Social, self, (situational), and affective processes in medial prefrontal cortex (MPFC): Causal, multivariate, and reverse inference evidence


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ABSTRACT

The medial prefrontal cortex (MPFC) has been postulated to serve a variety of social, affective, and cognitive functions. These conclusions have largely been driven by forward inference analyses (e.g., GLM fMRI studies and meta-analyses) that indicate where domain-specific tasks tend to produce activity but tell us little about what those regions do. Here, we take a multi-method, multi-domain approach to the functionality of MPFC subdivisions within Brodmann areas 9-11. We consider four methods that each have reverse inference or causal inference value: lesion work, transcranial magnetic stimulation, multivariate pattern analysis, and Neurosynth analyses. The Neurosynth analyses include multi-term reverse inference analyses that compare several domains of interest to one another at once. We examine the evidence supporting structure-function links in five domains: social cognition, self, value, emotional experience, and mental time travel. The evidence is considered for each of three MPFC subdivisions: dorsomedial prefrontal cortex (DMPFC), anteromedial prefrontal cortex (AMPFC), and ventromedial prefrontal cortex (VMPFC).

1. Introduction

The medial prefrontal cortex (MPFC) has been postulated to serve a variety of social, affective, and cognitive functions. These conclusions have largely been driven by forward inference analyses (e.g., GLM fMRI studies and meta-analyses) that indicate where domain-specific tasks tend to produce activity but tell us little about what those regions do. Here, we take a multi-method, multi-domain approach to the functionality of MPFC subdivisions. We consider four methods that each have reverse inference or causal inference value: lesion work, transcranial magnetic stimulation, multivariate pattern analysis, and Neurosynth analyses. The Neurosynth analyses include multi-term reverse inference analyses that compare several domains of interest to one another at once. We examine the evidence supporting structure-function links in five domains: social cognition, self, value, emotional experience, and mental time travel. The evidence is considered for each of three MPFC subdivisions: dorsomedial prefrontal cortex (DMPFC), anteromedial prefrontal cortex (AMPFC), and ventromedial prefrontal cortex (VMPFC). Although there is evidentiary variability across methods, the results suggest that social processes are functionally linked to DMPFC, and affective processes are linked to AMPFC and VMPFC. There is also a relatively non-selective region of VMPFC that may support situational processing, a process key to each domain, but also independent of each.

To paraphrase William James (1890), there are probably as many theories of medial prefrontal cortex (MPFC) as there are people who study MPFC. These theories of MPFC function are almost assuredly informed by forward inference analyses which may not be the best tool for this job. Forward inference analyses from individual articles and meta-analyses are a highly valuable source of information that indicate where there tends to be increased neural activity when particular task demands are present. For example, when individuals are asked to consider whether a trait is self-descriptive, there will be reliable activity in anteromedial prefrontal cortex (AMPFC; Kelley et al., 2002).

Cautionary tales abound regarding the dangers of ‘affirming the consequent’. In logic, it is a well-known error to conclude from “If A then B” that the presence of B also implies the presence of A. Knowing
that “If it rains, the picnic will be canceled”, does not allow us to infer from a canceled picnic that it must have rained (e.g. people might have gotten sick instead). Within neuroimaging, this has been characterized as the issue of invalid reverse inference (Poldrack, 2006; Yarkoni et al., 2011). Specifically, an instance of invalid reverse inference would occur if we concluded that since self-reference tasks activate AMPFC, then MPFC activity implies that self-reference processes are occurring. More broadly, this error would occur if we assume that since self-reference activates AMPFC, this implies that AMPFC’s function is self-reference. Forward inference studies (i.e. identifying activations based on which processes are induced) cannot in themselves tell us what we typically want to know: what are the psychological functions of different brain regions.

Indeed, a casual inspection of forward inference data makes clear that this data will not greatly aid our understanding of MPFC function. There are three anatomical subdivisions of MPFC that we will consider in this review (see Fig. 1A). Dorso medial prefrontal cortex (DMPFC) consists of the medial aspect of Brodmann area (BA) 9. AMPFC is defined as the medial aspect of BA 10. Finally, ventromedial prefrontal cortex (VMPFC) is defined here as the medial aspect of BA 11. Other characterizations of MPFC exist based on different considerations such as connectivity or co-activation (e.g. de la Vega et al., 2016), however most fMRI studies of MPFC focus on one or more of these subregions. Neurosynth (http://neurosynth.org) is an automated brainmapping database housing more than 10,000 functional MRI studies and produces the most bias-free forward inference analyses (as meta-analyses allow for numerous researcher degrees of freedom). As seen in Fig. 1B, various common accounts of MPFC function produce forward inference effects in largely overlapping swaths of all three MPFC divisions. If all of these psychological processes reliably activate most of MPFC, how can any patch of MPFC be reliably associated with just one of these processes? These forward inference analyses (and related meta-analyses) are of great value, but are not well-suited for making claims about structure-function links.

If we want to pursue an understanding of the psychological function of different MPFC subdivisions we have a number of more appropriate tools at our disposal. Lesion data, transcranial magnetic stimulation, multivariate pattern analysis, and Neurosynth reverse inference analyses can all be of use. To our knowledge, there are currently no broad reviews of MPFC examining these sources of data across common psychological accounts. We consider five major accounts of MPFC function: social cognition, self, value, emotional experience, and mental time travel. Based on the initial results of these reviews, we will also consider evidence for a novel domain of situational processing.

2. Methods

For each domain of interest, we will briefly review the existing meta-analytic and forward inference data. We will then turn to the other sources of data relevant to reverse inferences. Here we provide some context for how those reviews were carried out.

We searched for articles in each domain on Google Scholar and also searched through the citations of relevant articles for additional papers. Our searches each involved Boolean search terms (i.e. ‘AND’, ‘OR’) combining methods and domains. For searching different types of methods, we used terms including: lesion, damage, transcranial magnetic stimulation, tms, multivariate, multivariate pattern classification, multivoxel, mvpa, and meta-analysis. For the social domain, we used terms including: social, social cognition, theory of mind (ToM), mentalizing, and emotion perception. Because emotion perception is fundamentally about recognizing the psychological state of others, we have included this with social, while emotional experience is considered separately below. For the self domain, we used terms including: self, self-awareness, belief, and intentions. Here, studies of belief and intention refer to those in which participants reflect on their own beliefs and intentions. If a paper focused on understanding others’ beliefs or intentions it was included in the social domain. For the value domain, we used terms including: value, reward, reinforcement, incentive, and anticipation. For the emotion domain, we used terms including: emotion, affective, and valence. For the mental time travel domain, we used terms including: episodic, time travel, future thinking, prospection, and prospective memory. Because the term ‘autobiographical’ links to both self and mental time travel domains, these papers were searched for but only included in one domain or the other if the study clearly emphasized one of the two domains. If the study met criteria for inclusion for other reasons, we will also mention the results with respect to autobiographical memory.
For the most part, we only included papers that were relevant to linking one or more of the domains to particular MPFC subdivisions. A lesion paper that describes patients with general MPFC or prefrontal lesions would not have been included because it did not reach the degree of specificity needed for this review. It is also noteworthy that we initially began with a larger pool of domains. Some of these did not have enough data across the different methods we are considering to provide insight about their relation to MPFC subdivisions (e.g., narrative, counterfactual thinking, gateway hypothesis, and internal monitoring).

In contrast, MPFC-related studies in the choice domain strongly overlapped with the value domain. Thus, while we think we have selected the domains that are frequently associated with MPFC function across studies, a key caveat is that all analyses and inferences described here are limited to those five domains. Thus, if we speak of a region showing preferential involvement with a particular domain, we mean relative to the other domains considered in this article. We suspect many of these conclusions will hold up more broadly, but here we are focused only on these five domains.

It is also important to note that we are not claiming that any of these domains of interest are only processed in MPFC. Rather, we are focused on the extent to which MPFC subdivisions (or subareas within these subdivisions) are reliably associated with these domains at all, relative to the other domains of interest. Clearly, all of the domains of interest also involve processes outside of MPFC.

For all Neurosys analyses, we constructed regions of interest (ROIs) for medial BA 9, medial BA 10, and medial BA 11 (Fig. 1A). We also constructed a combined medial BA 9/10/11 ROI. These were created using the following procedure. ROI Masks for BA 9, BA 10, and BA 11 were generated from the Talairach Daemon database (Lancaster et al., 2000; Maldjian et al., 2003). The resulting masks were warped into Montreal Neurological Institute coordinate space (MNI; Evans et al., 1993) and edited using the FMRIB Software Library (FSL; Jenkinson et al., 2012). The masks were combined into a single MPFC mask and spherically dilated by 3 mm for improved gray matter coverage. Voxels beyond 15 mm of the midline were excluded in order to localize analyses to medial sections of the BAs. BA 9 and BA 10 masks were divided by the z-plane of +22. BA 10 and BA 11 masks were divided by the z-plane of -10. These ROI masks are all available at https://github.com/MetaD/MPFC-ROIs

We report five kinds of Neurosys analyses. Most of these analyses were conducted using NS+ (Du and Lieberman, 2018), a tool that extends what Neurosys can do in a standalone application that does not require Python installation. First, we report single-term forward inference analyses. These examine which voxels are more frequently activated by the tasks in a particular domain (e.g. self) than would be expected in a null distribution. More generally, forward inference analyses tell us where tasks from particular domains tend to produce effects in MPFC. Second, we report single-term reverse inference analyses. These analyses focus on the likelihood (i.e., posterior probability) that an activation seen in a particular MPFC region would come from a particular domain (e.g. self) rather than from any of the Neurosys studies that are not tagged for self, assuming equal numbers of domain-specific and non-domain studies (e.g. a pool of 500 self studies and 500 non-self studies). Essentially, these analyses set the Bayesian prior to 0.5 and, as a result, Bayes’ Theorem reduces down to a comparison between the hit rate at each voxel for a term of interest and the aggregate hit rate of all other terms in the database. Technically, when we create or assume an equal pool of term and non-term studies (i.e. prior = .5), the posterior probability at each voxel is:

\[
\text{Posterior probability (Term)} = \frac{\text{Hit rate (Term)}}{\text{Hit rate (Term) + Hit rate (Non – term)}}
\]

Third, we report multi-term reverse inference analyses. Conceptually, these are no different from the single-term reverse inference. However, these analyses compare a term of interest (e.g. self) to another term of interest (e.g. value). Here the formula is essentially the same:

\[
\text{Posterior probability (Term)} \times \frac{\text{Hit rate (Term)}}{\text{Hit rate (Term) + Hit rate (Term)}}
\]

These are frequently more useful than the single-term analyses as we think most researchers are more interested in whether some part of the brain is more associated with one of a handful of candidate functions. Two domains can both show strong single-term reverse inference with a region, but one region can have a higher posterior probability when the two terms are compared directly. In these analyses, we typically use a posterior probability of 0.60 as our critical threshold because it identifies voxels that in a balanced pool of, say, self and value studies, would be at least 50% more likely to come from one term or the other.

Fourth, we combine across all the multi-term reverse inference analyses to find voxels that meet the 0.60 threshold in each of the comparisons of a particular term to the other four terms of interest. Thus, this analysis would yield for the term ‘self’, those voxels that met the 0.60 threshold when ‘self’ was compared to ‘social’ and when ‘self’ was compared to ‘value’ and when ‘self’ was compared to ‘emotion’ and when ‘self’ compared to ‘mental time travel’. If an active voxel is 50% more likely to come from a ‘self’ study than any one of the other four terms, this is reasonable evidence that this voxel shows preference for ‘self’ relative to the other four terms.

It should be noted that whenever domains are compared to one another in Neurosys, any study tagged for both domains is necessarily excluded. The results could not be computed otherwise. Also, as reported below, we created our own domain-specific terms by combining studies from multiple terms relevant to a domain. For instance, mental time travel is not a term in Neurosys so we created a domain-specific term from all the studies tagged with any of the following terms: episodic, future, past, retrieval, prospective, and memory retrieval.

Fifth and finally, we took the clusters that emerged for the multi-term reverse inference analyses, created ROIs, and examined which terms out of Neurosys’s library of 3107 terms had the highest posterior probability. That is, for each voxel within one of these ROIs we computed the posterior probability of all 3107 terms. These posterior probabilities were then averaged across all the voxels within the ROI to give an unbiased estimate of the terms with the strongest reverse inference value, beyond the five domains we have focused on. We performed the same analysis on the ROIs created for the anatomical subdivisions of MPFC. It should be noted that for the tables that report these results, any terms that could not be construed as referring to psychological functions (e.g. ‘block’, ‘prefrontal’, ‘taken’) were excluded.

3. Results

3.1. Social cognition

Social cognition is largely identified with perceiving and understanding the thoughts, feelings, and motivations of others, of understanding the psychological causes of their behavior, and building mental models of the enduring psychological characteristics of other people and groups. In other words, social cognition is the study of how people make sense of other people. Studies considered below largely focus on mentalizing, attribution, and emotion perception processes. Historically, social cognitive processes have been associated with DMMPFC along with tempoparietal junction, posterior superior temporal sulcus,
precuneus, and the temporal poles (Lieberman, 2010; Van Overwalle, 2009).

3.1.1. Forward inference

There are eleven formal meta-analyses of the neural bases of social cognitive processing (Murray et al., 2012; Dricu and Früehholz, 2016; Fusar-Poli et al., 2009; Sabatinelli et al., 2011; Lamm et al., 2011; Bzdok et al., 2012; Schurz et al., 2014; Spreng et al., 2009; Denny et al., 2012; Gilbert et al., 2006; Van Overwalle, 2009). Given that many of these were based on overlapping sets of papers, it is unsurprising that there was general consistency across meta-analyses. Ten of the meta-analyses revealed effects in DMPFC and nine also showed effects in AMPCF. In contrast, only three meta-analysis showed effects in VMPFC.

Some of the meta-analyses made distinctions suggesting possible functional differences across MPFC subdivisions. For instance, Van Overwalle (2009) and Murray et al. (2012) localized general social judgments and judgments about close others separately. Both of these meta-analyses found that general social cognition was restricted to DMPFC, whereas thinking about close others was constrained to AMPCF. Given that VMPFC is frequently associated with affective processes, it is of note that none of the three meta-analyses of emotion perception showed effects in VMPFC, while two produced effects in DMPFC. Finally, like several of the meta-analyses, Schurz et al. (2014) examined theory of mind processes, but also computed contrasts for six different types of theory of mind tasks (c.f. Lieberman, 2010). Among MPFC regions, only DMPFC showed meta-analytic effects for all six task types. In contrast, AMPCF was significant for three of the tasks.

Examining the forward inference maps from Neurosynth (as opposed to the 11 formal meta-analyses), a somewhat different picture emerges (see Fig. 1b). The term ‘social’ produces broad coverage of DMPFC, AMPCF, and VMPFC, however, AMPCF disappears when terms such as ‘social cognition,’ ‘mentalizing,’ or ‘ToM’ are used.

Across meta-analyses and forward inference Neurosynth maps, it is clear that studies of social cognitive judgments produce reliable effects in DMPFC. However, methods vary in whether they also point to AMPCF or VMPFC as regions active during studies of social cognition.

3.1.2. Lesion studies

The most well-known lesion study of MPFC and social cognition is likely the case study by Bird et al. (2004). The authors examined a patient with extensive MPFC damage across BA’s 9/10/11 using a battery of five different mentalizing tasks. With the exception of one aspect of one task, the patient performed in the normal range on all tasks. This prompted the concern that the reliable MPFC effects observed in fMRI studies may not, in fact, reflect a causal role in social cognition. The limitation of the Bird et al. (2004) study is that it is an examination of a single case and thus generalizing from it is difficult.

Although lesion studies are a gold standard for assessing causality, there are significant limitations. First, lesions rarely respect anatomical boundaries. For instance, most VMPFC lesions also extend into AMPCF making it difficult to tease apart which tissue damage is actually critical to observed function loss, except in very large lesion mapping studies. Second, lesions are not randomly distributed around the brain. Although there are many reports of VMPFC and AMPCF lesions, only a tiny handful involve DMPFC damage.

Several studies examining patients with VMPFC and AMPCF lesions found alterations in emotion perception (Adolphs et al., 2002; Heberlein et al., 2008; Mah et al., 2005), implicit stereotype associations (Gozzoli et al., 2009; Milne and Grafman, 2001), moral judgment (Ciaramelli et al., 2007, 2012; Koenigs et al., 2007; Moretto et al., 2010; Anderson et al., 1999), and theory of mind tasks (Channon et al., 2007, 2010; Leopold et al., 2011; Shamay-Toory et al., 2005, 2009; Stone et al., 1998; Umeda et al., 2010; Croft et al., 2010; Burin et al., 2014; Roca et al., 2011). It is important to note that several of the papers (Leopold et al., 2011; Shamay-Toory et al., 2005; Umeda et al., 2010) examining theory of mind found a dissociation, such that AMPCF and VMPFC were associated with affective mentalizing deficits (e.g. faux pas detection), but spared cognitive mentalizing (e.g. false belief).

In contrast to Bird et al. (2004), a small handful of other studies including DMPFC lesion patients have found some evidence of social cognitive deficits. Hornak et al. (2003) reported on a set of patients with DMPFC lesions who were impaired at emotion perception. Anderson et al. (1999) reported alterations in moral judgments in a sample of patients that included some with DMPFC damage. Lee et al. (2010) reported on impaired faux pas identification in a sample that was mixed between DMPFC, AMPCF, and VMPFC patients. Finally, Herbet et al. (2013) reported on a set of five patients who had maximal lesion overlap in DMPFC and were impaired on a standard theory of mind task shortly after surgical resection (but not three months later).

At this point, results from lesion studies strongly suggest that VMPFC and/or AMPCF are involved in more affectively-focused social processes (e.g. emotion perception, faux pas identification). The limited set of studies examining DMPFC suggest this region may play a causal role in more cognitively-focused social processes, but given the paucity of relevant lesion studies, this is a weak conclusion at best. It should be noted that for the lesion studies in each of the five domains, assigning lesions to the subregions of MPFC was done by eyeballing the figures showing the lesions. Thus, we cannot be certain that the lesions are confined only to the subregions that they appear to be in the figure.

3.1.3. Transcranial magnetic stimulation

What is missing in the lesion work on social cognition is made up for in TMS research. Here, the majority of studies focus on modulating DMPFC responses in order to examine whether this region causally contributes to social cognitive processes. These studies were evenly split between repetitive and single pulse TMS approaches.

Three TMS studies from the Cattaneo group have found that TMS targeting BA9 leads to alterations in trait judgments (Ferrari et al., 2016, Ferrari et al., 2016b, in press). Two others from this group (Ferrari et al., 2017; Gamond et al., 2017) found that TMS to BA9 prevents social stereotypes from being applied. Three TMS studies have looked at theory of mind directly, though neither using a false belief task, with one showing deficits associated with TMS targeting AMPCF (Lev-Ran et al., 2012). The second failed to find a main effect of DMPFC TMS on two theory of mind tasks (Krause et al., 2012), however, did find that those high in trait empathy did show reduced accuracy with TMS applied to DMPFC – a moderation effect also seen in another study of emotion perception (Balconi and Bortolotti, 2013). The third found that continuous TMS applied to DMPFC improved theory of mind performance for women but not men (Adenzato et al., 2017). Additionally, a transcranial direct current stimulation (tDCS) study found that continuous anodal stimulation over DMPFC improved visual perspective-taking as well (Martin et al., 2017). Finally, multiple studies have shown that TMS aimed at BA9 produces impaired emotion perception (Balconi and Bortolotti, 2013; Gamond and Cattaneo, 2016; Mattavelli et al., 2011).

In summary, in the domain of TMS research there is consistent evidence that DMPFC plays a causal role in social cognition. This was primarily observed for studies of emotion perception and trait judgments. It should be noted that TMS has the opposite limitation in MPFC, relative to lesion studies. While lesion studies largely focus on VMPFC and AMPCF, TMS studies have largely focused on DMPFC due to methodological constraints (e.g. TMS cannot reach VMPFC) and thus TMS is ill-suited to weigh in on contributions of VMPFC to any of the domains of interest.
3.1.4. Multivariate pattern analysis

In contrast to general linear model (GLM) univariate analyses, MVPA analyses are thought to reveal the neural bases of representational process. Because MVPA studies predict psychological/task states from neural patterns, rather than the reverse as typically seen in univariate studies, MVPA studies do not fall prey to issues of ‘affirming the consequent.’ However, functional claims in MVPA studies are always limited to the handful of psychological states/tasks being compared.

MVPA provides the most unambiguous evidence thus far that social cognition is primarily associated with DMPFC, rather than AMPC or VMPFC. Three studies performing whole-brain searchlight analyses (i.e. a technique for identifying voxels throughout the brain that are good candidates to produce multivariate effects) have observed that DMPFC, but not VMPFC, is involved in decoding the perception of different emotions (Jastorff et al., 2015; Kim et al., 2015; Peelen et al., 2010). One study took an ROI-based approach, including a VMPFC but not a DMPFC ROI, and did observe that VMPFC successfully decoded emotion perceptions (Kragel and LaBar, 2016).

Two other studies of emotion perception highlight the role of DMPFC in making mental state attributions of emotion, rather than being sensitive merely to the superficial features of different emotional expressions. In one study (Skerry and Saxe, 2014), participants had to identify the emotion a target would be experiencing either from their facial expression or from observing the situation the target was in without ever seeing the target. In a whole-brain searchlight analysis, DMPFC contained the only cluster that could accurately cross-classify (i.e. train on facial expressions and then test on situations, or the reverse). This suggests that DMPFC is decoding what is common across these stimuli, which is a representation of the mental state of emotion in others, rather than being sensitive to superficial features (e.g. visual aspect of facial expressions).

Skerry and Saxe (2015) followed this up by showing that in a searchlight analysis, DMPFC was the only MPFC subdivision that could successfully decode 20 different emotion states in others. Furthermore, using representational similarity analysis (RSA; a technique that examines how similar and dissimilar different neural states are from one another), they demonstrated that in DMPFC and AMPC, “the similarity of emotion conditions in voxel level patterns was positively correlated with similarity in the space of 38 appraisal dimensions.” Once again, this suggests that DMPFC is remarkably sensitive to subtle variations in the mental state correlates of different perceived emotions.

Tamar et al. (2016) asked participants to think about whether vignettes would induce certain mental states. They observed that the extent of rational vs. emotional responses induced by the vignette could be decoded by DMPFC and AMPC, but not VMPFC activity, whereas the social intensity of the mental state could be decoded by both DMPFC and VMPFC activity.

Other studies also demonstrate that DMPFC, but not VMPFC, decodes mental state inferences versus non-mental state inferences (Corradi-Dell’Acqua et al., 2014; Dungan et al., 2016), or decodes levels within a mental state inference (e.g. degree of reported perspective-taking from trial to trial; Tusche et al., 2016).

Hassabis et al. (2013) reported a particularly interesting MVPA study of trait knowledge. Participants learned about four targets whose personality characteristics filled the four cells created by crossing high and low extraversion with high and low agreeableness. Participants then imagined these targets in different scenarios. In a whole-brain searchlight analysis, only a single cluster in DMPFC was able to discriminate which of the four targets was being imagined from one trial to the next.

In summary, MVPA provides strong evidence that within MPFC, it is primarily DMPFC that is involved in social cognitive processes. Although AMPC and VMPFC showed significant effects sporadically, both were absent from a majority of the critical analyses from studies using whole-brain searchlight analyses.

3.1.5. Single-term reverse inference

Examining the generic Neurosynth reverse inference maps for terms including ‘social,’ ‘social cognition,’ ‘mentalizing,’ and ‘ToM’ (each compared to all other terms in the database) all produce similar cluster distributions in MPFC and all differ from the analogous forward inference maps in an important way. Specifically, DMPFC and VMPFC appear robustly, however AMPC is conspicuously absent from each of the relevant reverse inference maps in contrast to its presence in some of the forward inference maps.

3.1.6. Summary

Across forward and reverse inference maps, TMS, and MVPA analyses, there is clear and consistent evidence implicating DMPFC in social cognition and mental state inference processes. Lesion data is equivocal regarding DMPFC’s role in social cognition, but this may be due to the dearth of studies examining social cognition in DMPFC lesion patients.

There is also evidence linking AMPC and VMPFC to social cognitive processes, though it is less consistent than the evidence for DMPFC. Lesion data clearly links these regions to affective aspects of social cognition, though these studies typically lack the ability to differentiate BA10 and BA11 effects. MVPA studies did not strongly implicate AMPC or VMPFC in social cognition processes. In contrast, reverse inference maps suggest a role for VMPFC, but not AMPC, in social cognitive processes.

3.2. Self-processes

Self-processes encompass a wide array of topics within nearly endless hyphenated self topics (e.g. self-concept, self-esteem, self-enhancement, etc.). Within the neuroscience literature, self-concept and self-reflection are the two primary areas of self study. Self-concept refers to the knowledge structure that characterizes who we are, what we’ve done, and what we hope to do. This encompasses self-reference, self-knowledge, and autobiographical memory. Note that since autobiographical memory involves self and episodic memory processes, it was largely excluded from analysis here as indicated above in the methods section. Self-reflection, along with introspection and metacognition, involves thinking about the self, one’s goals and intentions, or one’s own thoughts more generally. Historically, self-processes have been identified with AMPC along with precuneus (Kelley et al., 2002) and more recently with ventral striatum (Falk et al., 2015; Rameson et al., 2010; Tamir and Mitchell, 2012).

3.2.1. Forward inference

There are eight meta-analyses of the neural bases of self-processes (Cona et al., 2015; Stawarczyk and D’Argembeau, 2015; Denny et al., 2012; Northoff et al., 2006; van der Meer et al., 2010; Murray et al., 2012; Van Overwalle, 2009; Martinelli et al., 2013). Of these, six report on the common neural basis of self-reference and accessing conceptual knowledge about oneself (Denny et al., 2012; Northoff et al., 2006; van der Meer et al., 2010; Murray et al., 2012; Van Overwalle, 2009; Martinelli et al., 2013) and all find a predominance of activity in AMPC. Two of these also find reliable self-reference effects in DMPC (Denny et al., 2012; van der Meer et al., 2010). The meta-analysis by Denny et al. finds that although both DMPC and AMPC are reliably associated with self and social judgments, there is a dorsal/ventral gradient such that more dorsal activations with higher z-coordinates are more likely to come from social tasks in which participants think about other people and more ventral activations with lower z-coordinates are more likely to come from self-reference tasks.
One of these meta-analyses (Martinelli et al., 2013) also distinguished between conceptual self-knowledge (e.g. “I am funny”), semantic self-memories (e.g. “I often spent weekends at the shore as a child”) and episodic self-memories (e.g. “I remember this one time at the shore in 1982, when I...”). Within MPFC, each of these component self-processes (conceptual, semantic, episodic) produced meta-analytic effects in AMPFC. Conceptual self-knowledge also produced a modest cluster in DMPFC. None of the three components produced peaks in VMPFC.

Two meta-analyses also examined focusing on one’s personal goals and intentions (Coda et al., 2015; Stawarczyk and D’Argembeau, 2015). The results were mixed with one reporting increased AMPFC for personal goals (Stawarczyk and D’Argembeau, 2015) and the other reporting reduced AMPFC for intention processing (Coda et al., 2015). We were not able to identify any meta-analyses for metacognition focusing on MPFC effects.

The forward inference Neurosynth map for the term ‘self’ is largely consistent with the meta-analyses in this domain. Large clusters cover most of DMPFC and AMPFC, extending down to the most dorsal portion of VMPFC.

Across meta-analyses and forward inference Neurosynth maps, it is clear that tasks invoking self-processes produce reliable effects in AMPFC. There are also multiple pieces of evidence to suggest that self-processes evoke DMPC activity as well. In the domain of self-processes, there is little forward inference evidence of VMPFC’s involvement.

3.2.2. Lesions

There have been several lesion studies that focus on at least one aspect of self-processing. Three lesion studies have focused on self-reference and each of these found that AMPFC damage was associated with impaired self-referential processing and conceptual self-knowledge (Marquione et al., 2016; Kurczek et al., 2015; Philipp et al., 2012a). In a case study (Marquione et al., 2016), a patient with AMPFC damage displayed poor self-knowledge, but spared social knowledge of another person. Another important dissociation was observed by Kurczek et al. (2015). In this study of five patients, primarily with AMPFC damage but with some VMPFC damage as well, participants showed a significant reduction in self-references in written narratives. However, these patients also showed a normal level of past and future thinking in these narratives. Hippocampal patients showed the opposite pattern of results with respect to self-reference and mental time travel. Note that another study (Bertossi et al., 2016b) did not replicate these effects from Kurczek, however the lesions in the Bertossi study were centered in VMPFC, rather than AMPFC.

Six lesion studies also examined metacognitive processes that relate to self-awareness and self-insight. These studies examined feeling of knowing (Modirrousta and Fellows, 2008; Schnyer et al., 2004), self-conscious emotion (Beer et al., 2003), and metacognition more generally (Budsn et al., 2005; Fleming et al., 2014; Mah et al., 2004). Across these studies, deficits were reliably associated with AMPFC lesions in BA10 with a few studies also showing VMPFC effects.

Finally, one case study (Philipp et al., 2012b) examined introspection and autobiographical memory in a patient with AMPFC damage that appears to extend into VMPFC. This patient had mostly spared self-related processing, but showed significant deficits in autobiographical memory.

In general, lesion studies of self-processes strongly implicate AMPFC in self-reference and metacognitive tasks. When VMPFC damage was present in studies, this region was implicated as well. Consistent with the general dearth of DMPFC lesion studies, there were no DMPFC lesion studies of self-processes.

3.2.3. Transcranial magnetic stimulation

There are a relatively small number of TMS studies of MPFC and self-processing. Coordinates of stimulation sites are not always given or are only estimates when they are. With these caveats in mind, three TMS studies that appear to stimulate AMPFC (and possibly DMPFC) show altered self-processing. One study (Luber et al., 2012) shows a reversal of self-enhancing to other-enhancing judgments and the second shows reductions in private self-awareness (Gruberger et al., 2015). Another study (Barrios et al., 2008) stimulated DMPFC and found self-enhancement disrupted here as well. Finally, stimulation of DMPFC does not diminish the enhanced efficiency associated with self-reference (Lou et al., 2010). It is also worth noting that a tDCS study found that continued anodal stimulation over DMPFC eliminated the self-reference effect (Martin et al., 2017). At this point, there is some general evidence that TMS in MPFC regions might alter some self-processes, but there are simply too few studies to suggest any strong conclusions. At best, there is some moderate evidence that DMPFC stimulation can alter some self-processes.

3.2.4. Multivariate pattern analysis

A half dozen MVPA studies have examined self-processes. All of these implicate AMPFC in self-related cognition. One study has examined MPFC involvement in distinguishing autobiographical memories from another’s memories. Rissman et al. (2016) found that patterns of activity in AMPFC and DMPFC could distinguish between pictures taken over the past three weeks from a camera hanging around the participants’ necks and pictures from another participant’s camera. Furthermore, only AMPFC distinguished between strong and moderate recollections of autobiographical memories.

Three other MVPA studies have looked at forming, maintaining, and remembering personal intentions. For instance, in one study by Haynes et al. (2007), participants would secretly choose which of two kinds of tasks to do next. From neural activity in AMPFC during the intervening delay, the selected task could be decoded. The other two studies also showed multivariate links between AMPFC and personal intentions (Gilbert et al., 2012; Mommennejad and Haynes, 2012), with one also showing DMPFC involvement (Mommennejad, and Haynes, 2012).

Finally, Chavez et al. (2016) were able to train a classifier on positive versus negative images and successfully use this classifier to discriminate between judgments of self and a close other. The fact that this cross-classification succeeded was taken as evidence that there is a positive bias (or self-enhancement) inherent in self-evaluation that is not present in the evaluation of others.

In summary, though MVPA studies of self processes are still rare, those that have been published show clear consistent evidence of AMPFC in self-processes. Some evidence for DMPFC or VMPFC was present as well.

3.2.5. Single-term reverse inference

We examined the generic Neurosynth reverse inference map for ‘self.’ Here, robust effects were observed in AMPFC and DMPFC, but effects were largely absent in VMPFC. These results indicate that activations present in AMPFC and DMPFC are more likely to come from studies tagged for ‘self’ than from other non-self tagged studies in the Neurosynth database.

3.2.6. Summary

Across forward and reverse inference maps, lesion, and MVPA analyses, there is clear and consistent evidence implicating AMPFC in self-processes. TMS data is more equivocal given the small number of studies and difficulty using TMS to stimulate AMPFC. In each method-
ological domain, there were studies that occasionally indicated DMPFC or VMPFC, but there was little consistency in these effects.

3.3. Value

Value, quite simply, refers to how we order our preferences for things, material and immaterial, relative to one another. The neuroscientific study of value primarily focuses on preferences between options, anticipation of rewards, and the receipt of rewards. Historically, valuation processes have been associated with VMPFC and ventral striatum.

3.3.1. Forward inference

Although there are a handful of meta-analyses of valuation, reward, and/or preference-based choice, the meta-analysis from Bartra et al. (2013) has already been cited over 700 times and is arguably the gold standard in this domain. These authors examined the effects of valence (positive vs. negative), processing stage (decision stage vs. outcome receipt), and reward type (primary vs. secondary). MPFC effects are evident in nearly every contrast with the exception of punishments/absence of reward. The clusters observed span AMPFC and VMPFC in each of these analyses, however, the peak voxel tends to be right at the border of AMPFC and VMPFC, most often in the former.

Liu et al. (2011) found similar effects, but suggested MPFC responses were driven more by outcome receipt than anticipation. Hayes et al. (2014) found results primarily in AMPFC that were associated with appetitive rather than aversive stimuli. Finally, a meta-analysis from Sescousse et al. (2013) compared primary and secondary rewards and found that only secondary reward (e.g. money) produced effects in VMPFC and AMPFC, while primary rewards (e.g. food) were associated with rostral anterior cingulate cortex.

Within the Neurosynth database, the forward inference map for the term ‘value’ (344 studies) primarily covers AMPFC and bleeds into the dorsal aspects of VMPFC. There is also a modest cluster present for ‘value’ in the DMPFC. The term ‘reward’ produces a similar pattern, with the term ‘incentive’ yielding a more modest footprint in AMPFC and VMPFC, with no DMPFC.

Across meta-analyses and Neurosynth forward inference maps, it is clear that studies that focus on valuation processes produce substantial effects in MPFC. The effects appear to be most concentrated in AMPFC and VMPFC.

3.3.2. Lesions

As in the previous domains, the lesion studies skew strongly towards damage in more ventral regions. There are no valuation lesion studies that focus on DMPFC. Of the 19 lesion studies of valuation included here, all have significant coverage of VMPFC and nine show patient lesion overlap in AMPFC as well.

Half of the lesion papers focused on updating the value associated with different stimuli. The canonical task in this domain is the Iowa Gambling Task (IGT) in which participants choose from decks of cards that contain mostly small rewards and occasionally lead to large punishments. Participants must learn to integrate across these to discover the average value of drawing from each deck to succeed at the task. Almost all of the studies using this task, and variants of it, have found poor task performance in patients with VMPFC damage (Gläscher et al., 2012; Bechara et al., 1999, 2000; Fellows and Farah, 2003, 2005a; Hochman et al., 2010; Rolls et al., 1994; Tsuchida et al., 2010), with a few also including samples with significant coverage of AMPFC (Fellows and Farah, 2003, 2005a). Only one study of VMPFC patients observed normal performance on the IGT (Manes et al., 2002). In one very large lesion mapping study (Gläscher et al., 2012; N = 344), VMPFC was the only region of the brain for which lesion size was associated with IGT performance.

Riskier decision-making in response to different incentives has been shown in multiple studies to be associated with lesions in both VMPFC and AMPFC (Levens et al., 2014; Clark et al., 2008; cf. Pujara et al., 2015). Both VMPFC and AMPFC have also been implicated in making transitive valuation errors (i.e. choosing A over B, despite having already chosen B over C and C over A) (Henri-Bhargava et al., 2012; Camille et al., 2011).

There is mixed data on VMPFC and consideration of future rewards, with one study showing blunted responses in VMPFC lesion patients to delayed financial gains (Moretti et al., 2009), two others showing an altered temporal discounting profile in VMPFC patients (Peters and D’Esposito, 2016; Sellitto et al., 2010), and a fourth showing unchanged temporal discounting in these patients (Fellows and Farah, 2005b).

There is also a single study of how individuals weight different attributes in assigning value to art. In this study (Vaidya et al., 2017), VMPFC gave less weight to certain attributes (e.g. emotionalicity, warmth, complexity) but the same weight to other attributes (e.g. concreteness, balance).

Finally, a single study of reward sensitivity to different levels of reward, as measured by saccades, found altered sensitivity in VMPFC patients (Manohar and Husain, 2016). Oddly, VMPFC patients were more sensitive than controls to reward levels, rather than showing the expected blunting.

In summary, there is consistent evidence from lesion studies suggesting that VMPFC plays a causal role in the processing of value and reward. There was some evidence of AMPFC involvement when AMPFC was damaged in the sampled group it was often implicated. Finally, the lesion data cannot speak to DMPFC involvement in value processes as only a single study reported on DMPFC (Tsuchida et al., 2010) and found no DMPFC damage-related effects.

3.3.3. Transcranial magnetic stimulation

To our knowledge, only a single TMS study focused on MPFC in the domain of valuation has been published. Cho et al. (2015) stimulated AMPFC and observed participants were less likely to discount future rewards. It is likely that there have not been more studies in this area because most reward effects are observed in MPFC regions that are difficult to access with TMS.

3.3.4. Multivariate pattern analysis

One of the signature findings from univariate fMRI studies of value is that VMPFC and AMPFC serve to put stimuli from different categories onto a ‘common value’ scale (Levy and Glimcher, 2012). These findings generally take the form of common activation for high versus low reward value stimuli from two categories (e.g. money and social reward). MVPA serves as an important complement to univariate studies to further examine whether regions in MPFC perform value computations that are independent of stimulus class. MVPA cross-classification across reward categories would seem to be one of the holy grails of true valuation.

Four MVPA studies have now examined the common scale notion (Gross et al., 2014; Howard et al., 2015; McNamee et al., 2013; Pogoda et al., 2016). Somewhat surprisingly, these studies consistently point to AMPFC rather than VMPFC as central to valuation independent of stimulus class. In all four studies, cross-classification analyses used a classifier trained on one class of reward (i.e. high vs. low value food rewards) and then tested this classifier on another class of rewards (i.e. high vs. low value trinket rewards). In each study, AMPFC had a cluster that succeeded during cross-classification and VMPFC did not. In contrast, for two of the studies (McNamee et al., 2013; Pogoda et al., 2016), VMPFC could classify within reward class, but could not train on one class and successfully decode rewards in the other class. In a related study, Kahnt et al. (2011) did find a cluster that spanned AMPFC.
and VMPFC that decoded the integrated value of a multi-attribute stimulus, rather than just the individual values of the different attributes. Another study (Brosch et al., 2012) asked participants to reflect on traditionally valuable activities (e.g. playing tennis) and on core values (e.g. fighting injustice). Univariate effects were observed for valuable activities in VMFC and for core values in AMPFC, but no multivariate effects were observed in either area.

There have been three MVPA studies of reward-guided choice (Bedi et al., 2015; Hampton and O’Doherty, 2007; Tsuche et al., 2010). In each of these, clusters in AMPFC could decode choices. Two of the studies also showed effects for VMPCF or DMPFC. A fourth MVPA study looked separately at valuation and selection in a choice task (Domenec et al., 2017) and found that VMFC contributed to the valuation of each option but not to the integration and selection across options.

Two studies have looked at reward anticipation and receipt using MVPA. One of these (Kahnt et al., 2010) found that neural activity in DMPFC and VMFC during an anticipatory period could discriminate the reward values being anticipated. Yan et al. (2016) found no multivariate effects for anticipation, but did find that activity in AMPFC and VMFC at reward receipt discriminated the value of the rewards obtained.

One study (Burke et al., 2016) examined relative value using MVPA. There were ‘gain’ blocks and ‘loss’ blocks. During gain blocks, participants won 10 points or 0 points on each trial. During loss blocks, participants lost 10 points or 0 points. They looked for classifiers that would either code the absolute value of each outcome (i.e. gain 10 > gain 0; gain 0 = loss 0; loss 0 > loss 10) or the relative value of each outcome (i.e. loss 0 > gain 0) and found that VMFC was sensitive to relative rather than absolute value.

Also of note in the Burke et al. (2016) study is that participants both played the game and watched another person play the same game. VMFC was only sensitive to relative value (or any value metric) for one’s own reward trials and not for the trials of a stranger. Another study from Skerry and Saxe (2014) also found that VMFC could decode personal levels of reward, but not good and bad outcomes occurring for other people. This is consistent with a univariate study (Morelli et al., under review) that found VMFC for personal reward outcomes, a small amount of VMFCF when observing a close other receive rewards, and no VMFC when observing a stranger receive rewards (e.g. Mobbs et al., 2009).

In summary, MVPA studies point primarily to AMPFC for amodal reward processes, ignoring stimulus or category information. VMFC was more identified with reward processes specific to a particular domain and the processing of reward values that were contextually sensitive. Finally, VMFC was present for personal valuation, but not consideration of another’s outcomes.

3.4. Emotion

Emotion research is largely separated along perceptual and experiential lines. As we have included emotion perception as part of the social processes above, the focus in this section is on emotional experiences (e.g. responses to emotion inductions). Historically, emotional experience has been associated with VMPCF, DMPCF, amygdala, and anterior insula (e.g. Kober et al., 2008).

3.4.1. Forward inference

There are three recent meta-analyses of emotion (Kober et al., 2008; Lindquist et al., 2012; Wagner et al., 2008). However, for the current purposes, the Wagner et al. (2008) meta-analysis is most instructive as it separates out studies of emotional experience (i.e. experiencing the emotion) from emotional perception (i.e. perceiving another’s emotion). This meta-analysis found DMPFC and VMPCF effects associated with emotional experience more so than emotion perception across 163 studies.

Within the Neurosynth database, the forward inference map for ‘emotion’ reveals broad coverage of DMPFC, AMPFC, and VMFC. Though it should be remembered that these studies represent a mix of emotional experience studies and emotion perception studies. Still, forward inference and the one relevant meta-analysis suggest that emotion tasks recruit DMPFC and VMFC.

3.4.2. Lesion

A small number of lesion studies have examined emotional experience or behavior, independent of valuation and reward, in a way that allows for inferences about subdivisions of MPFC, rather than MPFC or prefrontal cortex more generally. Two studies (Anderson et al., 2006; Hornak et al., 2003) observed general changes in emotional experiences of patients with VMFCF/AMPFC damage, though one of these (Hornak et al., 2003) reported that of the 21 patients with differential lesions, the three with the largest change in emotional experience had damage localized to DMPFC.

Three other studies examined more self-conscious emotions. Beer et al. (2003) reported that patients with VMFCF/AMPFC damage presented inappropriate self-conscious emotions (e.g. embarrassment). Two other studies examined regret with one study (Camille et al., 2004) showing that patients with VMFCF/AMPFC lesions did not show normal levels of regret after bad outcomes in a gambling task. The second study (Levens et al., 2014) did not show altered regret responses after poor gambling in patients with VMFCF/AMPFC lesions.

In summary, lesion evidence suggests that VMFCF/AMPFC lesions may interfere with emotional experience. Only one study (Hornak et al., 2003) included DMPFC patients and these patients showed a larger change in emotional experience compared to VMFCF/AMPFC patients.

3.4.3. Transcranial magnetic stimulation

We were not able to locate any TMS studies targeting MPFC contributions to emotional experience.

3.4.4. Multivariate pattern analysis

There are six MVPA studies of emotional experience that include coverage of MPFC regions. Four of these induced emotions using provocative images, movies, or music (Kragel and LaBar, 2015; Chang et al., 2015; Saarimäki et al., 2016). Saarimäki et al. (2016) observed clusters throughout DMPFC, AMPFC, and VMFC that decoded at least one of several emotions. Chang et al. (2015) also found that clusters throughout all of MPFC could decode ratings of emotional experience after looking at evocative images. Tsuche et al. (2016) found similar decoding effects for ratings of affective experience, but only in AMPFC. In contrast, Kragel and LaBar (2015) found little involvement of MPFC
regions in decoding seven different potential emotions. Only a small AMPFC cluster was involved in decoding the experience of contentment, but not any of the other emotions.

Tusche et al. (2014) conducted another study that examined emotionally-tinged thought, both directed and during rest. Participants were asked to imagine themselves behaving in ways that are consistent with a variety of traits that are positive (e.g. generous) or negative (e.g. vain). A cluster in VMPFC decoded positive from negative imaginings. This same cluster was then able to predict whether an individual was having spontaneously positive or negative thoughts during rest.

Finally, Kassam et al. (2013) asked actors to try to experience nine different emotions. A cluster in AMPFC successfully decoded positive from negative emotions. In contrast, a cluster in DMPFC successfully decoded social emotions that likely involve mentalizing (e.g. jealousy) from non-social emotions that do not (e.g. physical disgust).

In summary, AMPFC was most robustly associated with emotional experience among multivariate studies. This appears to primarily represent a valence dimension, which potentially relates to the valuation and self-relevance functions already ascribed to AMPFC above. DMPFC and VMPFC were each also identified in multiple studies, but less consistently than AMPFC.

3.4.5. Single-term reverse inference

The reverse inference Neurosynth map for ‘emotion’ produces modest clusters in DMPFC, AMPFC, and VMPFC. None of these clusters appear especially strong or cover most of the anatomical territory within each of these regions. Again, it should be remembered that ‘emotion’ as covered by Neurosynth includes many emotion perception studies that would fall into our social domain.

3.4.6. Summary

Most of the other domains covered thus far tend to show consistent evidence of relying on one or two areas of MPFC. Across the different methods we examine in this paper, emotional experience tends to link to DMPFC, AMPFC, and VMPFC (except for TMS, a domain for which there were no relevant papers). It is possible that all of these regions are doing emotion specific work, but it is also possible that some or all of these MPFC correlates of emotional experience reflect non-emotion specific functionality that is often called upon and used in the process of constructing emotional experiences. Many emotional experiences involve mentalizing, which could explain DMPFC effects (Kassam et al., 2013) and it is plausible that self-relevance processes which could explain AMPFC effects. These different accounts will be addressed in the section below on multi-term reverse inference.

3.5. Mental time travel

Mental time travel is a growing area of interest within psychology and cognitive neuroscience. The vast majority of mental time travel studies examine episodic memory and, as it pertains to MPFC specifically, episodic memory retrieval. More recently there have numerous studies focusing on mental time travel divorced from memory, in the form of future and past thinking and imagining. For instance, thinking about fictional pasts and futures is not strictly speaking an episodic memory task, but does require mental time travel. As mentioned above, autobiographical memory also involves mental time travel. However, given its overlap with the self domain, it is not focused on in either section unless the study is clearly emphasizing one of the two domains. Historically, mental time travel has been associated with AMPFC, VMPFC, medial temporal lobe, and posterior cingulate (Benoit and Schacter, 2015).

3.5.1. Forward inference

Mental time travel includes multiple concepts such as episodic retrieval, episodic past thinking, and episodic future thinking. There are multiple meta-analyses that focus on the neural basis of episodic memory, but these often focus exclusively on medial temporal lobe (Viard et al., 2012; Kühn and Gallinat, 2014). One meta-analysis (Gilbert et al., 2006) focused on frontal pole, but identified episodic retrieval with rostral-lateral PFC, rather than MPFC.

Meta-analyses that focus on both memory retrieval and future-focused thinking all show more MPFC involvement. Spreng et al. (2009) found that both autobiographical memory and future thinking recruits AMPC. Similarly, Benoit and Schacter (2015) found that both episodic retrieval and episodic future thinking recruit AMPC along with a dorsal region of VMPFC and a small cluster in DMPFC. Finally, Stawarczyk and D’Argeanbeau (2015) found that episodic future thinking produced clusters in AMFC and dorsal VMPFC.

The AMPC is robustly present in the forward inference Neurosynth maps for ‘episodic’, ‘future’, and ‘past’. Effects were exclusively in AMPC for ‘episodic’ and ‘future’, with respect to MPFC, whereas ‘past’ also produced VMPFC and DMPFC clusters.

Across meta-analyses and forward inference maps, there is clear evidence that mental time travel tasks produce activations in AMPC and the dorsal-most region of VMPFC. There is more modest evidence of DMPFC involvement in these tasks.

3.5.2. Lesion studies

The greatest number of lesion studies focusing on the role of MPFC in episodic memory primarily focus not on retrieval processes themselves, but rather the internal meta-cognitive judgments made about the information that has been retrieved. For instance, Gilboa et al. (2009) found that AMPFC and VMPFC lesions were associated with poorer metacognitive decision-making regarding the contents that come to mind during episodic retrieval. In other words, retrieval processes may yield multiple possible answers to an episodic memory search and then metacognitive processes are involved in judging between them (e.g. “which of those did I really see?”). Three other studies (Ciaramelli and Ghietti, 2007; Ciaramelli et al., 2006; Gilboa et al., 2006) demonstrate links between VMPFC and confabulation (i.e. the tendency to recall things that are not true or did not happen). These effects are generally understood in terms of meta-cognitive ‘feeling of rightness’ processes handled in VMPFC (Gilboa et al., 2006). Note that this kind of metacognitive process was also considered a component of self processes considered above.

Six other lesion studies focused on future thinking (Fellows and Farah, 2005b; Bertossi et al., 2016a; Urcztky and Gilboa, 2010; Volle et al., 2011; Umeda et al., 2011). All of them found a causal link between AMPFC damage, with three also pointing to VMPFC and two others showing effects associated with DMPFC.

Two studies from Bertossi et al. (2016a, b) were focused on further decomposing the contributions of MPFC to mental time travel. In one of these (Bertossi et al., 2016a), patients with AMPFC/ VMPFC damage produced fewer details related to their psychological experience and construal of past and future events, but had similar levels of details of external features of the events compared with control participants.

In the second study (Bertossi et al., 2016b), participants were asked to imagine future events as well as fictitious events that were not linked to any point in time (e.g. imagining a “bustling street market”). The AMPFC/VMPFC lesioned patients were impaired at constructing both types of scenes relative to other non-MPFC patients and healthy controls. Critically, lesion size in BA 10, but not BA 11, correlated with deficits in imagining future events, whereas lesion size in BA 11 was associated with deficits in imagining both future and fictitious events. The authors suggested that the results do not support a specific role for
BA 10/11 in mental time travel. Rather, they suggested that BA 11 is central to scene construction more generally (i.e., imagining a scene or situation) as lesion size there was related to deficits in imaginary scene construction whether or not the scene was not linked to a particular time. They also argued that the BA 10 effects may be more related to the additional self-relevant details involved in imagining future events than imaginary events. They point to other studies that suggest episodic future thinking is more related to personal goals and relies on details of self-knowledge in order to construe plausible personal future events (D’Argembeau and Mathy, 2011). Plausibility of fictitious events is not required and thus may depend less on self-knowledge.

In summary, lesion studies of mental time travel mostly point to AMPFC and VMPFC as key regions. Yet, some of these studies suggest that these regions might not be specific to mental time travel and instead might contribute to representations and processes that are relevant to, but also distinct from, mental time travel, per se. AMPFC and VMPFC lesions were associated with poor metacognitive decisions in episodic retrieval, which may be part of more general metacognitive or self-reflective processes in AMPFC. Finally, Bertossi et al. (2016b) suggests that VMPFC contributes to mental time travel because of a more general scene construction function that might also be invoked in other tasks that have little to do with mental time travel. We will return to this point towards the end of the paper.

3.5.3. Transcranial magnetic stimulation

We were not able to locate any TMS studies examining mental time travel effects associated with MPFC regions.

3.5.4. Multivariate pattern analysis

Of the three MVPA studies that examined decoding effects for mental time travel in MPFC regions (Johnson et al., 2009; Kuhl et al., 2012; Lewis-Peacock et al., 2016), only one had a positive result. Kuhl et al. (2012) asked participants to encode faces and scenes. A MPFC ROI that spanned BA9/10/11 could classify the faces versus scenes at encoding. This same ROI could also use the encoding data to classify subsequent memory performance.

3.5.5. Single-term reverse inference

We examined the generic Neurosynth reverse inference maps for ‘episodic’, ‘past’, and ‘future’. ‘Episodic’, and ‘future’, produced reverse inference effects in AMPFC. ‘Past’ also showed modest coverage in the dorsal aspect of VMPFC. It should be noted that while we did not intentionally include ‘autobiographical’ in the self or mental time travel Neurosynth analyses, 74 of the 108 studies tagged with autobiographical ended up in our mental time travel analysis because these studies were also tagged with another relevant term such as ‘episodic’ or ‘past’.

3.5.6. Summary

Across forward and reverse inference maps, meta-analyses, and lesion data, AMPFC and the dorsal aspect of VMPFC were consistently implicated in mental time travel tasks. TMS and MVPA effects were absent or too limited to draw any conclusions. Finally, multiple lesion studies raised issues of whether the MPFC link to mental time travel tasks reflects mental time travel processes, per se, or separate psychological processes (e.g. metacognition, self-knowledge, scene construction) that are relevant to mental time travel as well as other processes.

3.6. Multi-term reverse inference

Thus far, each psychological domain has been analyzed in isolation for evidence of its role in the functioning of the MPFC subdivisions. This is because the techniques we have reviewed rarely provide comparative data indicating whether a region of interest in the brain is more likely to be involved in one process rather than another. Although the web-based Neurosynth tools do not allow particular psychological terms to be compared to one another, Neurosynth’s Python-based core tools can be used to compare terms directly (e.g. ‘social’ versus ‘self’).

For our five domains of interest, we used these tools in the following way. First, we created our own domain-specific terms aggregating the studies from multiple terms in the Neurosynth database. For the social domain, we included the terms ‘social’ and ‘mentalizing’ which together yielded 1045 studies (i.e. studies tagged with either ‘social’ and/or ‘mentalizing’). For the self domain, we just used the term ‘self’ (903 studies). For the value domain, we used the terms ‘value,’ ‘reward,’ and ‘incentive’ (906 studies). For the emotion domain, we used the terms ‘emotion,’ ‘emotional,’ ‘emotionally,’ and ‘emotions’ (1690 studies). Finally, for the mental time travel domain, we used the terms ‘episodic,’ ‘future,’ ‘past,’ ‘retrieval,’ ‘prospective,’ and ‘memory retrieval’ (1395 studies). Note that some terms that were used in earlier parts of this paper to search for articles were not available as search terms in Neurosynth.

We used Neurosynth to directly compare, via random sampling, the maximum number of studies in each pairing that was possible while producing equal numbers per term. Thus, we created a fair empirical prior of 0.50 for each term. Matched random samples of studies were generated 500 times for each term comparison and then the results of those iterated samples averaged together.

We examined posterior probabilities and used a threshold of 0.60 in these head-to-head term comparisons to indicate a voxel is more likely to be associated with one psychological domain rather than another. Because these are head-to-head match-ups, when one term has a posterior probability of at least 0.60 in a voxel, the other term must have a posterior probability of 0.40 or less, as posterior probabilities in a head-to-head match up always add to 1. Thus, if in a ‘social’ versus ‘self’ comparison, a DMFP vacel has a posterior probability of 0.60 for the social domain and 0.40 for the self domain, then an observed effect seen in this voxel in a study drawn at random from this sampling is 50% more likely to have come from the social domain than the self domain (i.e. 0.60 is 50% greater than 0.40). Note that in this case, there is still a reasonable chance that a study came from the non-winning domain. But voxels present in this analysis were substantially more likely to have come from the ‘winning’ domain. Voxels that meet the 0.60 threshold are referred to as dominant win voxels in contrast to voxels that are merely greater than 0.50, which are referred to as simple win voxels.

We ran all 20 possible combinations of our five domains in one-on-one matchups (see Fig. 2). We next identified voxels that had posterior probabilities of 0.60 in each and every comparison of a target domain to the remaining four domains. Thus, when ‘social’ was the target domain, we identified voxels that had posterior probabilities of at least 0.60 in. (‘social’ versus ‘self’) AND (‘social’ versus ‘value’) AND (‘social’ versus ‘emotion’) AND (‘social’ versus ‘mental time travel’).

Fig. 3 shows the resulting maps with one panel per domain showing the sagittal slice with the most voxels for that domain. For each domain, yellow voxels represent dominant wins against all four other domains, and red voxels represent dominant wins against three of the other four domains.

As can be seen in Fig. 3, the social, self, value, and emotion domains each have sizable clusters in distinct regions of MPFC that are associated with that domain more than every other domain of interest. The social domain produced higher posterior probabilities than the self, value, emotion, and mental time travel domains primarily in DMFP (254 voxels) with another smaller cluster in posterior VMFP (111 voxels). The self domain produced higher posterior probabilities than the social, value, emotion, and mental time travel domains primarily in AMPFC (143 voxels). The value domain produced higher pos-
terior probabilities than the self, social, emotion, and mental time travel domains in multiple clusters within AMPFC (161 voxels) and VMPFC (471 voxels), somewhat right lateralized. The emotion domain produced higher posterior probabilities than the self, social, value, and mental time travel domains in anterior VMPFC (107 voxels), somewhat left lateralized. Finally, there were only 27 voxels for which mental time travel had at least a 0.60 posterior probability against self, social, value, and emotion domains. However, closer inspection suggests that most of these are frontopolar rather than on the medial PFC wall.

In this paper, we have chosen to focus on posterior probabilities rather than Z-scores and their associated p-values (Yarkoni, 2015). That said, some are likely to value knowing the p-values associated with the analyses from the previous paragraph. In order to estimate the p-values, we identified voxels just meeting our minimum threshold (i.e. between 0.60 and .61) and identified the Z-score for each of these voxels. We averaged these Z-scores and then computed the associated p-value. The resulting p-values from each of the four analyses that contribute to each four-way conjunction analysis (e.g. ‘social’ > ‘emotion’ AND ‘social’ > ‘mental time travel’ AND ‘social’ > ‘self’ AND ‘social’ > ‘value’) were multiplied together to yield the probability of a voxel being significant in all four analyses. For voxels associated with the social domain more than the other domains, the four-way conjunction p-values were <.00033. For the self domain they were <.00027. For the value domain they were <.00016. For the emotion domain they were <.00053. And for the mental time travel domain they were <.00041. In each domain other than mental time travel, the clusters typically involved a few dozen voxels at a minimum and thus the combination of voxel-level probability and cluster extent indicates that these are meaningful conjunction clusters.

It is worth noting that of the dominant winners (when one domain wins over the other four, each at the 0.60 threshold), 85% of the dominant winners in all of DMPFC were accounted for by the social domain. Within AMPFC, the self and value domains accounted for 36% and 40% of dominant winners, respectively. Finally, in VMPFC, value accounted for 64% of the dominant winners.

Although only 17% (1429 of 8429) of all MPFC voxels are accounted for by dominant winners, 88% (7426 of 8429) are accounted for by simple winners (when one domain wins over the other four, each at a > .50 threshold), substantially higher than the 6% rate that would be expected from chance alone. Fig. 4A displays simple winners from domains that ‘won’ sizable chunks of MPFC including social, self, and affective domains. Affective refers to value and emotion domains combined. Fig. 4B shows simple winners from each domain within each MPFC subdivision. Notable here is that social wins 55% of DMPFC voxels, self and value each win 30% of AMPFC voxels, and value wins 37% of VMPFC voxels. In total, simple winners account for 99% of DMPFC voxels (2124 of 2154), 98% of AMPFC voxels (2960 of 3035), but only 75% of VMPFC (2406 of 3240). We should note that while the general pattern associated with the simple winners is informative, it assuredly includes numerous Type I errors.

Given that nearly all of MPFC was accounted for by simple winners except in VMPFC, we ran an additional analysis in order to characterize the no-winner voxels in VMPFC. Specifically, we looked for voxels that were not won by any one domain, but that instead showed single-term reverse inference effects for each of the five domains at a posterior probability of 0.60. Such voxels are presumably relevant to all five domains but not preferentially related to any of them of the others. Although we searched the entire MPFC ROI, almost all of the non-selective voxels emerging from this analysis were in VMPFC, largely in a single cluster (329 voxels; see the pink region in Fig. 4A) that fill the gap described in the previous analysis.

One plausible explanation for this non-selective cluster is that it performs a function that is distinct from all of our domains of interest, but that it often makes an important contribution to the functioning of

Fig. 2. Multi-term head-to-head reverse inference maps. Each row shows reverse inference maps of voxels for which the term at the start of the row has a posterior probability of at least 0.60 when compared with one of the other four terms. The parenthetical number under each term at the start of the row indicates the total number of studies for that term in the Neurosynth data (though most terms are aggregates of multiple terms, as described in the text). The parenthetical number next to each brain image indicates the number of studies from each term used in that comparison. Thus, the 866 in the social > value image indicates that there were 866 studies tagged with social terms and 866 tagged with value terms considered in each iteration of this analysis. Arrows indicate regions that were present in each comparison in that row and thus are present in Fig. 3.
those domains. For instance, Bertossi et al. (2016b) suggested that what might appear to be mental time travel effects in VMPFC may really reflect scene construction. As it turns out, the single-term reverse inference maps for ‘scene’ and ‘events’ looks quite similar to the non-selective clusters in VMPFC (see Fig. 5). In a later section, we will consider the possibility that scene construction is one of a class of processes involved in situational processing more broadly that may be linked to this region of VMPFC.

3.7. Neurosynth analyses for all functional terms

It is plausible that despite our best efforts to choose domains that are strong candidates for MPFC functionality, there are better functional descriptions of these regions that we neglected. There are 3107 terms in the Neurosynth database (though many do not describe psychological functions) and we have only considered a handful. Thus, in a final set of analyses, we examined our ROIs for the set of terms, out of all functional-related terms in the Neurosynth database, that produced the highest average posterior probability for each ROI.

Table 1 shows the top 30 psychologically-meaningful terms for the three anatomical subdivisions of MPFC. Terms that were left out were almost uniformly anatomical names (e.g. ‘medial prefrontal’, ‘dorsomedial’, etc.) Note that the bolded capitalized terms are the terms we constructed for the multi-term reverse inference analyses above. As can be seen, the top terms for DMPFC are dominated by social cognition terms. The top terms for AMPFC tend towards self and value processes, but show a mix across domains. For VMPFC, the top terms focus on emotion, value, and social processes with some other clinical relevant terms such as ‘age’, ‘disorder’, ‘regulation’, and ‘disease’. These results largely confirm our initial choice of domains.

Table 2 shows the same type of analysis conducted on the clusters identified in the multi-term reverse inference analyses above, based on voxels that are dominant winners for one term over each of the four other terms. Thus, for the cluster that emerges for the social domain in the multi-term reverse inference analysis, our constructed social term is the highest functional term in the entire database (followed closely by a variety of other social cognitive terms). Here, our constructed terms were the highest term for clusters associated with social, self, value and emotion. Mental time travel was near the top of the list for its cluster, preceded only by other related memory terms. We see this analysis essentially as a post-hoc manipulation check against the possibility that other unexamined terms actually account for the function of these regions better than those we chose to look at.

4. Discussion

4.1. Integrating the results

Prior to the current review, previous reviews have relied almost exclusively on forward inference to summarize the role of mPFC in social, self, affective, and mental time travel processes. In each of these domains, meta-analyses or forward inference analyses suggest a reliable presence in all three MPFC subdivisions (Fig. 1B).

By looking to other sources of data (lesion, TMS, MVP, Neurosynth), we hoped that collectively they would provide additional insight into psychological functionality within MPFC subdivisions. There are clearly limitations to this approach. For instance, DMPFC lesions are rare, TMS in VMPFC is currently impossible, and Neurosynth is based on linking article text with peak activations using automated algorithms that are assuredly an imperfect way to link structure to func-

Fig. 3. Multi-term reverse inference maps comparing all five domains. For each map, yellow voxels indicate that the associated term had at least a .60 posterior probability in all four head-to-head matchups against the other terms. The bar graph shows this for a single voxel within DMPFC for the ‘social’ analysis. At this voxel, the posterior probability exceeds the dotted line representing .60 against mental time travel AND self AND value AND emotion. Red voxels indicate that the .60 threshold was met for three of the four head-to-head matchups. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)
Fig. 4. Multi-term reverse inference maps showing ‘simple winners’. (a) Showing results for social, self, and affective (value + emotion) that each ‘won’ sizable clusters of MPFC. Green, blue, and yellow voxels indicate that the associated term had >.50 posterior probability in all four head-to-head matchups against the other terms. The pink area indicates voxels deemed as non-selective because they show single-term reverse inference posterior probabilities of at least 0.60 for each of the five domains of interest, but are not dominate by any single domain. Based on literature reviewed in the text, we speculate that this area of VMPFC may be involved in situational processing; (b) The percent of simple winners (i.e. >.50 posterior probability against each of the other four terms) for each term in each MPFC subdivision. Here, pink indicates the percent of voxels unaccounted for by any of the domains within each subdivision. 
(For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Fig. 5. Single-term reverse inference maps for ‘scene’ and ‘events,’ both relevant to situational processing.

tion. Nevertheless, we believe that this review does make some progress towards linking psychological functions with MPFC subdivisions.

Table 3 represents our summary of the evidence within each method (lesion, TMS, MVPA, single-term reverse inference, multiple-term reverse inference) supporting links between the five domains of interest (social, self, value, emotion, mental time travel) and each MPFC subdivision (DMPFC, AMPFC, VMPFC). For each method, we indicated whether the evidence was absent (‘none’), ‘weak’, ‘moderate’, or ‘strong.’ ‘None’ indicates that analyses were run that could have yielded evidence linking a particular domain to a particular subdivision but that the evidence did not show this relationship. In contrast, “n/a” was used when there was little or no data available for making this assessment. To generate an overall assessment of each domain’s link to each subdivision, we converted our labels to a scale: none = 1, weak = 2, moderate = 3, strong = 4. All numbers for a row were averaged together (with "n/a" cells ignored). The overall assessment was then converted back to labels: ≥3.5 strong, ≥2.5 moderate, ≥1.5 weak, <1.5 none.
Table 1

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</table>

This summary data suggests reliable separation of psychological function across the three subdivisions of MPFC. Specifically, only the social domain received an overall assessment of “strong” in DMPFC. Both the self and value domains received an overall assessment of “strong” in AMPFC. Finally, only the two affective domains of value and emotion received overall assessments of “strong” in VMPFC. There was moderate overall evidence linking mental time travel to both AMPFC and VMPFC.

One surprising finding seen in Fig. 4A (and consistent with Table 3), is that there is a ventral cluster in VMPFC that is more strongly associated with social processes than the other constructs examined in this review. This was unexpected because this region does not typically appear in meta-analyses of social cognition, nor did it appear in our forward inference Neurosynth analysis of the social domain. A likely culprit for this disparity between forward and reverse inference analyses is signal dropout. The ventral surface of VMPFC is one of the regions most susceptible to dropout effects, which leads to Type II errors, the failure to reveal true effects. The Neurosynth database only has about a quarter as many studies overall producing effects at the center of this VMPFC social cluster as it does at the center of the DMPFC social cluster. This might impair the ability of forward inference analyses, like meta-analyses, to detect the VMPFC cluster because forward inference depends on accumulated evidence across a large number of studies. In contrast, reverse inference is about probabilities of one domain being responsible for observed effects in a region, relative to one or more other domains and thus, these will be less affected by raw counts.

To inspect things further, we looked at all 3000+ terms in the Neurosynth database to see which terms ranked highest as reverse inference targets for activations associated with this VMPFC ‘social’ cluster. The terms ‘social’ and ‘social cognitive’ had the first and third highest posterior probabilities across all psychological terms (‘impaired’ was second). Other terms in the top 30 included ‘interpersonal’, ‘beliefs’, ‘traits’, ‘social interaction’, ‘social cognition’, and ‘autism’. There were also some emotion related terms including ‘positively’, ‘negatively’, ‘loss’, and ‘emotional’. Finally, two terms, ‘Alzheimer’ and ‘demential’ were potentially related to memory.

4.2. Situational processing in VMPFC

As noted above and seen in Fig. 4A, another substantial cluster in VMPFC is non-selective within MPFC among the five domains of interest. Here, we consider the possibility that this general region may be associated with situational processing. Unlike the evidence for all the other domains considered in this paper, there are many fewer studies specifically examining the neural bases of situational processing and its component processes. Thus, our suggestion is best taken as an educated guess and a call for further research – hence the parenthetical in the article’s title. Let us consider the constituent components of situational processing and how it is relevant to several of the other domains of interest.

The vicinity of this VMPFC cluster is often observed in studies of memory retrieval and mental time travel, but as Bertossi et al. (2016b) observed, VMPFC lesions may impair scene construction (e.g. imagining a “bustling street market”) rather than mental time travel, per se. Several studies implicate the VMPFC cluster of interest in the representations of scenes (Bertossi et al., 2016b; Hassabis et al., 2013, 2007; Addis et al., 2009; Summerfield et al., 2010). The ability to represent the spatial layout of scenes is frequently relevant to mental time travel. For instance, remembering where one parked in the parking lot is aided by being able to reconstruct an image of the layout of the lot. As noted above (see Fig. 5), the terms ‘scene’ and ‘events’ both produce single-term reverse inference effects that overlap substantially with the non-selective VMPFC cluster.

Evidence suggests that VMPFC may be doing more than representing the visual aspects of scenes. Instead, it may be representing a collection of associated bits of knowledge that go together with the scene or a given context (Aminoff and Tarr, 2015). Thus, when we say that VMPFC may support situational processing, we are referring to how a situation is represented more completely in terms of spatial, temporal, causal, evaluative, and social aspects. When these are considered together, they reflect an integrated set of situational associations.

Schemas are generalizations and associative sets that are abstracted from individual experiences and events, and thus might contain this kind of integrated situational knowledge base. Once schemas are in place they serve several functions including (a) providing context to guide interpretation of ambiguous stimuli and events and (b) integrating new experiences into existing schemas. As with scene processing, there are a number of studies that link VMPFC to schematic processing (e.g. Lieberman et al., 2004). Patients with BA 11 lesions show diminished assimilation of new information to schemas (Spalding et al., 2015) and less schema-biased recall (Warren et al., 2014; see also Ghosh et al., 2014). Multiple studies have observed greater VMPFC activity or connectivity when encoding new information that is congruent with an existing schema (Bar et al., 2008; Aminoff et al., 2008; Schlichting and Preston, 2015; Sommer, 2016; Tse et al., 2011; van Kesteren et al., 2014).

Additionally, a series of studies have implicated VMPFC when a cue indicates the relevant situation for contextualizing the ambiguous material (Ames et al., 2015; Yeshurun et al., 2017; Maguire et al., 1999; van Kesteren et al., 2010). Building off of classic studies of situational cueing from Bransford and Johnson (1972), these studies present participants materials that are either unclear or can be understood in mul-
Table 2
Terms with greatest reverse inference evidence within functionally defined clusters derived from Fig. 3 (i.e. clusters for which each voxel was a dominant winner for one domain term over the four other domain terms).

<table>
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Table 3
Summary of results for each domain within each MPFC subdivision for each methodology. Note that ‘none’ indicates that analyses were presented that could have provided evidence but that little or no evidence was observed. In contrast, ‘n/a’ indicates that there were not enough studies that could have provided relevant evidence to assess the structure-function link at all. $R_{single}$ refers to single-term reverse inference and $R_{multi}$ refers to multi-term reverse inference.

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<td>n/a</td>
<td>Moderate</td>
<td>None</td>
</tr>
<tr>
<td>VMPF</td>
<td>Strong</td>
<td>Strong</td>
<td>n/a</td>
<td>Moderate</td>
<td>Strong</td>
</tr>
<tr>
<td>MTT</td>
<td>DMFFC</td>
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<td>Moderate</td>
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<tr>
<td>AMPFFC</td>
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<td>n/a</td>
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<td>Weak</td>
</tr>
<tr>
<td>VMFFC</td>
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<td>Strong</td>
<td>n/a</td>
<td>Moderate</td>
<td>None</td>
</tr>
</tbody>
</table>

tiple distinct ways. For instance, Ames et al. (2015) showed vignettes to participants that included ambiguous statements such as “kicking and stomping are usually required”. Sometimes these statements were disambiguated with a picture (e.g. someone waving a tire) and other times the picture shown was irrelevant. In this study, participants shown the correct situational cue, showed stronger intersubject correlations in VMFFC suggesting that VMFFC-based situational processes may help to bring individuals into a similar psychological state of understanding.

Based on this evidence, we echo a small number of other scientists who have posited this region of VMFFC is involved in situational processing (Krueger et al., 2009; Ranganath and Ritchey, 2012; for a review of similar account describing this region as involved in a contextual associations network, see Aminoff, 2014). This VMFFC cluster may appear in studies across various domains because situational processing and its components (scene construction and schema-based cognition) are relevant to the various domains. Scene construction and schema-based processes are increasingly identified as central to mental time travel without actually being mental time travel. Social cognition was partially founded as a field that examines how people are influenced by situations and how humans are more likely to attribute their own foibles to situational causes, but not to excuse the foibles of others in this way. In the context of mentalizing, some tasks require keeping a particular situation in mind within which the actors are thinking, feeling, and acting. For example, knowing whether two people are in a public or private setting alters the presumed links between their thoughts and their actions.
Finally, our emotional experiences and our assessments of value are influenced by our understanding of our situation or the context that a choice takes place in. If person A bumps into and knocks over person B, person B’s emotional reaction will depend on whether she sees the physical contact as intentional or accidental. If the situational context is a narrow icy path that A and B were walking on, this could certainly influence person B’s appraisal and subsequent emotional reaction.

Further investigating a link between situational processing and VMPCF, as well as the role of situational processing in other domains, requires new research. For instance, MVPA studies might focus on one or more of the different domains considered here and manipulate the presence/relevance of situational information. Comparing mentalizing tasks that do and do not depend on situational processing on different trials could help tease apart regions that are intrinsic to mentalizing and regions that support situational processing, but not mentalizing per se. The same could be done in each of the other domains as well. Additionally, future studies could examine which features and dimensions of situations are and are not represented here and how collectively these dimensions produce integrated outputs that can motivate situationally-guided behavior.

Given the well-known finding that people tend to overlook or under-estimate the impact of situational processes in general (Gilbert and Malone, 1995), it would be important to identify the neural bases of successful situational processing, to identify individual differences, moderators, and even training that might enhance the application of these neural processes. Some have suggested that over-looking the power of situations is one of the greatest sources of error in human interactions and yet, to date, this has largely been overlooked within the social neuroscience literature.

5. Conclusion

As we said at the opening of this article, each mPFC researcher probably has at least a slightly different theory of mPFC function. To be sure, we came to this article with our own conceptions. We employed a data-driven approach relying on different sources of evidence relevant to making claims about MPFC function. Some of the results surprised us. We expected social to be strongly represented in DMPCF, but did not expect the cluster to VMPCF that was more strongly associated with social than any of the other domains. We expected the value domain to be primarily localized to VMPCF, but it is similarly represented in VMPCF and AMPCF. Situational processing was not even on our radar when we began this review, but the evidence suggests it would be a valuable addition to social and affective neuroscience research.

Some may object to our giving Neurosynth-based multi-term reverse inference analyses significant weight in helping to assign functions to regions. However, whatever limitations it may have, it is a superior tool for this job than using forward inference analyses (e.g. meta-analyses) which are typically used to inform reverse inference intuitions and yet logically inappropriate for doing so.

We have no doubt that our review is not the final word on MPFC function, but we do hope that our review has helped to clarify some issues and perhaps spur new research in the future.

Uncited references

Hornak et al. (1996) and Irish et al. (2013).

References


