (The redline depicts the area of mPFC mask used in SVC analysis.)

Given the complexity of the imagined-value task, it is important to rule out other explanations for the main mPFC result. This is particularly important given the overlapping nature of certain experimental factors (see Methods). In short, none of the subsequent analyses in Experiment 2 showed an effect in mPFC, even at a lenient $p<.001$ uncorrected threshold. However, these analyses did reveal effects in other regions at this threshold. These results were reported for completeness but note they should be treated with caution given that they do not survive correction for multiple comparisons.

3.4.2. Imagining states of need, and item congruency with need (GLM2)

Compared to imagination of a neutral state, imagination of states of physiological need showed greater activation in bilateral insula (MNI coordinates of peak activations: -39, -6, -3, Z = 3.27; +45, +15, +3, Z = 3.15; $p < .001$, uncorrected; Figure 13A). By contrasting imagery for congruent versus incongruent items, a region in the basal ganglia was identified – the caudate nucleus (+3, +9, +6, Z = 3.60; -6, +9, +6, Z = 3.56, p< .001, uncorrected; Figure 13B). Since congruent items had higher subjective value than incongruent ones, a small volume corrected analysis for the congruent-incongruent contrast in the mPFC ROI was also carried out, but found no significant effect.

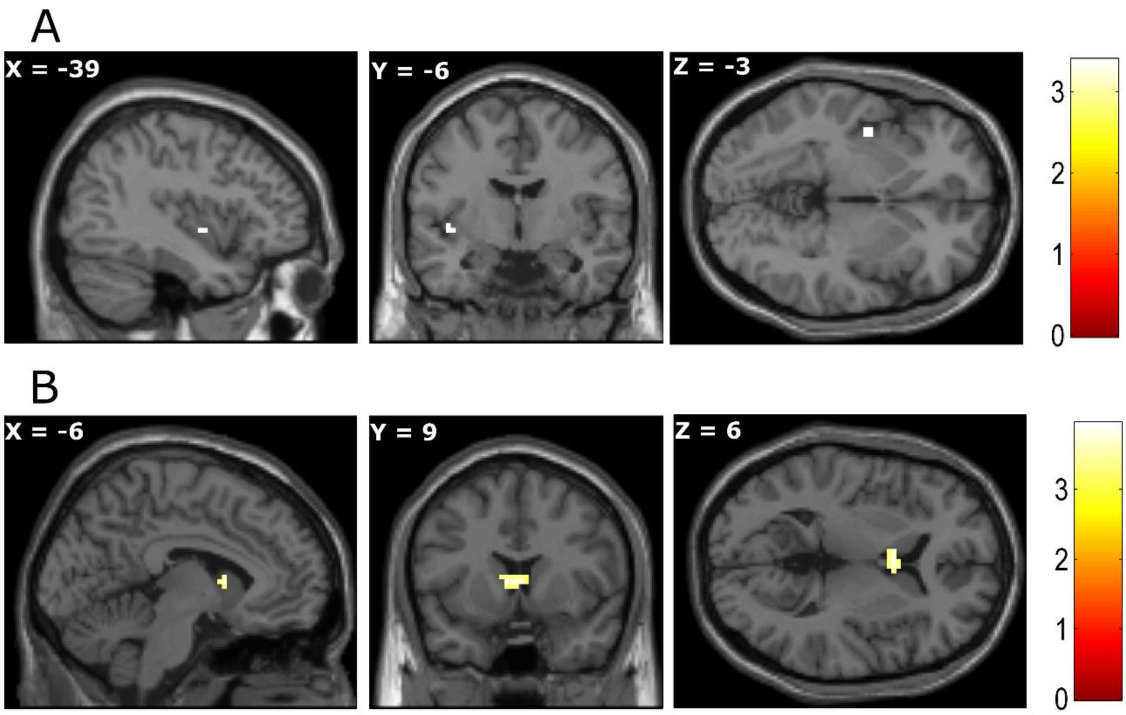


Figure 13. Imagining states of need> imagining the neutral state

A, Bilateral insula showed higher activation when participants were imagining states of need compared to imagining the neutral state. B, The caudate showed greater activation for imagining a state-congruent item than a state-incongruent item. All peaks significant at p< .001, uncorrected (colour bars indicate equivalent Z scores).

I also investigated whether the fMRI correlates of an item's value or state-congruency varied between the first and second item, finding a non-significant trend towards a greater effect of state-congruency for the first versus second item in the vmPFC (-3, 33, -12; p=0.083 FWE, SVC). However, these could not influence the findings themselves, as the manipulation of state-congruency was counterbalanced across items.

3.4.3. Subsequent memory effects (GLM3)

This parametric modulation analysis showed that BOLD signal in right amygdala (+33, -3, -30; Z = 3.27) and left anterior hippocampus (-21, -12, -18; Z = 3.33), when participants were imagining items, were significantly correlated with participants' subsequent memory (p< .001, uncorrected, Figure 14). Note, the subsequent memory modulator combined categorical subsequent memory status (i.e., hits and misses) with subjective confidence, revealing linear increases in BOLD response from -4 (high confidence misses) to +4 (high confidence hits). No other significant activity was revealed in this analysis.

No significant activations were found corresponding to subsequent source memory effects for state (GLM4) or for context (GLM5), i.e. the comparisons of imagery for items that became source hits versus source misses. This may reflect a lack of power, given the relatively low trial numbers in specific conditions (i.e., source misses for state), and the absence of a parametric measure like the confidence ratings used for item memory.

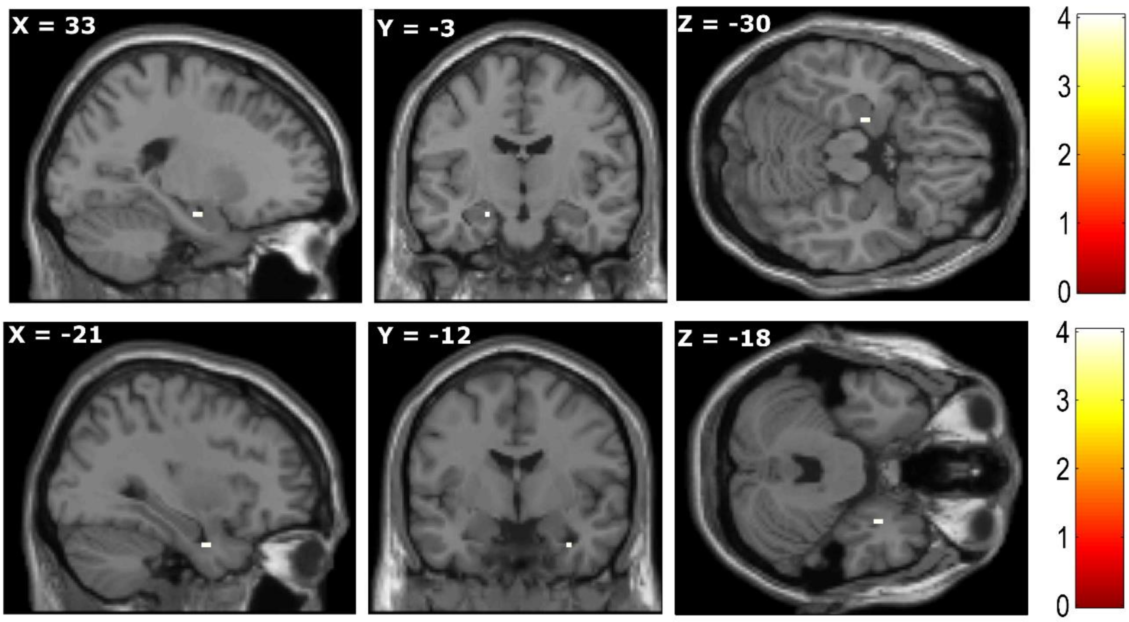


Figure 14. Subsequent memory

Greater activity was seen during encoding in left hippocampus (upper row) and right amygdala (lower row) for items that were subsequently correctly recognised with high confidence compared to subsequently non-recognised items. All peaks significant at p< .001, uncorrected.

3.5. Discussion

I was interested in the potential role of medial prefrontal cortex in contributing subjective value to the contents of imagery. The imagined-value paradigm provides a way to measure this by manipulating subjective value of imagined items with respect to imagined physiological need. In line with the results of Experiment 1, the behavioural results of Experiment 2 suggest the manipulation was valid and the imaging results support the hypothesis that mPFC activity reflects the subjective value of elements in imagined scenarios.

The manipulation of imagined need succeeded in altering the subjective value of elements within imagined scenarios in that participants indicated higher ratings for items congruent with (i.e. likely to satisfy) the state of need. The subsequent recognition memory for items also supports the success of this manipulation. Items which were able to fulfil people's imaginary needs showed greater subsequent memory, both in being better recognized and by being better associated to the state of need in which they were presented. This could be because to imagine a congruent item in the imagined scenario is more consistent with our daily life experiences and this enabled participants to have a richer imagination. Similarly, congruent items might fit more readily into a pre-existing 'schema' allowing for a more rapid integration of the item and imagined state (Bartlett, 1932; Bransford & Johnson, 1972; Tse et al., 2007). Equally, congruent items might have been better remembered because more valuable scenarios tend to be more strongly represented in memory-related areas (Lebreton et al., 2009; Wittmann et al., 2005).

The instruction to imagine states of physiological need was accompanied by increased activity in the insula compared to neutral states, albeit at an uncorrected threshold. This would be consistent with studies showing insular activation corresponding to interoception of actual physiological states (Craig, 2003), including thermo sensation (Craig, Chen, Bandy, & Reiman, 2000), and hunger (Tataranni et al., 1999). One might wonder whether people are able to imagine themselves in different physiological states, because physiological states are not usually thought to be under cognitive control. However, involuntary physiological signs can be influenced by imagination, e.g. pupil dilation can be affected by imagining dark or light environments (Laeng & Sulutvedt, 2013).

I was interested in the process by which subjective value is afforded to an item within an imagined scenario. To investigate this I looked for an fMRI signal matching the modulation of an item's subjective value by the imagined state of need, i.e. a regressor formed from the subjective rating of the item when imagined as part of a specific scenario minus the subjective rating of that item in daily life. I found of activity in mPFC, both in a more superior region and the ventral region of mPFC (albeit at an uncorrected threshold for the latter region), following this pattern. This is consistent with our hypothesis for the role of mPFC in imagery. Thus, beyond the representation of the subjective value of choices in decision making, the mPFC may also play a role in representing the value of items in imagined scenarios more generally. This more general role might begin to explain its involvement in autobiographical memory retrieval or episodic future thinking, as well as tasks with an implied component of choice such as planning. Indeed, mPFC activation has been seen together with hippocampal activation during the imagination of rewarding future situations in a decision task (Lebreton et al., 2013).

In general, congruent items were rated as more valuable than incongruent ones. Congruent items might be valuable because of their utility in a specific context (i.e., a congruent state) (Hare, Malmaud, & Rangel, 2011) or because congruent items are more self-relevant in a congruent state (D'Argembeau, 2013). Could the results been observed in mPFC be caused by semantic congruency effect? To examine the effect of semantic congruency itself, I simply compared the imagination of explicitly congruent or incongruent items, finding activity in the caudate nucleus (but not in mPFC, where the difference in activity was some way below threshold, at p=0.06 uncorrected). Thus, there is little support for a semantic interpretation of the mPFC activity I observed. The representation of the combined scenario may involve the striatum, via increased consolidation of the congruent state-item association, consistent with some rodent studies of consolidation (Pennartz et al., 2004). Alternatively, the striatal activation may reflect the involvement of these areas in reward-related processing (e.g., Brian Knutson, Rick, Wimmer, Prelec, & Loewenstein, 2007), in the sense that the imagined interaction with the congruent item seems more rewarding in nature (although we forbade imagined consummation of items).

Although in general, congruent items have higher subjective ratings and incongruent items have lower subjective ratings, but there was no mPFC effect in the congruent vs. incongruent contrast. A potential explanation is because the power of parametric modulator analysis is stronger than that in a pairwise comparison.

The behavioural results demonstrate a higher recognition rate for congruent items. This memory effect could relate to schema theory: perhaps the encoding of new information (i.e. a congruent item) benefits from being congruent rather than incongruent with the existing scenario. The mPFC has been implicated in incorporating new information into existing knowledge structures (Benchenane et al., 2010; Tse et al., 2011; van Kesteren et al., 2013; van Kesteren, Rijpkema, Ruiter, & Fernández, 2010; van Kesteren, Ruiter, Fernández, & Henson, 2012). However, mPFC did not show a significant subsequent memory effect. Subsequent memory for items was related to activity in the anterior medial temporal lobe during encoding, consistent with several previous studies implicating the hippocampus (Wagner, 1998). Our subsequent memory effects also extended into the amygdala. This may be consistent with a role for the amygdala in item memory (Farovik, Place, Miller, & Eichenbaum, 2011; Kensinger, Addis, & Atapattu, 2011; Kensinger & Schacter, 2006; Ranganath, 2010), or with amygdala involvement in enhancing memory for items with affective salience (Hamann, Ely, Grafton, & Kilts, 1999) or intrinsic value as a reinforcer (Rolls, 2005). Unfortunately, we did not have enough statistical power to analyse subsequent memory effects separately in congruent, neutral and incongruent items to address these possibilities.

The recollection of autobiographical information has been associated with a network of brain regions. Although many posterior regions have a hypothesized functional role within this network (Byrne et al., 2007; Cabeza & St. Jacques, 2007; Hassabis & Maguire, 2009; Schacter et al., 2012), the mPFC has received somewhat less attention. Autobiographical memories tend to be highly personal and value-laden. For example, we are more likely to remember the experience of having a cup of hot tea after walking outdoors for hours on a cold winter day than having a cup of tea in an ordinary afternoon. Given its association with value in decision making, and with the value afforded by imagined scenarios in the present study and related studies (Benoit, Szpunar, & Schacter, 2014; Gross et al., 2014; Nieuwenhuis & Takashima, 2011), mPFC activity may reflect representation of the value of recollected information (see also D’Argembeau, 2013). This is perhaps one reason why mPFC is typically not seen in more traditional episodic memory tasks, such as word recognition, where memory for such items may be high, but little value is associated with the retrieved items. Indeed, the subjective value associated with items may be one critical difference between typical autobiographical and episodic memory tasks.

To conclude, we have developed a new paradigm for looking at the interaction of imagery and value. We have validated it behaviourally via subjective value ratings and subsequent memory effects. Supporting our hypothesis, we found activity in the mPFC corresponding to the subjective value that an item is afforded by the imagined scenario. This suggests an extension of the well-known role of mPFC in representing value during decision making, and offers a potential explanation of its involvement in imagery and autobiographical memory retrieval.

Chapter 4. Experiment 3- mPFC activity in autobiographical memory recall

*This chapter derives partly from Lin, W.-J., Horner, A. J., & Burgess, N. (2016). Ventromedial prefrontal cortex, adding value to autobiographical memories. Scientific Reports, 6, 28630. http://doi.org/10.1038/srep28630

The medial prefrontal cortex (mPFC) has consistently been shown to play a role in autobiographical memory (AM) recall (for reviews, see Addis et al., 2007; Cabeza & St. Jacques, 2007; Hassabis & Maguire, 2009; Svoboda, McKinnon, & Levine, 2006), recollection of self-relevant information (Macrae et al., 2004; Martinelli, Sperduti, & Piolino, 2013; Moore III, Merchant, Kahn, & Pfeifer, 2014; Summerfield, Hassabis, & Maguire, 2009), the imagination of novel scenarios (for reviews, see Buckner & Carroll, 2007; Schacter et al., 2012), emotional regulation during autobiographical memory recall (Ford, Morris, & Kensinger, 2013; Holland & Kensinger, 2012) and linking self-relevance and value (D'Argembeau, Stawarczyk, Majerus, Collette, Van der Linden, Feyers, et al., 2010; D'Argembeau et al., 2012), with the ventromedial prefrontal cortex (vmPFC), in particular, being reliably involved. Whilst this highlights that mPFC has an important role in AM and imagery, it remains unclear exactly what functional role it provides.

It is well-established that mPFC also plays a role in representing the values of choice during decision making (for a review, see Levy & Glimcher, 2012). In addition, judgements relating to the self are believed to be processed in more ventral mPFC while other-relevant processing is associated with more dorsal mPFC (for a review, see Denny, Kober, Wager, & Ochsner, 2012). Taken together, these observations suggest that mPFC might contribute to imagination and AM by representing the subjective value of the contents of imagined or recollected scenarios, and that increasing the personal relevance of these contents might involve more ventral regions of mPFC.

The predicted modulation of mPFC activity by the value of elements within imagined scenarios has recently been observed (Benoit et al., 2014; W.-J. Lin, Horner, Bisby, & Burgess, 2015). In both studies, participants imagined novel scenarios and rated the subjective values of the imagined contents, with these ratings being found to correlate with activity in mPFC. Here we sought to investigate the hypothesis that activity in mPFC might reflect the values of elements of autobiographical memories, and the related hypothesis that the more personally relevant AMs used here might be reflected in activity in more ventral regions within mPFC than seen with the novel scenarios used in previous studies.

In Experiment 2, activity in mPFC was modulated by participants' subjective evaluation of common items present in newly imagined scenarios. In the present study, we used a similar procedure but replaced the imagined scenarios and imagined items with participants' real autobiographical memories and the items that were remembered within them. On day1 I asked participants to recall AMs, including six items within each event that were either liked or disliked at the time of the event. They characterized each AM in terms of its pleasantness, recall vividness (Daselaar et al., 2008), personal significance, recall frequency, recall difficulty, emotional intensity and time since it happened, and also reported the familiarity of the items at the time of the event (as familiarity has also been linked to mPFC activity during imagery (Benoit et al., 2014; Szpunar, Chan, & McDermott, 2009)). On day 2, in an fMRI scanner, participants recalled AMs and then rated the values of four of the items in each event, and the vividness with which each was brought to mind.

4.1. Behavioural Pilot

Before I carried out the current experiment in the fMRI scanner, the experimental paradigm was tested without scanning. This behavioural pilot was carried out to make sure that participants were able to recall enough memories and were able to provide those necessary details.

Nine participants were recruited from UCL (age range= 20-32 yrs). All participants gave written informed consent before taking part in the experiment. All experimental protocols were approved by the UCL research ethics committee (1338/006), and all data collection and analyses were carried out by the approved guidelines.

The test contained in two parts: AM-interview in Day1 and test in Day2. In the AM-interview, participants had to recall and elaborate 40 autobiographical memory events based on free association with word-cues we provided. Then they had to choose six items from each event; three were items which they liked at the time when the event occurred, and the other three were items which they did not like at that time. They also had to rate each remembered event for the level of detail, emotional valence, personal significance, vividness, and recall frequency, using a 4-point scale.

In the test phase, cues were presented one by one and participants had 8-12 seconds to recall the corresponding events again. Four items were selected from each event, and these items were presented as words one by one on the screen. Participants had to recall each item. Half of these items were those identified as liked by participants in the AM-interview and the other half were disliked ones. Participants also rated how much they liked each item on a 5-point scale immediately after recalling it.

All the participants were able to recall and elaborate 40 specific memories based on the cues we provided. They were also able to provide enough important and non-important items within each memory. Moreover, they gave liked items higher likability ratings than disliked items during recall (see Figure 15), which suggests that participants did not randomly categorise items into liked and disliked categories. In general, the results of this behavioural pilot experiment suggested the feasibility of this paradigm.

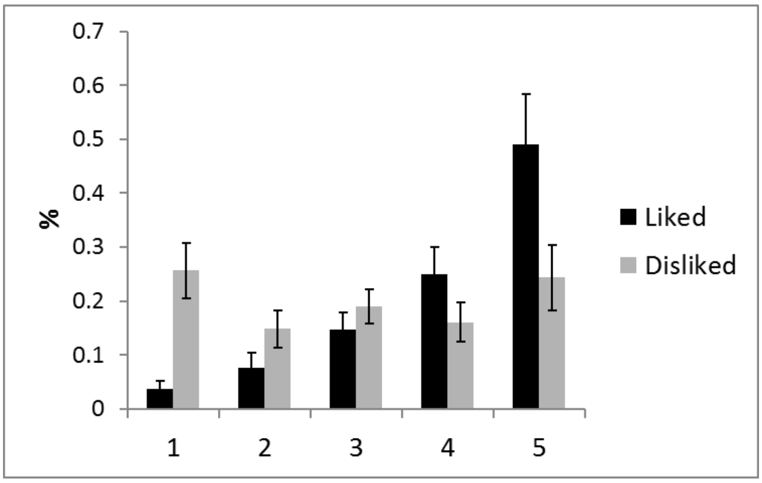


Figure 15. Percentage of liked and disliked items across ratings 1-5 during recall

4.2. Methods

4.2.1. Participants

Twenty-seven right-handed participants from University College London were recruited via advertisement. Two participants failed to finish the experiment and therefore all the results reported here were from the remaining 25 (11 males, mean age=25.6, SD=4.62, range=20-35). All participants gave written informed consent before taking part in the experiment. All experimental protocols were approved by the UCL research ethics committee (1338/006), and all data collection and analyses were carried out in accordance with the approved guidelines.

4.2.2. Stimuli

An AM interview procedure (Maguire, 2001) was adopted to collect participants' autobiographical memories. Cue words used in the AM interview were 40 nouns chosen from Clark and Paivio's (Clark & Paivio, 2004) extended norms. All of these words have high ratings in frequency (mean Thorndike-Lorge frequency=1.88, SD=0.15), imageability (mean=6.32, SD = 0.39), and concreteness (mean = 6.59, SD = 0.55).

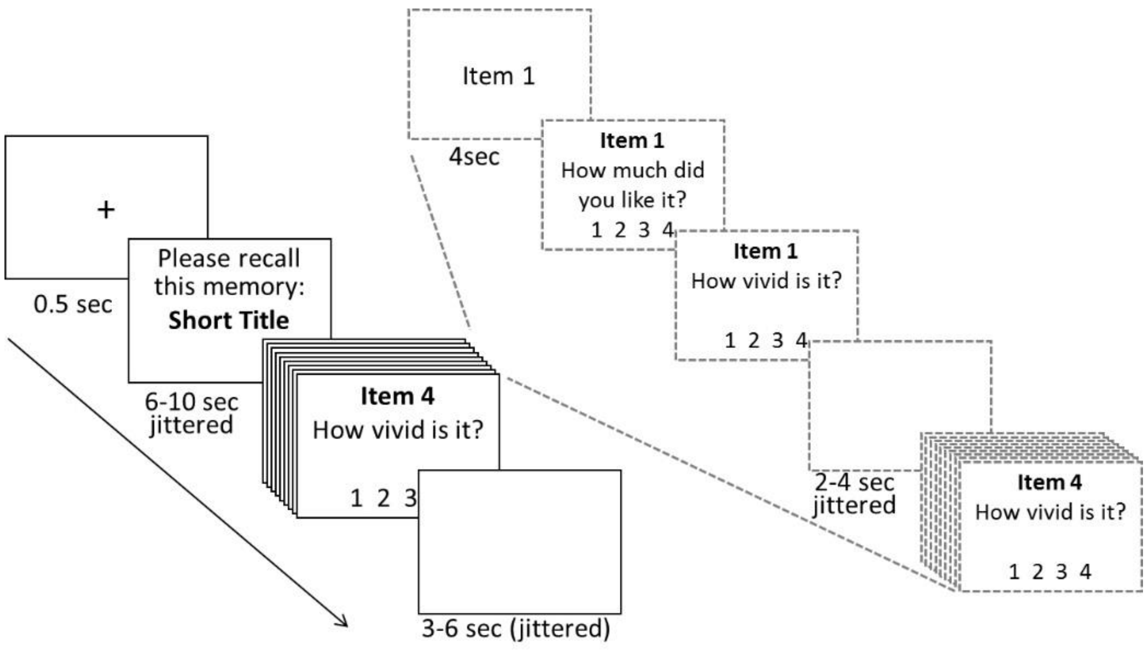


Figure 16. Day 2: Recall in scanner

Procedure of autobiographical memory recall and item rating in the scanner on Day2.

4.3. Procedure

All participants took part in the experiment on two consecutive days – the AM interview on Day 1 and recall in the scanner on Day 2 (Figure 16). Conducting a separate scanning session (on Day 2, as opposed to scanning the Day 1 interview) allowed us to have better control over several factors during memory and item retrieval in the scanner on Day 2, for instance, counterbalancing the order in which liked and disliked items were recalled and controlling the duration allowed for AM retrieval which can be extremely varied on Day 1. Although retrieval on Day 2 might be affected by the recall or rating process on Day 1 (Cabeza & St. Jacques, 2007), participants were instructed to focus on their original memories. During the AM interview, all of the forty cue words were presented to participants one by one. Participants were instructed to freely associate one time- and location-specific autobiographical event to each cue word and verbally elaborate the details of the event. Details included the age of the event, location, people involved, and things that happened in the event. Events could range in age from their childhood to the day before the interview. A succinct memory title for each event was created by participants themselves as a reminder of the event to be used for recall on Day 2.

Ratings for each event were also required, including the pleasantness, recall vividness and emotional intensity evoked by the event, as well as its personal significance, recall frequency since the experience, and recall difficulty. These ratings are common in autobiographical memory studies (e.g., Bonnici et al., 2012; Ryan et al., 2001). Some of these ratings may be highly correlated with each other, for example, personal significance and emotional intensity.

However, they were not identical, for example one participant had a highly positive affect when having delicious ice cream on a hot summer 10 years ago but this delicious-ice-cream memory did not have much personal significance. Participants also had to provide three items they liked and three they did not like from each event, as well as rating how familiar they were with each item at the moment when the event originally occurred. People could not be given as liked or disliked items. All the ratings in this study were on a scale from one to four. To give readers a better understanding of the types of event that were described, we present an example event from one of the participants:

'The word "Journal" reminds me that I once stole my sister's diary. This happened when I was 12, so that's 2005 and it was December. My sister was keeping a diary since that summer but she never allowed me to read it. One day, I decided to steal it. It wasn't so hard because I knew exactly where she hid it in our bedroom. I took her diary and sat on the floor next to my bed and began to read it. I liked the cover of the diary, it's my favourite colour. In the first few pages, most of the contents were mundane things, so I got bored very soon. But I found one exciting page just before I wanted to stop reading - she was secretly in love with Orlando Bloom! She kept all the information about him and described how much she loves him. Just a few seconds after I found out this secret, I heard footsteps outside the room in the corridor. It was my sister. I was panicked and found no time for me to put the diary back in its place so I hid it under my duvet. She came into the room and realized what I was doing immediately. She got furious. We definitely had a very serious fight but I don't really remember that part actually. So the three things I liked were the cover of that diary, the carpet on the floor I was sitting on, and my duvet. I didn't like the drawer my sister hid her diary, the pair of shoes my sister was wearing and maybe the dome light in our room. I'm going to name this memory "Stealing my sister's diary".'

Although six items were obtained for each event on Day 1, only four were presented on Day 2 - two liked and two disliked items. Only four items were used in the recall task to (1) shorten the duration that participants had to stay in the scanner and (2) avoid potential categorical differences between the ‘liked’ and ‘disliked’ items used for a given participant (e.g., avoiding all the liked items being snacks and all the disliked items being vegetables). The items used on Day 2 were selected by the experimenter and participants did not know which had been included until they saw them in the scanner. A liked item was chosen if (1) the same item or a very similar item had not been chosen yet, or (2) a similar item also existed among disliked items. The same principles applied when choosing disliked items.

During the recall task in the scanner on Day 2, participants recalled all forty memories and four of the items from each memory that they had provided on Day 1. There were two sessions in the recall task, each containing twenty trials. For each trial, participants were first required to retrieve the complete memory, followed by focussing their attention on specific items related to the memory. During memory retrieval, participants were instructed to reconstruct the scenario as closely as possible to the real situation when the event originally happened. They were encouraged to bring visual, auditory, tactile, olfactory and any other details into the reconstructed scenario. For instance, the beds, carpet, light, drawer and any other furniture in the bedroom, the setting of furniture, the sensation of holding the diary, the feeling of reading the diary, the sister’s handwriting, the sister’s footsteps and all the other details in the memory “Stealing my sister’s diary” should be reconstructed. While recalling and evaluating an item, attention should be focused on that item only. Specifically, participants were instructed to evaluate how much they liked this item and how vividly they recalled it.

Each trial consisted of the following sequence of stimuli: (1) a centrally presented fixation cross for 0.5 sec, (2) a title for memory retrieval, whose duration was randomly chosen between 6 to 10 seconds (jittered, based on a uniform distribution), (3) a blank screen for 0.5 sec, (4) an item's name for evaluation (item1) from the memory, presented for four sec, (5) 'how much did you like item1?' presented until a response was made (participants answered rating questions on a scale of 1 (not at all) to 4 (liked it very much) by pressing a button box with their right hands), (6) 'how vivid is item1 now?' presented until a response was made, (7) a blank screen for 2 to 4 sec (uniform distribution), steps (4)-(7) were repeated for the other three items from the event (i.e. item2, item3 and item4). The order of the presence of liked and disliked items was randomised across trials. A practice trial was carried out outside the scanner before participants went into the scanner.

Note that I asked participants to rate how much they liked the item during the event. However, in case their evaluation was influenced by their general liking for that type of item during daily life, after scanning I also asked them to give a rating of each item type used in the experiment (i.e., rating in general). For instance, if a participant had included book items, regardless of whether it was a statistics textbook, a science fiction novel, or a romance novel; they rated how much they liked books in daily life. In Experiment 2, the subjective values of items in imagery were calculated by subtracting everyday values from imagined values. However, in Experiment3, participants did not rate each single item's everyday value. Instead, they provided the rating of each item type used in the experiment. The reason we did not ask for the everyday value of each item was that some items only appeared once in participants' life and there is no such 'everyday value' for this type of items.

4.4. fMRI Data Acquisition and Preprocessing

Functional imaging was performed on a 3T scanner (Siemens TIM Trio) during the autobiographical memory and item recall task. The functional data were acquired with a gradient-echo EPI sequence (TR, 3.36s; TE, 30ms; flip angle, 90°; resolution, 3×3×3 mm; 64×74; 48 slices per volume). The total number of volumes in each run varied across participants because of the variation of response time for each rating (the mean number of volumes was 329 per session, range = 248-468). A high-resolution T1-weighted 3-D structural image (1 mm3) was acquired after two sessions of functional scans. A double-echo FLASH fieldmap sequence was also recorded.

Functional images were processed and analysed with SPM8 (Wellcome Trust Centre for Neuroimaging, London UK, http://www.fil.ion.ucl.ac.uk/spm/software/spm8/). The first five volumes of each scan were discarded for T1 equilibration. Preprocessing procedures included bias correction, realignment, unwarping, coregistration, slice timing correction, and normalization to the MNI template using the Dartel toolbox. EPI images were smoothed with an isotropic 8mm full-width half-maximum Gaussian kernel.

4.4.1. Main Analysis

The preprocessed functional images were analysed with general lineal models (GLMs). Along with regressors of interest, each GLM included 6 movement regressors for each session, estimated during realignment, as well as two further regressors modelling each session. Based on our strong a priori hypothesis that mPFC activity is modulated by the subjective value of memory content, we performed small-volume correction (SVC) within an anatomical mask of bilateral mPFC (volume ~ 53,493 mm3). This mask was derived from the AAL atlas (Tzourio-Mazoyer et al., 2002), as implemented in the WFU PickAtlas Tool (Maldjian et al., 2003). Within this small volume we report effects that survive $p<.05$ family-wise error correction (FWE).

GLM1 was used for testing the hypothesis that mPFC represents value in autobiographical memory. According to our hypothesis, activity when recalling and evaluating liked items should be higher compared to recalling and evaluating disliked items. This model included five regressors per session: (1) recalling a memory, (2) evaluating a liked item from the memory (regardless of the item's subjective rating; 2 items per memory), (3) evaluating a disliked item from the memory (regardless of the item's subjective rating; 2 items per memory), (4) ITI periods and (5) key-presses. Trial periods were modelled with a boxcar function for the entire length of each period, convolved with the canonical HRF. Parameter estimates for regressors (1) to (3) were averaged across the two sessions and entered into a second-level model. The contrast between recalling a memory and evaluating an item (regardless of whether liked or disliked) was used to make sure participants were engaged in the AM recall task during scanning. We also compared the activity in mPFC when recalling a liked item versus recalling a disliked item.

GLM2 was used to further investigate the nature of the activity in mPFC found in GLM1 for liked versus disliked items, to see whether mPFC activity showed a parametric relationship to the subjective ratings of value given for each item. GLM2 included five regressors per session: (1) recalling a memory, (2) evaluating an item from the memory (regardless of liked/disliked), (3) a parametric modulator of the item regressor based on the participant's value of that item (i.e., how much did they like this item within the event; a rating from 1-4), (4) ITI periods and (5) key-presses. A one-sample t-test was carried out in the 2nd level analysis to test the effect of parametric modulator (regressor 3) averaged across the two sessions. Therefore, whereas GLM1 interrogates BOLD response for liked vs. disliked items (irrespective of their individual subjective rating in the scanner), GLM2 interrogates whether BOLD linearly varies with the individual subjective ratings of each item (irrespective of whether they are liked/disliked).

4.4.2. Further analyses of vmPFC activity

We found significantly increased activity in vmPFC in GLM1 and GLM2 for objects with higher subjective value. However, we also found weak but significant correlations between the ratings of item value, and ratings of item recall vividness and of the item's familiarity at the time of the event (see Results). Thus, these two factors might contribute to our observed item value effect. To investigate further, we also evaluated GLM3 within the vmPFC (an anatomical mask of bilateral vmPFC was derived from the AAL atlas, the volume ~ 15,513 mm^3), which included 7 regressors, five of them were the same from those in GLM2, plus another two parametric modulators (PMs) – based on the recall vividness ratings and familiarity ratings of each item – in the following order: (1) recalling a memory, (2) evaluating an item, (3) vividness PM of regressor 2, (4) familiarity PM of regressor 2, (5) item value PM of regressor 2, (6) ITI, and (7) key-presses. Parameter estimates for regressor5 were averaged across the two sessions and entered into a second-level model (a one-sample t-test). In SPM, the first PM is allowed to explain both unique and shared variance, with subsequent PMs explaining the remaining unexplained variance of the preceding PMs. Thus, any value effects found in GLM3 is variance uniquely explained by the item value PM after removing shared variance from the preceding familiarity and vividness PMs.

Similarly, to assess any effects of item familiarity or item recall vividness independently from the other factor and from item value, we evaluated GLM4 and GLM5 with the PMs from GLM3 re-ordered so that familiarity and vividness came last respectively. Regressors in GLM4 were (1) recalling a memory, (2) evaluating an item, (3) vividness PM of regressor 2, (4) item value PM of regressor 2, (5) familiarity PM of regressor 2, (6) ITI, and (7) key-presses. Regressors in GLM5 were (1) recalling a memory, (2) evaluating an item, (3) familiarity PM of regressor 2, (4) item value PM of regressor 2, (5) vividness PM of regressor 2, (6) ITI, and (7) key-presses. Finally, to examine whether the event-specific item value effects we observed in GLM1 and 2 could reflect the values in everyday life of the types of item retrieved, we built GLM6. All the regressors and PMs in GLM6 were identical as those in GLM3 except that the last PM was the general value rating for that type of item in daily life. GLM6 was meant to detect any general preferences for different types of item that might modulate vmPFC activity. However, we note that this analysis of general preferences differs in nature from the analysis of the values of specific items.

To investigate the relation of the event-specific item value effects seen in vmPFC during the item evaluation phase to activity during retrieval of the corresponding autobiographical memory, we used additional GLMs for each of the ratings given to characterise the AMs in the initial meeting. Each GLM contained five regressors: (1) recalling a memory, (2) one of the memory rating PM of regressor 1, (3) evaluating an item, (4) ITI, and (5) key-presses. The PM regressor was one of the seven memory ratings, i.e. memory pleasantness, personal significance, recall frequency, recall difficulty, emotional intensity, recall detail, and memory age. Parameter estimates for regressor 2 were averaged across the two sessions and the percentage signal change in a 10-mm-radius region of interest (ROI) in vmPFC centred on the peak item rating effect in GLM3 (-6, +33, -12) was extracted by using MarsBaR toolbox(Brett, Anton, Valabregue, & Poline, 2002). A one-sample t-test was carried out for each GLM to test if there was any modulation of vmPFC ROI activity by one of the memory ratings when recalling memories.

4.5. Behavioural Results

4.5.1. Memory

The memory age ranged from one day to 31 years old. Table 3 shows the distribution of different memory ratings across all participants. Correlation coefficients between any two ratings are also present in Table 4. To calculate correlation coefficients between memory ratings at the group level, I first acquired correlation coefficients for each participant. Then I ran a one sample t-test to test if the mean correlation coefficient of the entire group is statistically different from zero. It shows that significant correlations exist between several memory ratings. Correlation coefficients which survive the Bonferroni correction are listed as below: pleasantness* detail, pleasantness* significance, pleasantness* recall frequency, detail* significance, detail* recall frequency, detail* recall difficulty, detail* memory age, emotional intensity* significance, emotional intensity* recall frequency, significance* recall frequency, recall frequency* recall difficulty, and recall difficulty* memory age.

Table 3 The results of memory ratings

	1	2	3	4	Mean
How much did you like this event? (1 not at all-4 very much)	17%	18%	31%	33%	2.81
Level of detail? (1 vague-4 vivid)	11%	31%	36%	22%	2.69
Emotional intensity evoked by the memory? (1 non-emotional-4 highly-emotional)	17%	38%	31%	14%	2.41
Personal significance of this memory? (1 insignificance-4 life-changing)	27%	36%	27%	10%	2.20
How often do you recall this memory? (1 never-4 very often)	34%	45%	18%	4%	1.92
Difficulty of recall? (1 very easy-4 very difficult)	36%	42%	17%	5%	1.91

Table 4 Mean Spearman's rank correlation coefficients (rho) and standard deviation (in parentheses) between memory ratings.

	(1)	(2)	(3)	(4)	(5)	(6)	(7)
(1) pleasantness	-						
(2) detail	0.255*** (0.22)	-					
(3) emotional intensity	0.149** (0.26)	0.312 (0.24)	-				
(4) significance	0.195*** (0.23)	0.268*** (0.23)	0.602*** (0.17)	-			
(5) recall frequency	0.143*** (0.19)	0.406*** (0.23)	0.371*** (0.21)	0.423*** (0.18)	-		
(6) recall difficulty	-0.049 (0.17)	-0.491*** (0.24)	-0.139** (0.22)	-0.159** (0.21)	-0.369*** (0.19)	-	
(7) memory age	-0.059 (0.17)	-0.422*** (0.26)	0.064 (0.18)	0.102* (0.21)	-0.115* (0.22)	-0.407*** (0.21)	-

*significant correlation at $p < .05$

**significant correlation at $p < .01$

***significant correlation at $p < .001$

The Bonferroni corrected threshold is 0.002 (0.05/21).

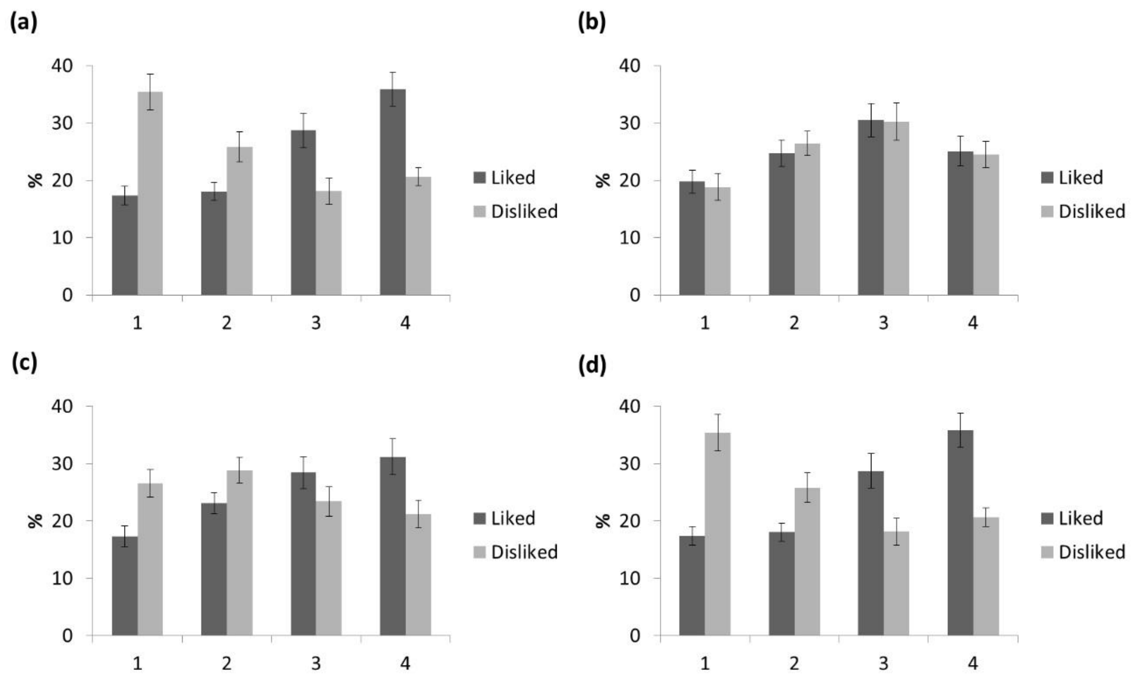


Figure 17. Percentage of liked and disliked items across ratings 1-4 on Day2. (a) Ratings for the specific items within an event that were initially identified as 'liked' or 'disliked' on Day1, showing higher ratings for the 'liked' items. (b) Ratings of participants' preferences for these types of items in daily life, showing no differences between the categories of items from which the 'liked' or 'disliked' examples came. (c) Recall vividness for 'liked' and 'disliked' items within an event. (d) Familiarity rating of items (at the time of the event). Liked items were rated as more vividly recalled and more familiar at the time of the event than disliked items. Error bars represent ±1 SEM.

4.5.2. Items

Only two liked and two disliked items from each memory were used in the scanning period on Day 2. Although some items appeared more than once across each participant's reported memories, the influence of repetition should be negligible because the number of items was small (mean number of repeated items out of 160 used for each participant = 2.99, SD= 4.22). A two-way repeated measures ANOVA on rating of items was conducted to verify the value differences between liked and disliked items, including factors of event-specificity (i.e. value of that specific item within the event versus value of that type of item in general life) and item type (liked versus disliked). There were main effects of both rating specificity ($F(1, 24) = 6.08$, $p = .021$) and item type ($F(1, 24) = 66.82$, $p < .001$) and the interaction between them ($F(1, 24) = 140.88$, $p < .001$). Further analyses showed that 'liked' items had higher event-specific value ratings ($t(24) = 13.17$, $p < .001$) but not higher general value ratings ($t(1, 24) < 1$, $p = .915$). This suggests that the item value ratings in the scanner and the liked/disliked categorization prior to scanning do indeed reflect the event-specific value of the items concerned, not just the general values of these types of items in other circumstances. A paired-samples t-test on recall vividness between liked and disliked items revealed that liked items were more vivid than disliked items, $t(24) = 10.85$, $p < .001$. Figure 17 illustrates the value and recall vividness rating of items on Day 2.

Correlation coefficients (Spearman's rank coefficient) between vividness rating and rating within events are listed in Table 5, as well as those between the familiarity rating and rating within events. In general, items with higher values tended to have both higher familiarity and vividness ratings.

Table 5 Mean Spearman's rank correlation coefficients (rho) between item ratings.

	(1)	(2)	(3)
(1)rating within event	-		
(2)recall vividness	0.238***	-	
(3)familiarity	0.151***	0.221***	-

***significant correlation at p< .001

4.6. fMRI Results

4.6.1. Autobiographical memory recall

We first searched for regions that showed a greater BOLD response when recalling a memory relative to evaluating an individual item (irrespective of liked/disliked) in GLM1, showing large regions of activity (p<0.05, whole brain FWE) throughout the network that has consistently been associated with autobiographical memory recall, including mPFC, medial temporal lobes, retrosplenial and medial parietal areas (Maguire, 2001; Svoboda et al., 2006) (Table 6; Figure 18).

Table 6 Results of the contrast comparing autobiographical memory recall to item recall

Region	Cluster Size	x	y	z	Peak T	Peak p (FWE-corr)
ventromedial Prefrontal Cortex	1660	6	42	-9	10.73	< .001
Inferior Frontal Gyrus	44	-30	33	-9	7.46	< .001
Middle Frontal Gyrus	103	24	30	39	7.15	< .001
Inferior Frontal Gyrus	35	48	30	9	6.81	< .001
Sub-Gyral	169	-21	27	39	8.98	< .001
Superior Temporal Pole	12	42	24	-24	5.22	0.016
Superior Temporal Gyrus	12	51	12	-9	5.83	0.002
Superior Temporal Gyrus	383	42	-54	21	9.02	< .001
Middle Temporal Gyrus	69	-54	-54	-6	6.26	< .001
Posterior Cingulate	4024	-9	-57	24	11.40	< .001
Middle Temporal Gyrus	296	-42	-69	24	9.33	< .001
Cerebellum	18	12	-45	-42	6.49	< .001
Cerebellar Tonsil	16	-9	-48	-45	5.55	0.005

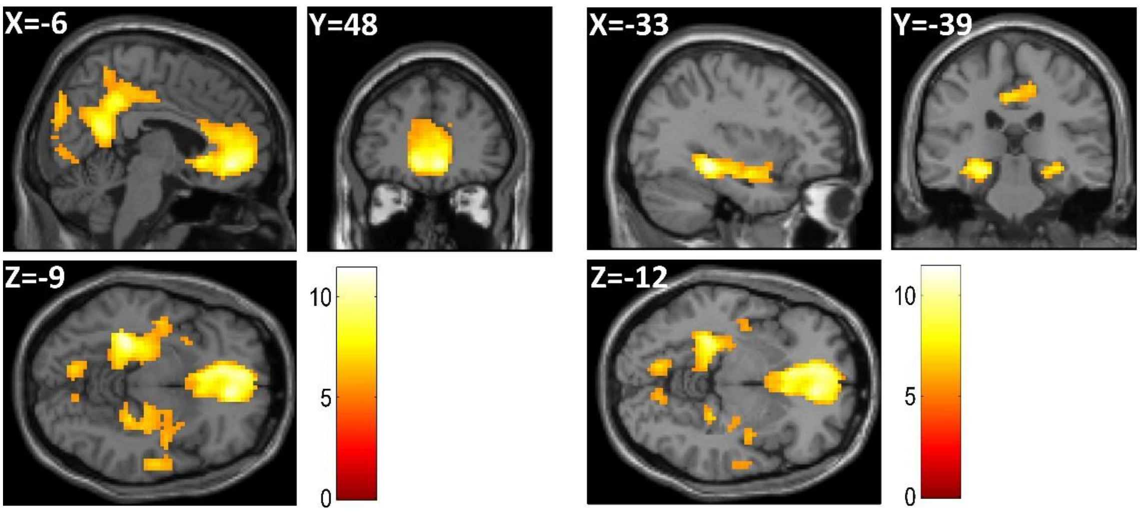
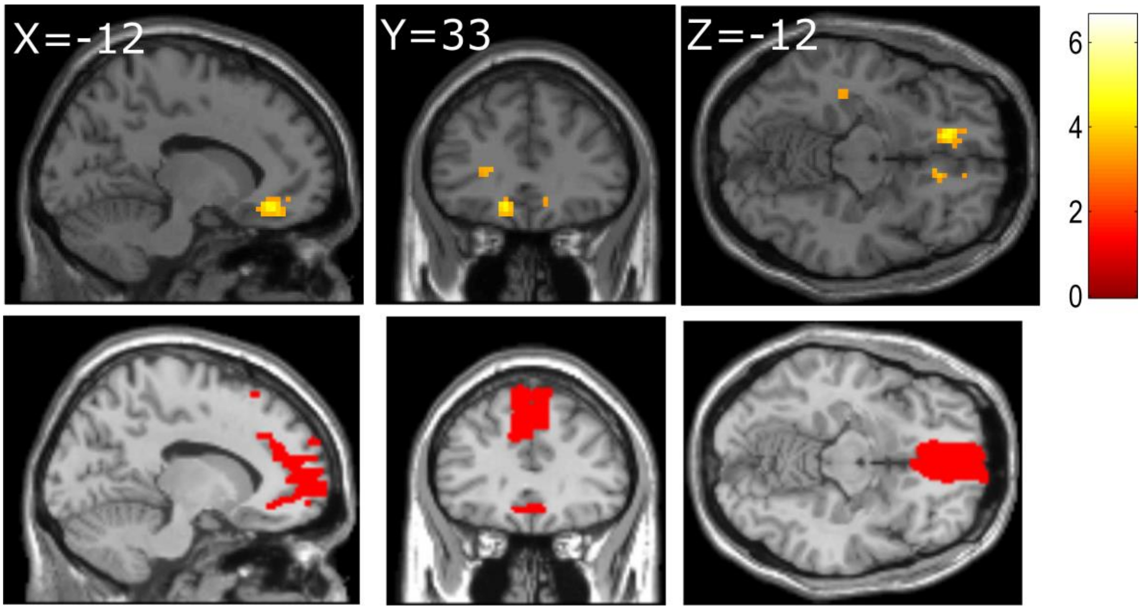


Figure 18. Autobiographical memory recall versus item memory.

Plots shown at p<0.005 FWE corrected, cluster size> 1000 voxels.

(a)



(b)

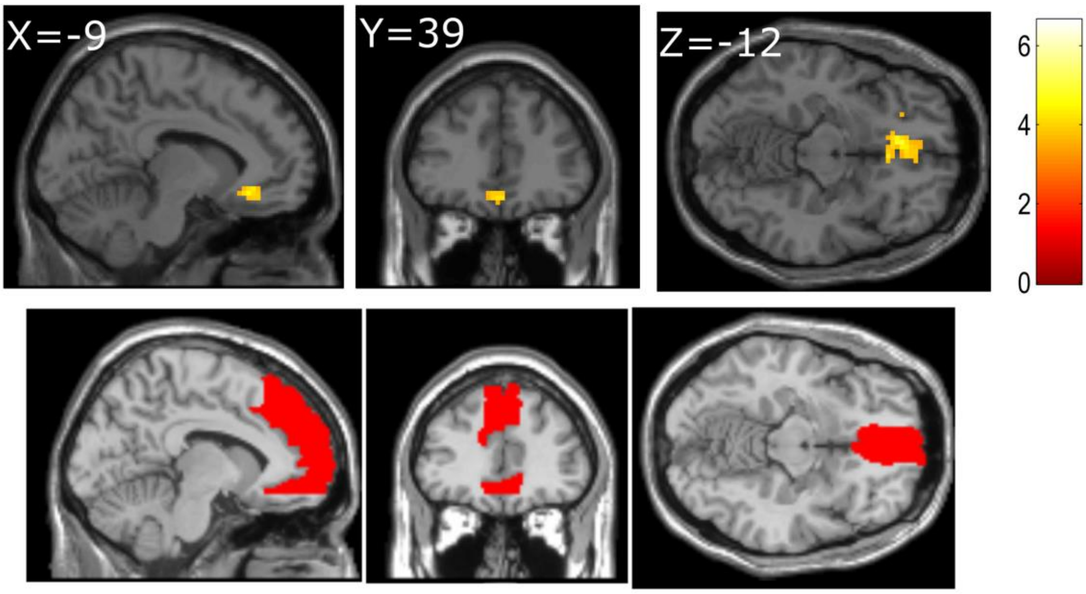


Figure 19. Item value effects.

(a) The Liked- Disliked item contrast. (b) Parametric effect of subjective rating of value within event. Plots shown at p< 0.05 FWE, small volume corrected (SVC) using the anatomical mask of mPFC. The lower panels of (a) and (b) depict the mask..

4.6.2. Subjective value of items in mPFC

To test our specific hypothesis, we first compared the evaluation of liked items to the evaluation of disliked items in GLM1 (liked > disliked). This contrast showed significantly greater activity in vmPFC (-12, +33, -12, Z = 4.23; p = .003 FWE SVC;

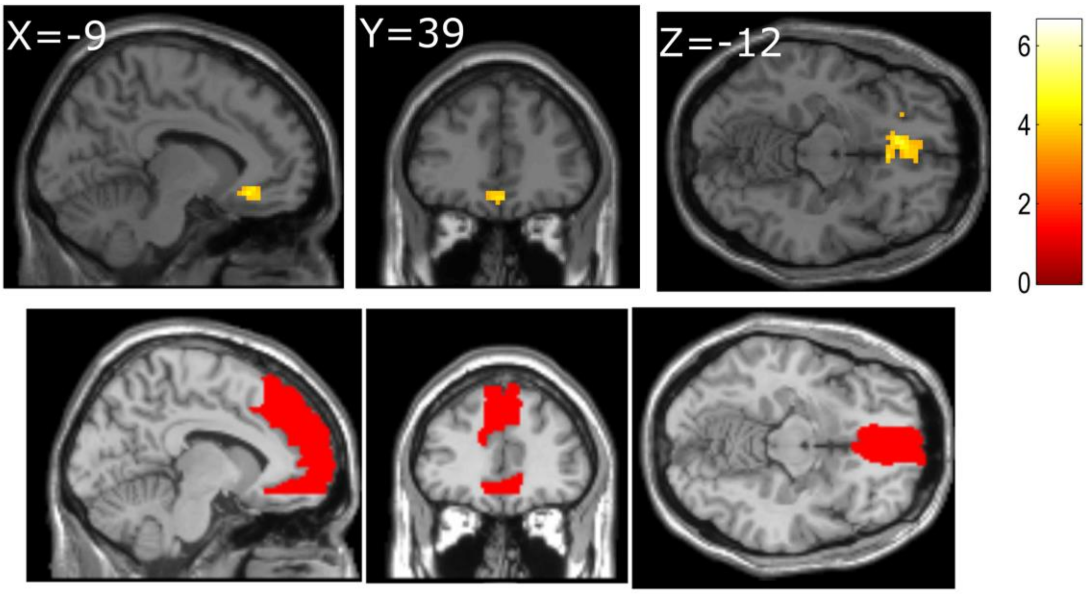


Figure 19). Furthermore, the parametric modulator of likability rating within event in GLM2 also revealed an effect in a similar area of vmPFC (-6, +33, -12,

Z = 4.02; p=.008 FWE SVC,

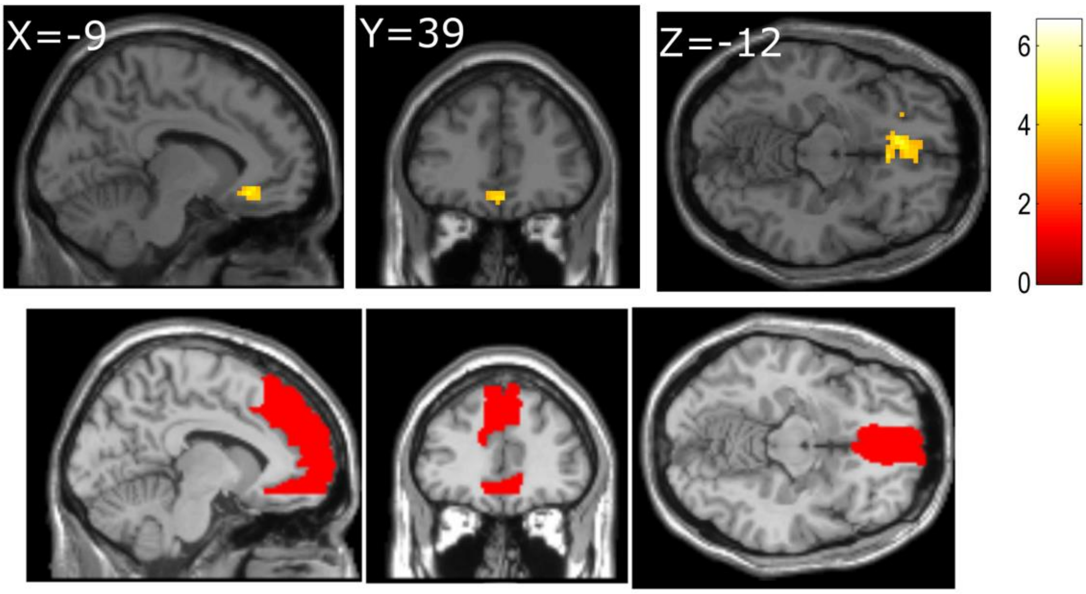


Figure 19). In summary, we provide evidence that vmPFC shows greater activity for liked items and its activity positively correlates with the values of individual items from recalled autobiographical memories.

4.6.3. Relation of vmPFC value effects to familiarity and vividness

We found significantly increased activity in vmPFC in GLM1 and GLM2 for items with higher subjective value, consistent with our hypothesis. However, we also found weak but significant correlations between the ratings of item value, item recall vividness and the familiarity of the item at the time of the event (the latter from the initial interview), see Table 5. Thus, it is possible that these two factors might contribute to our observed item value effect in vmPFC. Accordingly, we examined vmPFC activity in more detail by including parametric modulators for item value, vividness and familiarity, rotating the order of parametric modulators across analyses (see Methods), and testing for significance within the mPFC mask. There was no significant effect of mPFC mask. For an exploratory purpose, we ran a follow-up analysis again but used a mask focused on vmPFC using an SVC for this region. The value effect seen in vmPFC remained significant when familiarity and vividness were both included as parametric modulators in GLM3 (-6, +33, -12, $Z = 3.58$; $p=.034$ FWE SVC). These results support our hypothesis that vmPFC activity was modulated by the values of items in AMs, and that this effect cannot be fully explained by the familiarity of the item at the time of the event, or by the vividness of its recollection. However, there is a caveat: there might be the issue of 'double dipping' regarding using the vmPFC mask in this analysis.

According to Benoit et al. (2014), the same region within vmPFC represents both value and familiarity of an item. Therefore, an anatomical mask focused on vmPFC was used in GLM4 to test if there was familiarity effect within vmPFC in this experiment. The parametric modulator of item familiarity within event (GLM4) also revealed a significant unique effect in the vmPFC (-12, 42, -9, $Z = 3.55$; $p=.043$ FWE SVC; Figure 20), which was not caused by the value or vividness of the items. This is in line with the account that vmPFC integrates affective value and familiarity of AM contents (Benoit et al., 2014). However, there was no unique effect of recall vividness within vmPFC ($p> .05$, $Z = 2.83$ FWE SVC) in GLM5, which suggests that the vividness of an item's recall does not explain vmPFC activity beyond that explained by item familiarity or item value.

The involvement of vmPFC in value representation is well-known in decision-making tasks. However, there was no significant effect of the general every-day value of the types of items retrieved within vmPFC (GLM6). This suggests that the item value effect we observed in the present study reflected the memory-specific value of the item, rather than general preferences for different types of item. In sum, GLMs 3-6 suggest that, in our AM-focussed task, vmPFC independently tracks both the value and familiarity of the items within an event that is remembered in an autobiographical memory, rather than the non-specific values of these types of items in general.

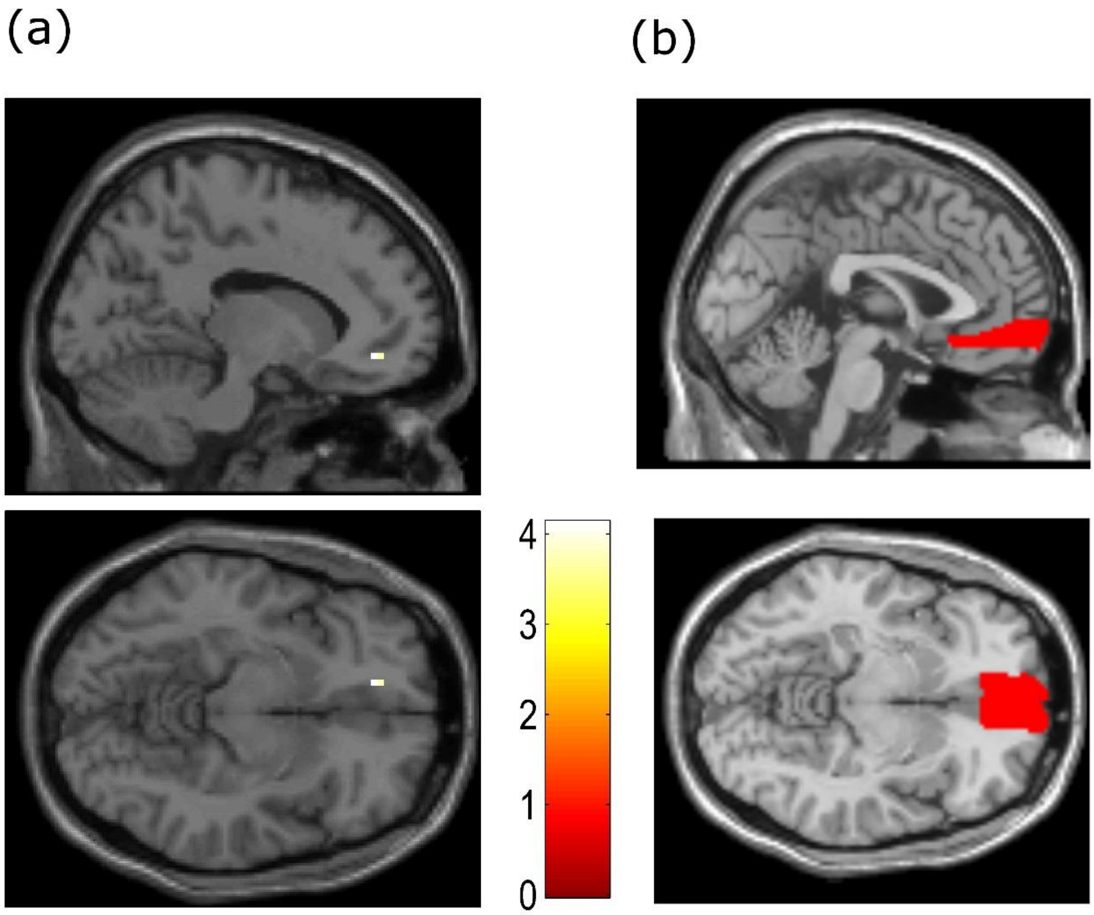


Figure 20. Effects of item familiarity.

Effects of the familiarity of the item at the time of the event (a), Plots shown at $p<0.05$ FWE, SVC on the vmPFC mask in (b).

4.6.4. Relation of vmPFC item value effects to the personal emotional significance of the memory

How might the subjective value of the items within an AM relate to processing during recall of the AM itself? The behavioural results show that there were significant correlations between the summed values of the items present in an AM and several of the ratings used to characterise that AM overall, including memory pleasantness, personal significance, recall frequency, recall difficulty, emotional intensity, recall detail, and memory age. We tested how activity in the vmPFC region showing the item value effect varied with these memory ratings during retrieval of the AM itself, using a separate GLM for each memory rating (see Methods). During recall of an AM, the mean activity in the vmPFC ROI varied with both the personal significance of the memory ($p= 0.038$) and the emotional intensity evoked by the AM ($p= 0.0435$). None of the other memory ratings showed significant modulation of vmPFC activity during recall of an AM.

It is likely that the subjective value of the items contribute to the personal emotional significance of the memories they occupy. This would explain the common response in this region to item value and to emotional intensity and personal significance. Example items include a birthday cake made by mom, a ticket to a favourite singer's concert, a seashell collected from the beach during a family trip, rocks from grandfather's collection, and a postcard from childhood friends.

4.7. Discussion

Participants in an fMRI scanner recalled personal autobiographical memories (AMs), and evaluated their liking for specific items within each remembered event. Half of the items used were identified as ‘liked’ and the other half as ‘disliked’ within the context of each AM. Compared to ‘disliked’ items, the ‘liked’ items (in a specific event) were reported as being more familiar at the time of the event, and were recalled more vividly during memory recall. Consistent with the hypothesis that mPFC represents the value of items within AMs, vmPFC activity while recalling and evaluating items was modulated by how much participants liked those items at the time when the events happened.

During recall of the entire AM, activity in the vmPFC location showing the item value effect was modulated by the personal significance and the emotional intensity of the memory. This finding is in line with the ideas that vmPFC plays a role in the generation of affective meaning (Roy et al., 2012), in the association of events with emotional responses (Euston et al., 2012), and in the modulation of emotional response via self-relevance (Sperduti et al., 2016). It is well recognised that the vmPFC is involved in self-relevant processing during autobiographical memory recall (e.g., Moore III et al., 2014; Summerfield et al., 2009). Consistent with the hypothesis by D'Argembeau that vmPFC assigns personal value to self-related information (D'Argembeau, 2013), our results suggest that one of its roles is to provide the subjective values of the items present in AMs, and that these values contribute to the overall personal emotional significance of the AM itself.

In Experiment 2, the activity of a region in mPFC (peak voxel coordinates: +9, +57, +12) was modulated by the subjective value of common everyday items that participants were imagining in novel scenarios. This region was more dorsal and anterior than the item value-related region in the present study (-6, +33, -12). A functional gradient along dorsal-ventral axis has been observed in mPFC, between making self- or other-related judgements, such that self-relevant information is believed to be processed in more ventral mPFC, whereas other-relevant information is processed in more dorsal mPFC (Denny et al., 2012; Nicolle et al., 2012; Sul et al., 2015). Similarly, vmPFC activity during memory for recent presentation of face stimuli is greater for personally relevant faces (Trinkler, King, Doeller, Rugg, & Burgess, 2009). Thus the more ventral location of the item value effect here, compared to Experiment 2, may reflect the greater personal emotional relevance of the items from participants' autobiographical memories compared to the photos of common everyday objects used in the Experiment 2.

Speer et al. (2014) discovered that mPFC activity was greater during the recall of AMs that made them feel happy compared to the recall of neutral memories, using a similar paradigm to our own. In their study, ventral striatum activity was also parametrically modulated by affective ratings of the memories. Both ventral striatum and mPFC also responded to monetary reward in their study, and participants were even willing to lose monetary reward to obtain chances to recall positive memories. Speer et al. (2014) suggested that positive memory recall is valuable, so that the reward system was recruited in positive memory recall. Compared to Speer et al. (2014), our study indicates that vmPFC can represent the values of different memory components separately, i.e., the items within memories. We also noticed that, during recall of an AM, vmPFC activity was modulated by the personal significance and emotional intensity of the AM, implying that the variation in vmPFC activity with the subjective value of items relates to the part those items play in the emotional self-relevance of the event. If the value-related vmPFC effect in our study reflects items' personal emotional relevance, this might explain the reduced involvement of ventral striatum (+12, +3, -3, $p = 0.25$) here compared to Speer et al. (2014), assuming that ventral striatal activity reflects the subjective consequences of recalling a positive memory (i.e. the feeling of happiness) which has direct value for the current state (equivalent to receiving money), consistent with its association with reward magnitude more generally (D'Argembeau, Xue, Lu, Van der Linden, & Bechara, 2008; Diekhof, Kaps, Falkai, & Gruber, 2012; B Knutson, Adams, Fong, & Hommer, 2001; Stott & Redish, 2014; Strait, Sleezer, & Hayden, 2015).

In addition to subjective value, greater levels of activity in vmPFC have also been reported when participants recalled a familiar memory or imagined personal future events within a familiar contextual setting, compared to imagining personal future events within an unfamiliar contextual setting (Benoit et al., 2014; Szpunar et al., 2009). Consistent with the results from these studies, vmPFC activity was also modulated by how familiar the items were at the time of the AM in our study, being greater when recalling and evaluating more familiar items. However, the unique effects of item value and item familiarity occur independently in vmPFC, and there were no significant correlation between a memory's personal significance or emotional intensity and the summed familiarity of the items within it. Further studies are necessary to clarify the nature and importance of item familiarity in modulating vmPFC activity.

In summary, we showed that vmPFC activity is modulated by the values of items within autobiographical memories. Taken together with Experiment 2, these results are consistent with the hypothesis that mPFC represents the values of elements within autobiographical memory and mental imagery, with the more ventral mPFC location found in the present study reflecting the greater emotional self-relevance of objects in autobiographical memories than those in arbitrary imagined scenarios. In addition, our findings support the association of vmPFC activity with processing of self-relevance and, in our study, with the contribution of liked objects to the personal emotional relevance of autobiographical memories.

Chapter 5. General Discussion

5.1. Overview

In this final chapter, I will discuss the similarities and dissimilarities between the two fMRI experiments. Afterwards, I will discuss a few issues which are highly relevant to value representation and/or function of the mPFC.

The motivation of this study was to investigate whether the common function of mPFC in episodic simulation and autobiographical memory retrieval is subjective value representation. More specifically, the aim of my thesis was mainly to answer two research questions:

1. Does the mPFC represent subjective values of imagined components during mental imagery?
2. Does the mPFC represent subjective values of elements during retrieval of autobiographical memory?

Experiment 1 was carried out to verify that the imagined-value paradigm is able to manipulate subjective values through mental imagination. Two fMRI studies, Experiment 2 and 3, were carried to answer each research question. Experiment 2 revealed that there was a positive correlation between the subjective values of imagined objects and the BOLD signals of mPFC, which implies that mPFC was involved in episodic imagination of subjective value representations. The possibility that the mPFC effect was modulated by participants' general preferences had been ruled out since the subjective rating was obtained by subtracting everyday value from imagined value. In other words, the effect was modulated by imagery-specific values rather than everyday values. Results of Experiment 3 show that there were also parametrical relationships between values of items in autobiographical memory and vmPFC activity. In the meantime, the vmPFC activity was also modulated by the personal significances and emotional intensities of recalled memory. However, the vmPFC activity was not modulated by the every-day values of items which suggests that the vmPFC effect in Experiment 3 was memory-specific. Taken together, findings in both Experiment 2 and 3 were not merely memory-independent or imagery-independent value representations. In short, these results support the hypothesis that mPFC represents subjective values of elements in autobiographical memory and episodic simulation.

5.2. Differences between Experiment 2 and Experiment 3

Experiment 2 shows that the mPFC activity was modulated by the subjective value of elements in the imagined scenarios and Experiment 3 shows that the vmPFC activity was modulated by the memory-dependent value, personal significance and emotional intensity of the contents of autobiographical memories. However, please bear in mind that the effect of the subjective value of items in mPFC was not based on the corrected subjective value, but based on the value within the events. Although there was no significant effect within mPFC for everyday value, it does not necessary guarantee that the mPFC effect we found from GLM2 could not be influenced by everyday value at all (Henson, 2005).

Both of them support the hypothesis that mPFC plays the role of value representation in autobiographical memory and mental simulation. Nevertheless, there are still differences between the results from these two experiments.

The main difference is that the effect in Experiment 3 was in a more ventral and posterior region within mPFC, compared to the one in Experiment 2. This could be explained by one or some of the following explanations. Functional segregation along dorsal-ventral axis has been observed in mPFC. When making self- or others-related judgements, mPFC is one of the brain areas involved. Within the mPFC, self-relevant information is believed to be processed in the more ventral part while others-relevant information is believed to be processed in the more dorsal part (for a review, see Denny et al., 2012), with gradual self-other representational changes along the ventral-dorsal axis (Nicolle et al., 2012; Sul et al., 2015; Van Overwalle, 2009). Similarly, vmPFC activity during memory for a recent presentation of face stimuli is greater for personally relevant faces (Trinkler, King, Doeller, Rugg, & Burgess, 2009). This could explain why the item value effect in Experiment 3 was more ventral than that in Experiment 2. The items in Experiment 3 were taken from participants' autobiographical memories and were, therefore, self-relevant to some degree, whereas the items in Experiment 2 were photos of arbitrary common objects.

In parallel to this argument, functional segregation along the mPFC anterior-posterior axis is a potential explanation for why the value representation in autobiographical memory recall was more posterior than that in mental imagery. Researchers suggest that representations of complex, secondary, abstract or intangible stimuli are located in the anterior mPFC while representations of simple, primary, or tangible stimuli locate in the posterior mPFC (for reviews, see Amodio & Frith, 2006; Kringelbach & Rolls, 2004). This hypothesis is not only supported by the anatomical fact that the anterior mPFC is more recently developed than the posterior mPFC (Öngür and Price, 2000), but also supported by experimental results (Sescousse, Caldú, Segura, & Dreher, 2013; Sescousse, Redouté, & Dreher, 2010; Suzuki et al., 2012; Wang et al., 2014). For example, Sescousse and colleagues found a dissociation in the mPFC depending on reward types (Sescousse et al., 2010). A posterior mPFC region responded to primary reward (i.e. erotic pictures) and an anterior mPFC region responded to secondary reward (i.e. monetary reward). Wang et al. (2014) showed that the values of immediate rewards were represented in a more posterior region of mPFC while the values of delayed rewards were represented in a more anterior region of mPFC. In another study, Koritzky et al (2013) also demonstrated that information with higher immediate effect engaged more posterior mPFC. Compared to mental imagery, the contents of autobiographical memory are less abstract and have lower uncertainty, therefore, this difference might explain why the value representations in Experiment 3 were more posterior than that in Experiment 2.

In this section, I tried to explain why the proposed common role of subjective value representation did not recruit the same region within mPFC in the two different tasks of autobiographical memory recall and episodic imagery. The first argument argues that these two tasks involve different degrees of self-related components. This would support the existence of an anatomical gradient concerning the extent to which self-relevance contributes to the valuation of an item. The second one argues that the anatomical location of value representation for different types of items varies. These two arguments are not mutually exclusive. It is possible that both of them contribute to the differences in the location of activity between two experiments. One can imagine that self-relevance could modulate value in several ways, e.g., multiply the basic value by the importance of the item to oneself, or contribut to the valuation itself due to the intrinsic emotional importance of the item conferred by memories of previous experiences with it.

Further experiments are necessary to refine this interpretation. For example, it would be nice to recruit participants to imagine items from their memory appearing in a novel and fictitious situation. Researchers would then have the chance to compare the value representations of the same item in different situations.

5.3. General Perspectives

In this section, I will discuss some topics which I believe are highly relevant to the aim of my thesis. Since this thesis focuses on value representation and the function of mPFC, I will start from discussing the valuation system. I will then explore two relevant topics, social valuation and self-concept representation, both of which have been associated with processing in vmPFC. I will also briefly describe the impairments in memory resulting from vmPFC lesions and link these to the hypothesis of my thesis. Finally, I would close by discussing some clinical applications of imagery training on mental diseases and some potential therapeutic strategies inspired by the results of my experiments on mental diseases and memory deficits.

5.3.1. Automatic valuation system

An automatic ‘Brain Valuation System’ has been proposed to include posterior cingulate cortex (PCC), hippocampus, ventral striatum and vmPFC. This system is modulated by preferences even when participants were engaging in a preference-irrelevant task, which implies that this valuation system is an automatic system (Lebreton et al., 2009; Kim 2007). The activation in the mPFC when participants were passive viewing different goods (e.g., books, CDs, lotteries) was able to predict their preferences between two different goods in an independent task (Levy & Glimcher, 2011). In other words, the valuation system is still working under circumstances when no decision has to be made.

In Experiment 3, the value and familiarity of items were rated based on the value and familiarity at the time when those events happened. These ratings must be different from the current value and familiarity ratings of items. But the vmPFC was modulated by the ratings then, rather than by the ratings now. One potential explanation is that during item retrieval and evaluation, the valuation system automatically activated and began evaluating items in participants’ recall. But this cannot explain why the other parts of the valuation system (i.e., PCC, hippocampus, and ventral striatum) did not show the same pattern as vmPFC did. An alternative explanation is that the values of items were encoded when the event happened and the values were retrieved during memory recall. Studies have shown that brain regions activated during encoding a memory also reactivated during retrieving the same memory (see Danker & Anderson, 2010 for a review). Regions included primary sensory cortices (Stock, Röder, Burke, Bien, & Rösler, 2008; Wheeler & Buckner, 2003; Wing, Ritchey, & Cabeza, 2014), emotional processing areas (Smith, Henson, Dolan, & Rugg, 2004), and encoding strategic processing regions (Nyberg et al., 2001). The vmPFC effect in Experiment 3 implies that the values of items are part of the memory reinstatement process.

5.3.2. vmPFC and social valuation

As mentioned in Chapter 1, the mPFC has been seen as the centre for common value representation because values of items from different categories have been found to be represented in mPFC. The attributes of these items were highly divergent, from commercial reward such as food, trinket and money to those uncommercial or abstract ones such as charitable donations (Hare et al., 2010), people (Cunningham, Johnsen, & Waggoner, 2011), to win or lose in bids (van den Bos, Talwar, & McClure, 2013), attractive faces (Smith, Clithero, Boltuck, & Huettel, 2014), social appraisal (Lin, Adolphs, & Rangel, 2011), in-group membership (Morrison, Decety, & Molenberghs, 2012), closeness of relationship and trustworthiness of partner (Fareri, Chang, & Delgado, 2015), etc. (for a review, see Ruff & Fehr, 2014). The values of these rewards are built upon social norms or experiences of social interaction and social learning. For example, in a 150-trial charitable donation fMRI experiment (Hare et al., 2010), participants were allowed to decide how much money ($*x*) they would like to donate to a charity organisation (*x* ranged from 0 to 100) in each single trial and they were also told that they would receive $(100- *x*) afterwards. Only one of the 150 trials (randomly decided) became the implemented trial. The subjective value of charitable donation was defined by combing both the deservingness rating of a charity and the amount of money participant would like to donate to that charity. The fMRI results showed that BOLD signal in vmPFC was the only region which showed a positive correlation with the subjective value of charitable donations during decision-making phase (i.e., when deciding how much you would like to donate?). In another recent study, participants were shown faces of others along with positive or negative comments (e.g., 'you are kind', 'you are unreliable') while they were in the fMRI scanner. The BOLD signal in vmPFC was higher when receiving positive comments than receiving negative ones (Kawasaki et al., 2016). In general, this evidence supports the idea that vmPFC is critical to abstract and social value representation.

If vmPFC is involved in social valuation and social decision-making, it is reasonable to assume that brain regions which are commonly been found in social cognition also collaborate with vmPFC, for instances, the temporal-parietal junction (TPJ) and inferior frontal gyrus (IFG). Some sub-regions of TPJ has been found to be involved in theory of mind as the function of reasoning other people's minds (e.g., Mars et al., 2012; Saxe & Kanwisher, 2003) (for reviews, see Saxe, 2006; Van Overwalle, 2009). In the meanwhile, the IFG has been found to be critical in emotional empathy or affective empathy (Hooker, Verosky, Germine, Knight, & D'Esposito, 2010; Shamay-Tsoory, Aharon-Peretz, & Perry, 2009). Indeed, studies have shown that the functional connectivity between vmPFC and TPJ or between vmPFC and IFG were greater while participants were engaged in social decision-makings compared to while they were engaged in non-social tasks (Hare et al., 2010; Smith et al., 2014).

How about social tasks without decision-making or value evaluation? Do these tasks involve vmPFC? If the valuation system is automatic, then the vmPFC should be involved in most social tasks even those one without intentional valuation. There are plenty supporting evidence from neuroimaging and neuropsychological studies showing that the vmPFC is involved in different social tasks (for a review, see Bzdok et al., 2013). Figure 5 illustrates some of these functions, including emotional empathy, theory of mind, personal traits inference and so on (for reviews, see Saxe, 2006; Van Overwalle, 2009; Van Overwalle & Baetens, 2009), although some studies found a dmPFC region for theory of mind (e.g., Zerubavel, Bearman, Weber, & Ochsner, 2015). Taken together, the involvement of vmPFC in social valuation and social cognition tasks imply that the function of vmPFC is related to subjective value processing or representation. This is in line with the main hypothesis of the present thesis- the mPFC represents the subjective value of components in our autobiographical memory and episodic imagination.

5.3.3. Self-conception in mPFC?

Is there a brain region or 'centre' responsible for the generation or processing of the concept of the self? One of the first groups of studies which attempted to answer this question used trait adjectives judgment task. In their highly cited paper, Kelley et al (2002) scanned participants while they were making trait judgements. In each trial, participants saw a trait adjective word and had to answer one of these questions, depending on the trial types: (1) Does the adjective ascribe you? (2) Does the adjective ascribe George W. Bush (i.e. an other) or (3) Is the adjective printed in uppercase? Compared to other-related judgements, mPFC had greater activity during self-judgement, which implies that mPFC is relevant to the processing of the self-concept. Further studies support this implication by showing greater mPFC activity during self-judgement than other-judgement, including familiar famous people, unfamiliar friends, close friends or family members (D’Argembeau et al., 2012; Denny et al., 2012; Heatherton et al., 2006; S. C. Johnson et al., 2002; Joseph M. Moran, Heatherton, & Kelley, 2009; van der Meer et al., 2010; Zhu, Zhang, Fan, & Han, 2007). However, there is another potential hypothesis which can also explain these results.

As mentioned in Chapter 1, a large literature agrees that mPFC represents the values of elements in tasks with or without decision-makings and evaluations. In general, the self-concept is highly valued by most people across different cultures. Compared to the value attributed to others, the value attributed to the self is usually higher. Could this be the reason why the differences in self vs. others trait judgements appear to increase activity in mPFC (D’Argembeau, 2011, 2013)? This account could be supported by results that participants valued their present selves higher than their selves in the past or future, and the mPFC activity pattern changed accordingly (D’Argembeau, Stawarczyk, Majerus, Collette, Van der Linden, & Salmon, 2010). Furthermore, other studies also demonstrated that the activity differences in mPFC between self and close-others (i.e., participant’s own mother) vary across participants from different cultures (Wuyun et al., 2014; Zhu et al., 2007). One alternative explanation for this is that the mPFC does not represent the self-concept but just reflects the fact that we care about ourselves most (Gillihan & Farah, 2005), and then our close families and friends, and so on.

The present thesis may provide some further insight towards resolving this disagreement. Experiment 3 shows that vmPFC activity was modulated by how much participants liked each item, and how familiar each item was to them, while they were recalling and evaluating items. While recalling memories, the same region was also modulated by how personally significant each memory was and by how strong the emotional intensity evoked by each memory was, but not by how much participants liked each memory. If the involvement of mPFC in self-concept representation in the literature was only because of the high value of self-relevant components, then the vmPFC activity should also be correlated with the memory pleasantness in Experiment 3. This implies that the representation of self in mPFC may not merely reflect the high value of self-relevant items but also because of involvement in processing of the self.

Furthermore, the mPFC region represents item value within memory was more ventral than the region represents item value in imagery (i.e., Experiment 3 versus Experiment 2). This result is in line with the argument that the ventral region involves more self-relevant processing or is more self-relevant than the dorsal region.

5.3.4. Confabulation in vmPFC patient

Based on the hypothesis that mPFC represent the subjective values of components in memory and imagination, what symptom would manifest if there is a partial or complete loss of this function? One possibility is that the subjective values of all items in a memory become the same and values of items across different memories also become equivalent. In this circumstance, people may become less able to differentiate one memory from another memory and they may misrecognise elements from one event to another event. An alternative possibility is that people may misattribute values to elements of memories during autobiographical memory recall. In this situation, people may fail to retrieve critical elements of an event because the values of the elements they retrieved are low. Meanwhile, people may misrecognise one item from a different memory because they erroneously believe this item to have significantly high value. Whether which situation is true, it is reasonable to speculate that mPFC lesioned patients may have difficulty in retrieving details of autobiographical memories accurately.

One of the most common memory deficit after vmPFC lesion (Figure 21) is confabulation (Turner, Cipolotti, & Shallice, 2010), especially spontaneous confabulation. Patients with confabulation provide false information unintentionally when they are requested to recall memories (Gilboa, 2006; Moscovitch & Melo, 1997; Turner et al., 2010). Although there is no consensus on whether the confabulation would have the same or different amount of influence on semantic and episodic memory, one study shows that it has equal influence on both types of memory (Moscovitch & Melo, 1997).

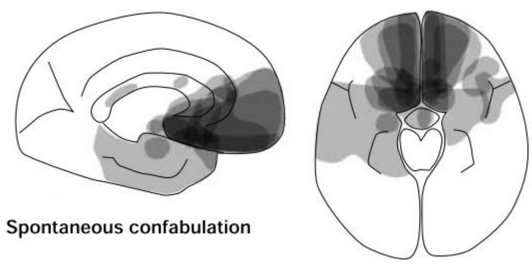


Figure 21. Lesion of confabulating patietns

Diagrams taken from Schnider (2003) shows lesion (shaded areas) overlap from different patients.

The underlying mechanism of confabulation is not yet clear but there are several hypotheses that try to explain it (for a review, see P. W. Burgess, 1996). One of these hypotheses is the temporality disturbance account (e.g., Barba, Cappelletti, Signorini, & Denes, 1997; Schacter, 1987; Williams & Rupp, 1938). This account suggests that confabulation is caused by disturbance of the temporal order of events. In other words, the contents of retrieved events by patients might be real but are retrieved with incorrect timestamps. However, there is growing evidence to imply that temporal order disturbance is not the only reason for confabulation (e.g., Gilboa, 2006; Moscovitch & Melo, 1997; Thaiss & Petrides, 2008). Another theory proposes the idea that confabulation is due to failure of suppressing currently irrelevant events (Schnider & Ptak, 1999; Schnider, Treyer, & Buck, 2000) (for a review, see Schnider, 2003). In a classical paradigm (e.g., Gilboa, Alain, He, Stuss, & Moscovitch, 2009; Schnider, 2000; Schnider & Ptak, 1999), pictures are presented to participants one by one and participants have to make a response when they detect a reappearance of the picture. The experiment consists of several runs and the same pictures are used across different runs, so that each picture appears more than once within the whole task. To perform this task well, participants have to be able to identify when the reappearance is within a single run or from previous runs. Specifically, target picture in the previous run are no longer relevant to the current run. Studies have shown that patients with confabulation have poor performance on this task- they mistook pictures appeared in earlier runs as if they appeared within the current run (Nahum, Ptak, Leemann, Lalive, & Schnider, 2010; Schnider & Ptak, 1999; see also Thaiss & Petrides, 2008; Turner et al., 2010). Studies have also shown that the engagement of vmPFC in healthy controls was necessary for this task (Schnider et al., 2000). A relevant but more general hypothesis suggests that impaired source monitoring or reality monitoring is the main cause of confabulation rather than simply unable to suppress irrelevant information (M. K. Johnson, 1991; Turner et al., 2010). In a source monitoring task, participants had to judge whether an item was imagined by themselves or was read out loud by examiner earlier. Compared to healthy controls and non-confabulating amnesic patients, confabulating patients tended to misrecognize imagined words as heard words (Turner et al., 2010).

Another different theory suggests that confabulating patients have impairment in strategic memory retrieval process (Gilboa, 2006; Moscovitch & Melo, 1997; Nahum et al., 2010; Turner et al., 2010). According to Moscovitch and Melo (Moscovitch, 1992; Moscovitch & Melo, 1997), strategic memory retrieval process includes to initiate a search through memory, to constrain searching area, and to evaluate and verify the accuracy of retrieved contents, contexts, and timestamps. This process proposed by Moscovitch includes multiple components and further researches are necessary to clarify whether vmPFC confabulating patients have deficits in all or some parts of these components. Given the significant overlap in neural basis between autobiographical memory recall and episodic future imagining, it may not be so surprising that some patients do not only confabulate past events but also confabulate future events (Barba et al., 1997; Bertossi, Tesini, et al., 2016). For example, a patient GA answered 'I will go out shopping alone by car' when examiner asked what she planned to do in the next day but what she described in her answer was impossible to accomplish. However, this phenomenon could be explained by both the reality monitoring account and the strategic retrieval account. Moreover, not every vmPFC amnesic patients suffered from confabulation (Bertossi, Aleo, et al., 2016; Ghosh, Moscovitch, Melo Colella, & Gilboa, 2014). It is not clear whether lesion within a specific vmPFC sub-region is sufficient to cause confabulation or lesion in both vmPFC and some other brain region is requisite for confabulation. In short, there are still discrepancies among different studies and further evidence is necessary to provide us with a better understanding of confabulation.

A lot of studies focuses on the role of mPFC in decision making and valuation (see Chapter 1). Therefore, it would be reasonable to speculate that mPFC lesioned patients may have issues on value processing or reward processing. Unfortunately, there is only one relevant study. In the study of Bertossi et al. (2016), vmPFC patients made choices between small, immediate rewards and large, delayed rewards. The results showed that there was a correlation between their temporal discounting rates and their ability to imagine future events- patients who were unable to imagine future event vividly also tended to choose immediate but small reward over delayed, large rewards.

5.3.5. Application of imagery and autobiographical memory recall

Both mental imagery and autobiographical memory retrieval contribute to potential therapeutic methods for certain mental diseases.

Experiment 2 revealed that participants changed their preferences and motivations after just being immersed in imagination for a few seconds. This is in line with a series of studies which improved participants' motivation to achieve their goals through imagery training. In a study carried out by Andrade and colleagues (Andrade, Khalil, Dickson, May, & Kavanagh, 2016), participants who wished to lose body weight and reduce high-calorie snacking were introduced to functional imagery training. During the training, participants were asked to imagine the positive outcome of reducing snacking for a year and how joyful it would feel. They also imagined themselves using techniques and methods which they believed were useful in their previous experiences. The imagery training lasted for two weeks and, compared to the control group, the training group consumed fewer snacks and had motivational thoughts more frequently (Andrade et al., 2016). Other studies also demonstrated a similar effect of imagery training on reducing food craving (Andrade, May, & Kavanagh, 2012; Kavanagh, Andrade, May, & Connor, 2014). In another study, the intensity of food craving decreased after participants imagining engaging in their favourite activities (Knäuper, Pillay, Lacaille, McCollam, & Kelso, 2011). Therefore imagery based training could be used for reduction of food craving and snacking, which could be used as a strategy to improve healthy eating behaviour. Moreover, this may be an alternative or supplemental treatment for substance abuse, for instances, tobacco, alcohol, and drugs. However, participants in these studies were healthy normal controls. It remains unknown if imagery based training could be applied to individuals who have eating disorders or substance abuse issues.

Imagery training could also be applied to individuals who are suffering from depression or anxiety disorders. Studies have demonstrated that imagery-based interpretive bias modification (CBM-I) can improve symptoms of anxiety (e.g., Mathews & Mackintosh, 2000) and depression (e.g., Holmes, Lang, & Shah, 2009; Torkan et al., 2014). CBM-I is a procedure that aims to change people's bias in a positive direction. In this training procedure, a narrator reads some virtual scenarios to patients, and patients have to imagine those scenarios vividly. All of these scenarios begin with an ambiguous start but end with a positive outcome. For example, "You are starting a new job that you very much want. You think about what it will be like and feel extremely optimistic" (Berna, Lang, Goodwin, & Holmes, 2011; Holmes et al., 2009). After practicing imagining lots of ambiguous situations that end with positive outcomes, participants showed decreased anxiety levels (e.g., Murphy et al., 2015), improvements in depressive symptom (Blackwell & Holmes, 2010; Lang, Blackwell, Harmer, Davison, & Holmes, 2012), and increased positive cognitive bias or decreased negative bias (Holmes, Mathews, Dalgleish, & Mackintosh, 2006; Lau, Molyneaux, Telman, & Belli, 2011; Torkan et al., 2014).

The findings of Experiment 2 could also be applied to develop new interventions for memory deficits. Items with higher values became better remembered in Experiment 2, a new intervention could involve imagery scenarios which raise the values of items to improve their subsequent memory.

Experiment 3 in the present study demonstrated that the vmPFC was involved in subjective value representation during autobiographical memory recall. Speer et al (2014) had similar results and they further demonstrated that participants were willing to lose monetary reward just for obtaining chances to recall positive memories. Speer et al. (2014) suggested that positive memory recall is valuable explaining why the reward system was recruited in positive memory recall. In a mouse study, researchers tagged neurones in the dentate gyrus which were activated during encoding of a positive experience and reactivated these neurones via optogenetic technique later (Ramirez et al., 2015). After reactivation of these neurones, depression-related behaviours were significantly reduced in the mice. This implies that positive memory retrieval may be able to alleviate symptoms of depression.

Depression does not only influence patients' emotion, but also impairs their ability to retrieve autobiographical memory. People who are suffering from depression may tend to collect negative memories, have difficulty accessing a specific memory or "overgeneral", and recall less details of positive memories (for a review, see Dalgleish & Werner-Seidler, 2014). This is not surprising given the involvement of mPFC in both the value/reward system and the autobiographical memory system. Therefore, it is reasonable to speculate that the incorporation of autobiographical memory training could be a potential therapeutic method for depression. In fact, interventions adopting autobiographical memory-based therapeutics have begun to be developed in the past decade and revealed some promising results (e.g., Dalgleish et al., 2014; Hitchcock et al., 2015, 2016; Neshat-Doost et al., 2013; Raes, Williams, & Hermans, 2009). For example, one of the training programme, MEmory Specificity Training (MEST), has been found to be able to enhance the specificity of autobiographical memory retrieval in depressed individuals (Raes et al., 2009) and also reduced the symptoms of depression (Neshat-Doost et al., 2013). The MEST consisted of four 1-hour sessions. During each MEST session, patients received some cue words and had to recall different life events. The event could be neutral or positive in the first two sessions and then negative events were included in the last two sessions. Patients were encouraged to recall as many specific details within each event as possible. They were also encouraged to focus on the details and elements which made those events specific. This practice provided chances for patients to retrieve memory-specific details and trained patients to focus attention on aspects other than generic components of events. A large number of practices were also carried out at home. After the training, the symptom of overgeneral autobiographical memory was reduced (Raes et al., 2009) and participants became less depressed at a 2-month follow-up (Neshat-Doost et al., 2013).

5.4. Conclusion

Since the last decade, cognitive neuroscientists have showed great interest in the similarity and dissimilarity between autobiographical memory recall and mental imagery. A network, i.e. the core-network, was recognised as the common network for both abilities (Buckner & Carroll, 2007). This core-network includes mPFC, medial temporal lobe, and posterior parietal cortex. In the present thesis, I primarily focused on examining whether the functional role of mPFC in autobiographical memory retrieval and mental simulation is subjective value representation.

Experiments from both fMRI studies have shown that (1) mPFC activity was parametrically modulated by the subjective value of imagined items during imagining those items in certain physiological states, (2) vmPFC activity was modulated by value and familiarity of items in autobiographical memory during recalling and evaluating those items, (3) vmPFC activity was also modulated by personal significance ratings and emotional intensity evoked by memories during recalling memories. Altogether, these findings suggest that the function of mPFC in autobiographical memory retrieval and mental imagery might be subjective or self-relevant value processing and representation.

Finally, it is important to note that this thesis does not suggest that subjective or self-relevant value processing and representation is the only function of mPFC. The mPFC is an extremely large structure in humans, with many anatomical subdivisions (see Section 1.2), and might be expected to contribute to a wide range of cognitive tasks, see e.g. Figure 5). Accordingly, several studies have demonstrated the involvement of mPFC in phenomena that cannot be fully explained by this account. For instance, vmPFC patients have impaired observational learning but not experiential learning of the association between reward size and pictures (Kumaran, Warren, & Tranel, 2015). vmPFC lesion induced the change of sleep patterns and depressive-like behaviour in rats (Chang, Chen, Qiu, & Lu, 2014). Depressed patients have lower vmPFC activation compared to healthy controls during self-inferential processing (for a review, see Lemogne et al., 2012). Therefore, it is highly possible that mPFC plays other different roles in tasks other than autobiographical memory retrieval and episodic imagery.

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