Distinct Regions of the Medial Prefrontal Cortex Are Associated with Self-referential Processing and Perspective Taking

Arnaud D'Argembeau[1], Perrine Ruby[1,2], Fabienne Collette[1], Christian Degueldre[1], Evelyne Balteau[1], André Luxen[1], Pierre Maquet[1], and Eric Salmon[1]

Abstract

■ The medial prefrontal cortex (MPFC) appears to play a prominent role in two fundamental aspects of social cognition, that is, self-referential processing and perspective taking. However, it is currently unclear whether the same or different regions of the MPFC mediate these two interdependent processes. This functional magnetic resonance imaging study sought to clarify the issue by manipulating both dimensions in a factorial design. Participants judged the extent to which trait adjectives described their own personality (e.g., "Are you sociable?") or the personality of a close friend (e.g., "Is Caroline sociable?") and were also asked to put themselves in the place of their friend (i.e., to take a third-person perspective) and estimate how this person would judge the adjectives, with the target of the judgments again being either the self (e.g., "According to Caroline, are you sociable?") or the other person (e.g., "According to Caroline, is she sociable?"). We found that self-referential processing (i.e., judgments targeting the self vs. the other person) yielded activation in the ventral and dorsal anterior MPFC, whereas perspective taking (i.e., adopting the other person's perspective, rather than one's own, when making judgments) resulted in activation in the posterior dorsal MPFC; the interaction between the two dimensions yielded activation in the left dorsal MPFC. These findings show that self-referential processing and perspective taking recruit distinct regions of the MPFC and suggest that the left dorsal MPFC may be involved in decoupling one's own from other people's perspectives on the self. ■

INTRODUCTION

With the emergence of social cognitive neuroscience (Adolphs, 2003; Ochsner & Lieberman, 2001), functional neuroimaging studies have started to identify the neural correlates of various aspects of self-referential processing, such as the recognition of one's own physical appearance (Sugiura et al., 2005; Platek, Keenan, Gallup, & Mohamed, 2004; Kircher et al., 2000), awareness of one's own actions (Blakemore & Frith, 2003), and knowledge of one's own personality traits and abilities (Heatherton et al., 2006; D'Argembeau et al., 2005; Ochsner et al., 2005; Lieberman, Jarcho, & Satpute, 2004; Lou et al., 2004; Macrae, Moran, Heatherton, Banfield, & Kelley, 2004; Schmitz, Kawahara-Baccus, & Johnson, 2004; Fossati et al., 2003; Johnson et al., 2002; Kelley et al., 2002; Kircher et al., 2002; Kjaer, Nowak, & Lou, 2002; Craik et al., 1999). Cortical midline structures appear to play a key role in these self-referential processes (Northoff et al., 2006; Northoff & Bermpohl, 2004). For instance, several studies have investigated the brain regions recruited when people evaluate the self-descriptiveness of adjectives or sentences describing personality traits (Heatherton et al., 2006; Ochsner et al., 2005; Lieberman et al., 2004; Lou et al., 2004; Macrae et al., 2004; Schmitz et al., 2004; Fossati et al., 2003; Johnson et al., 2002; Kelley et al., 2002; Kircher et al., 2002; Craik et al., 1999) or simply think freely about their own personality (D'Argembeau et al., 2005; Kjaer et al., 2002), as compared to when they reflect on the personality traits of another person or make judgments of factual knowledge. The neural correlates of self-referential processing most consistently observed across these studies are located in the medial prefrontal cortex (MPFC) and in medial posterior regions (in the posterior cingulate cortex or the precuneus), indicating that these structures are important for representing self-knowledge (Northoff et al., 2006; Northoff & Bermpohl, 2004).

Another line of research has highlighted the role of the MPFC in adopting the perspective of other people and representing their mental states (Decety & Jackson, 2004; Ruby & Decety, 2003, 2004; Frith & Frith, 2003; Gallagher & Frith, 2003). Some perspective-taking studies have investigated the brain regions recruited when we "put ourselves in another person's shoes" to

[1]University of Liège, Belgium, [2]INSERM, U280, Lyon, F-69500, France

represent his or her knowledge or experience (taking a third-person perspective), as compared to our own knowledge or experience (the first-person perspective) (Ruby & Decety, 2001, 2003, 2004; Vogeley & Fink, 2003). We take a third-person perspective, for instance, when we try to appreciate what another person thinks about a particular topic (Ruby & Decety, 2003, 2004) or how he or she would feel in a given situation (Ruby & Decety, 2004). Taking a third-person perspective, as opposed to a first-person perspective, in the domain of action, knowledge, or emotion has been associated with activation in the inferior parietal cortex (predominantly in the right hemisphere), the medial parietal cortex (in the posterior cingulate cortex/precuneus), and the MPFC (Ruby & Decety, 2001, 2003, 2004). Studies that have investigated the neural underpinnings of the ability to infer the mental states of others (i.e., "theory of mind" or "mentalizing") also point to the MPFC, along with the temporoparietal junction and the temporal poles, as being important for appreciating other people's intentions, beliefs, or desires (Frith & Frith, 2003; Gallagher & Frith, 2003).

This overview shows that the MPFC is not only recruited when one reflects on oneself but also when one adopts the perspective of others, suggesting that common component processes might underlie both of these mental activities (Decety & Jackson, 2004; Frith & Frith, 2003; Gallagher & Frith, 2003). However, it should be noted that there is considerable variance regarding the precise location of the reported medial prefrontal activations, both in studies of self-referential processing and in studies of perspective taking. Indeed, the reported activations encompass virtually the entire MPFC, spanning the dorsal (including Brodmann's areas [BAs] 6, 8, and 9) and ventral (BAs 10, 11, 14, and 25) MPFC as well as the anterior cingulate cortex (BAs 24 and 32) (see the review by Ochsner et al., 2004, and the meta-analysis by Northoff et al., 2006). It is therefore likely that different subregions of the MPFC mediate different processes or representations (Amodio & Frith, 2006; Northoff & Bermpohl, 2004), some of which may be specifically recruited for self-referential processing, and others for perspective taking. In this respect, Mitchell and colleagues (Mitchell, Macrae, & Banaji, 2006; Mitchell, Banaji, & Macrae, 2005b) have recently suggested that the ventral part of the MPFC is primarily involved in self-referential processing and is also engaged when judgments about others' mental states involve a self-referential component (i.e., during simulations), whereas the dorsal part of the MPFC may instantiate more universally applicable social–cognitive processes that can aid mentalizing when self-referential processing is inappropriate (e.g., when trying to understand the mind of people assumed to be dissimilar from oneself).

However, because self-referential processing and perspective taking have not been manipulated within a single study, it is difficult to conclude with certainty that these two processes recruit partly distinct regions of the MPFC. Cross-study comparisons of brain activation foci are indeed obscured by various factors that could lead to apparently similar or dissimilar patterns of activation, such as individual differences in functional brain anatomy and differences in methods used to spatially normalize and analyze data. Furthermore, the tasks that have been used in previous studies to investigate self-referential processing or perspective taking probably engaged a mixture of both types of processes. Indeed, at least in certain circumstances, we take the perspective of others by considering what would be our own mental state if we were in the other's situation (Gallese & Goldman, 1998). Self-knowledge may thus serve as an anchor point for understanding others (Epley, Keysar, Van Boven, & Gilovich, 2004), especially when trying to understand the mind of people who are perceived as being similar to, rather than dissimilar from, oneself (Mitchell et al., 2005b, 2006). It is therefore likely that at least some of the perspective-taking tasks that have been used in previous studies implicitly required some amount of self-referential processing. Conversely, self-knowledge may in part be derived from our perception of what others think of us (Tice & Wallace, 2003), so that the self-judgment tasks used in previous studies may have implicitly contained a perspective-taking component. In consequence, it is likely that the neural correlates that have been previously associated with perspective taking were in part contaminated by self-referential processing and vice versa.

Considering these issues, the aim of the present functional magnetic resonance imaging (fMRI) study was to disentangle the neural correlates of self-referential processing and perspective taking, using a 2×2 factorial design in which both dimensions were manipulated. Participants had to make four types of judgments on a series of adjectives describing personality traits. Two types of judgments required participants to adopt a first-person perspective when assessing the extent to which the adjectives described their own personality (first-person perspective on the self [1P_Self], e.g., "Are you sociable?") or the personality of a close friend (first-person perspective on the other [1P_Other], e.g., "Is Caroline sociable?"). By contrast, in the two remaining conditions, participants were asked to put themselves in the place of their friend (to take a third-person perspective) and estimate how this person would judge the adjectives, with the target of the judgments again being either the self (third-person perspective on the self [3P_Self], e.g., "According to Caroline, are you sociable?") or the other person (third-person perspective on the other [3P_Other], e.g., "According to Caroline, is she sociable?").

To the best of our knowledge, only one functional neuroimaging study has included conditions that required taking both first-person and third-person perspectives on one's own personality (Ochsner et al., 2005). It was found that both types of perspective activated similar regions of the MPFC (BAs 8, 9, 10, and 25) compared to baseline perceptual judgments, and a direct comparison between first-person and third-person perspectives did not reveal any differential activation in the MPFC. However, that study did not include a comparison condition that requires participants to take a third-person perspective on someone else's personality, and therefore did not allow one to fully disentangle the effect of judgment target (self vs. other) from the effect of perspective (third person vs. first person). Accordingly, a particular strength of our design was the opportunity to compare the effects of each of these dimensions in order to get a clearer picture of the specific neural correlates of self-referential processing and perspective taking. In addition, the factorial design we used enabled us to examine the neural correlates associated with the interaction between the two processes. In particular, we were interested in investigating the brain regions specifically recruited during the process of reflecting on what others think about the self, that is, when people try to disengage from their own perspective to consider the self (vs. someone else) from a third-person (vs. first-person) perspective.

METHODS

Participants

Data were acquired from 17 right-handed French-speaking young adults (11 women; mean age = 23 years, *SD* = 3.4 years). All participants gave their written informed consent prior to their inclusion in the study, which was approved by the Ethics Committee of the Faculty of Medicine of the University of Liège and was performed in accordance with the ethical standards described in the Helsinki Declaration. None of the participants had any relevant medical history or used any centrally acting medication.

Task Description

Before the experiment began, participants were asked to identify someone they personally knew well (a close friend or relative), who was used as the "close other" during the scanning session. We used a close other rather than a public figure as the comparison person to minimize the possibility that the observed activations reflect the amount of knowledge and/or affective response rather than the self versus other distinction per se (Gillihan & Farah, 2005). The tasks that were performed during the scanning session consisted in making judgments on a series of adjectives describing personality traits. The perspective taken by the participants when making their judgments and the judgment target were manipulated according to a 2 × 2 factorial design, resulting in four conditions: taking a first-person perspective when making judgments about the self (1P_Self), taking a first-person perspective when making judgments about a close other (1P_Other), taking a third-person perspective when making judgments about the self (3P_Self), and taking a third-person perspective when making judgments about a close other (3P_Other). The 1P_Self condition required participants to evaluate the extent to which the adjectives described their own personality traits (e.g., "Are you sociable?"), whereas the 1P_Other condition required them to evaluate the extent to which the adjectives described the personality traits of their friend or relative (e.g., "Is Caroline sociable?"). Both these conditions therefore required participants to express their own opinion when making their judgments. By contrast, in the 3P_Self and 3P_Other conditions, participants were asked to "put themselves in the shoes of their friend or relative" in order to estimate how this person would assess the adjectives. Specifically, the 3P_Self condition required participants to evaluate the extent to which the adjectives described the way they are perceived by their friend or relative in terms of personality traits (e.g., "According to Caroline, are you sociable?"). In the 3P_Other condition, participants evaluated the extent to which the adjectives described the way their friend or relative perceived their own personality traits (e.g., "According to Caroline, is she sociable?").

The same set of 40 trait adjectives was used in all four conditions. These adjectives were selected from those used in previous studies of self-referential personality judgments (Klein, Loftus, & Kihlstrom, 1996) and were translated into French. The four conditions were presented in a single session, using a block design. There were 10 blocks per condition. Each block consisted of four trials lasting 5 sec each; thus, each block lasted 20 sec. In each trial, an adjective was presented for 5 sec, during which the participants were required to make their judgment, by pressing one of four buttons (1 = *not at all*, 2 = *a little*, 3 = *quite well*, 4 = *completely*). Three seconds before the start of each block, a brief instruction appeared on the screen to inform participants about the type of judgment they had to make for the adjectives presented subsequently (1P_Self: "You are"; 1P_Other: "X is"; 3P_Self: "According to X, you are"; 3P_Other: "According to X, he or she is," where "X" was replaced by the first name of the selected friend or relative); then, the four adjectives were presented sequentially below this instruction, which remained on the screen for the entire duration of the block. Blocks were separated by a variable interval of 7–12 sec during which participants passively viewed a fixation cross that was used as a baseline. A different random order for the presentation of the four conditions was generated for each participant, and this order was repeated 10 times throughout the scanning session. Practice trials were performed before the scanning session in order to familiarize participants with the four types of judgments.

MRI Acquisition

Data were acquired on a 3-T scanner (Siemens, Allegra, Erlangen, Germany) using a T2* sensitive gradient-echo echo-planar imaging (EPI) sequence (TR = 2130 msec, TE = 40 msec, FA 90°, matrix size 64 × 64 × 32, voxel size 3.4 × 3.4 × 3.4 mm^3). Thirty-two 3-mm-thick transverse slices (FOV 22 × 22 cm^2) were acquired, with a distance factor of 30%, covering the whole brain. Structural images were obtained using a T1-weighted 3-D MP-RAGE sequence (TR = 1960 msec, TE = 4.4 msec, FOV 23 × 23 cm^2, matrix size 256 × 256 × 176, voxel size 0.9 × 0.9 × 0.9 mm). In each session, between 629 and 650 functional volumes were obtained. The first three volumes were discarded to account for T1 saturation. Head movement was minimized by restraining the subject's head with a vacuum cushion. Stimuli were displayed on a screen positioned at the rear of the scanner, which the subject could comfortably see through a mirror mounted on the standard head coil.

MRI Analyses

Data were preprocessed and analyzed using SPM2 software (Wellcome Department of Imaging Neuroscience, www.fil.ion.ucl.ac.uk/spm) implemented in MATLAB (Mathworks Inc., Sherborn, MA). Functional scans were realigned by using iterative rigid body transformations that minimize the residual sum of squares between the first and subsequent images. They were normalized to the MNI EPI template (voxel size 2 × 2 × 2 mm) and spatially smoothed with a Gaussian kernel with full width at half maximum (FWHM) of 8 mm.

For each participant, brain responses were estimated at each voxel, using a general linear model with block regressors. Block regressors looked for brain activity separately for the 1P_Self, 1P_Other, 3P_Self, and 3P_Other conditions. For each condition, blocks pertained to the period from the appearance of the first adjective to the disappearance of the last adjective; therefore, the duration of each block was 20 sec. Boxcar functions representative of these block conditions were convolved with the canonical hemodynamic response. The design matrix also included the realignment parameters to account for any residual movement-related effect. A high-pass filter was implemented using a cutoff period of 128 sec in order to remove the low-frequency drifts from the time series. Serial autocorrelations were estimated with a restricted maximum likelihood algorithm with an autoregressive model of order 1 (+ white noise). The resulting set of voxel values constituted a map of t statistics (SPM{T}). As no statistical inference was made at this (fixed-effects) level, summary statistic images were thresholded at $p < .90$ (uncorrected). These images were further smoothed (6-mm FWHM Gaussian kernel) to accommodate to interindividual variability in brain anatomy. The four conditions (1P_Self, 1P_Other, 3P_Self, and 3P_Other) were then entered in a second-level analysis of variance (ANOVA) corresponding to a random effect model. A nonsphericity correction was applied and "replication over subjects" and "correlated repeated measures" were selected in the SPM2 analysis. F contrasts assessed the main effect of judgment target (self vs. other), the main effect of judgment perspective (third person vs. first person), and the interaction between these two factors. The resulting SPM{F} maps were thresholded at $p < .001$. As a rule, statistical inferences were performed at the voxel level at $p < .05$ corrected for multiple comparisons across the entire brain volume. When a priori knowledge about the potential response of a given area was available from the literature, a small volume correction was computed on a 10-mm radius sphere around the coordinates published for the corresponding location of interest (see below).

A Priori Locations of Interest

The following a priori locations of interest were used for small volume corrections, based on published coordinates in the literature on self-referential processing or perspective taking. These regions concerned areas in the ventral and dorsal portions of the MPFC (we refer to ventral MPFC for z coordinate ≤10 and to dorsal MPFC for z coordinate >10) (Ochsner et al., 2005), medial posterior areas (precuneus), the inferior parietal lobe, the temporal pole, and the left lateral orbitofrontal cortex. All stereotactic coordinates refer to the MNI space (published coordinates that referred to the atlas space of Talairach and Tournoux [1988] were transformed to the MNI space). The a priori locations of interest were the following:

Self-referential processing: ventral MPFC (BA 10) [−4, 54, 2 and 10, 52, 2] (D'Argembeau et al., 2005; Schmitz et al., 2004; Johnson et al., 2002; Kelley et al., 2002); dorsal MPFC (BA 9) [−16, 40, 32 and 10, 50, 20] (Fossati et al., 2003); anterior cingulate cortex (BA 32) [6, 34, 4] (Craik et al., 1999); precuneus [4, −56, 46] (Johnson et al., 2002; Kelley et al., 2002; Kjaer et al., 2002).

Perspective taking: inferior parietal lobe (BA 40) [50, −58, 30 and −58, −58, 28] (Ruby & Decety, 2001, 2004); precuneus [−10, −62, 38] (Ruby & Decety, 2001); left temporal pole [−56, −4, −34] (Ruby & Decety, 2003, 2004); left lateral orbitofrontal cortex [−46, 56, −2] (Hynes, Baird, & Grafton, 2006).

RESULTS

Behavioral Data

Response times for judgments were analyzed using a 2 (target: self vs. other) × 2 (perspective: third person vs.

first person) ANOVA. There was a main effect of perspective, $F(1,16) = 18.69, p < .001$, which indicated that judgments were made more slowly when subjects took a third-person perspective (M = 2115 msec) than when they took a first-person perspective (M = 1970 msec). The main effect of judgment target and the interaction between judgment target and perspective were not significant, $F(1,16) = 0.68$, $p = .42$, and $F(1,16) = 2.23$, $p = .15$, respectively.

fMRI Data

Self-referential Processing: Main Effect of Judgment Target

The main effect of judgment target (judgments concerning the self vs. judgments concerning a close friend) yielded a large activation cluster (3052 voxels) in the MPFC, which encompassed the dorsal (BA 9) and ventral (BA 10) portions of the anterior MPFC and the anterior cingulate cortex (BA 32; see Figure 1A and Table 1, for coordinates and Z values). As illustrated by average parameter estimates, the difference between self targets and other targets in the dorsal anterior MPFC corresponded to an increase in neural activity relative to baseline, whereas the difference between self and other in the ventral anterior MPFC corresponded to a lesser decrease in neural activity relative to baseline (Figure 1A, right; see Discussion). The main effect of judgment target also yielded significant activation in the precuneus (Table 1).

Perspective Taking: Main Effect of Judgment Perspective

The main effect of judgment perspective (taking a third-person perspective vs. a first-person perspective when making the judgments) revealed activation in the left dorsal MPFC (BA 6), posterior to the medial prefrontal regions observed for the main effect of judgment target (see Figure 1B and Table 2). Average parameter estimates show that the responses in this area were increased for the third-person perspectives as compared to the first-person perspectives (Figure 1B, right). The main effect of judgment perspective also yielded activation in the lingual gyrus (BA 18), in the left inferior parietal lobe (BA 40), in the precuneus (BA 7), in the left temporal pole (BA 20), and in the left lateral orbitofrontal cortex (BA 10).

Interaction between Judgment Target and Perspective

The interaction between judgment target and perspective revealed a single focus of activation, located in the left dorsal MPFC (BA 9; $x = -16, y = 32, z = 30$; $Z = 2.98$, $p = .06$ after applying small volume corrections; number of voxels = 15; see Figure 2). As shown by average parameter estimates (Figure 2, right), responses in this area were increased when the target of judgment was self as compared to other, but only for judgments made with a third-person perspective. This was confirmed by post hoc t tests, which yielded significant activation in this region for 3P_Self minus 3P_Other, but not for 1P_Self minus 1P_Other (at $p < .05$ after applying small volume corrections).

DISCUSSION

The aim of this study was to disentangle the neural correlates of self-referential processing and perspective taking, using a factorial design in which we manipulated both the target (self vs. other) and the perspective (third person vs. first person) of judgments about personality traits. This design allowed us to compare the changes in neural activity associated with self-referential processing and perspective taking within a single study and to investigate their interaction. When the target of judgments was the self, as compared to a close friend, neural activation was detected in a large portion of the MPFC, which encompassed the ventral (BA 10) and dorsal (BA 9) parts of the MPFC, as well as the anterior cingulate cortex (BA 32). The main effect of judgment target also revealed activation in the precuneus, close to the medial posterior regions that had previously been observed to be active when reflecting on one's own personality (Johnson et al., 2002; Kelley et al., 2002; Kjaer et al., 2002). Activation of these medial prefrontal and posterior regions is therefore consistent with previous studies of self-referential personality processing (Heatherton et al., 2006; D'Argembeau et al., 2005; Schmitz et al., 2004; Fossati et al., 2003; Kelley et al., 2002; Kjaer et al., 2002; Craik et al., 1999) and confirms that these regions are important for representing self-knowledge.

With regard to perspective taking, we found that taking a third- rather than a first-person perspective yielded activation in the left posterior and dorsal MPFC (BA 6), the left inferior parietal cortex (BA 40), the precuneus (BA 7), the left temporal pole (BA 20), the lingual gyrus (BA 18), and the left lateral orbitofrontal cortex (BA 10).These activations are broadly consistent with previous studies (Ruby & Decety, 2001, 2003, 2004) and may be related to the various processes that are recruited for perspective taking. In order to adopt someone else's point of view, one has to infer that person's perspective, to distinguish between one's own and the other's perspective, and to inhibit a tendency to attribute one's own perspective to others (Decety & Jackson, 2004; Ruby & Decety, 2003, 2004). In agreement with the present study, activation in the posterior dorsal MPFC (BA 6) has previously been reported when subjects take a third-person perspective to infer knowledge states of others (Ruby & Decety, 2003). This region is

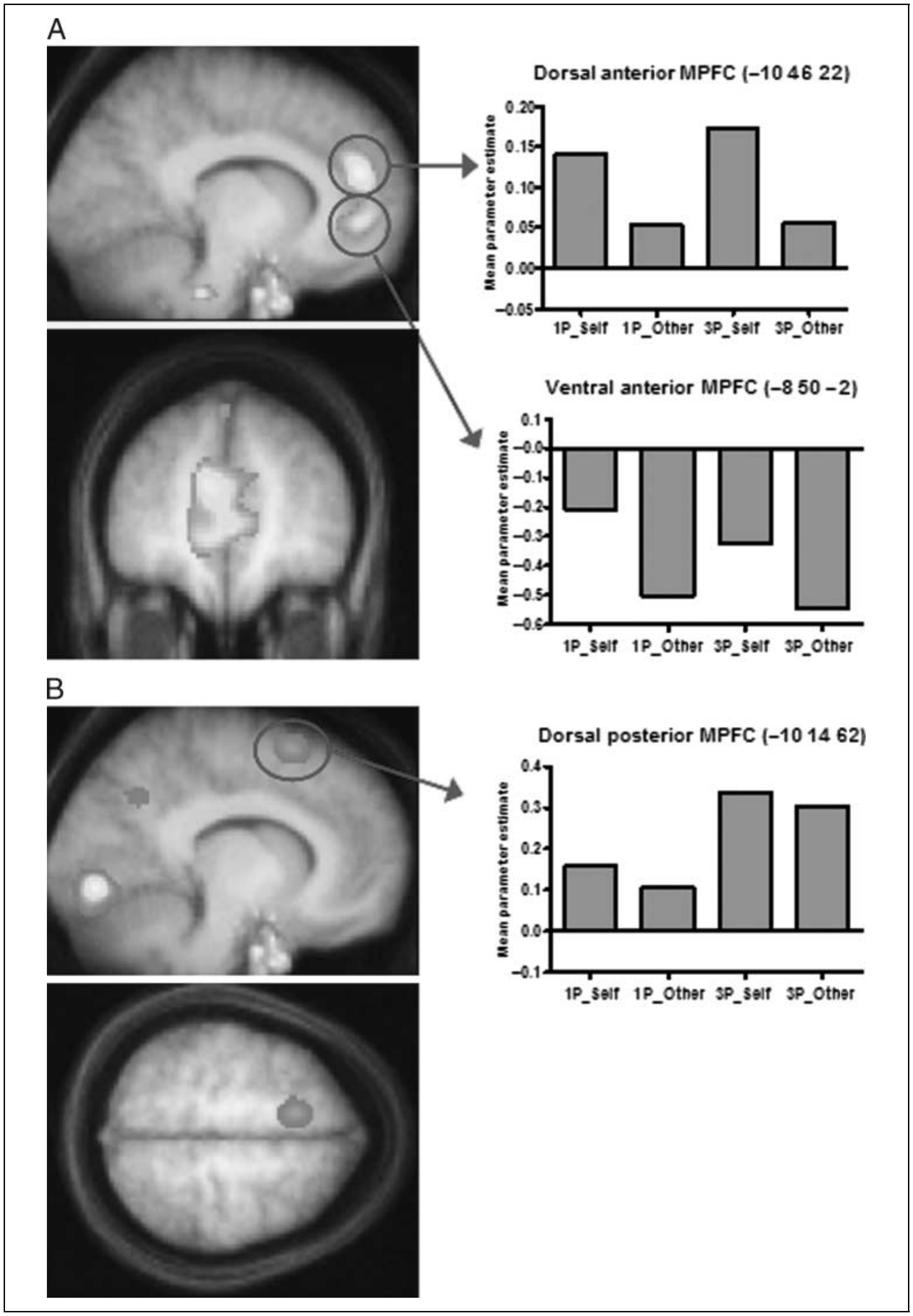

Figure 1. Neural response in the MPFC associated with the main effect of judgment target (self vs. other) and the main effect of judgment perspective (third person vs. first person). Displayed at $p < .001$ uncorrected, on the mean structural MRI of all participants. (A) Left: parasagittal and coronal sections showing activation of the ventral and dorsal anterior MPFC for judgments targeting the self compared to judgments targeting the other. Right: mean parameter estimates show that the difference between self and other in the dorsal anterior MPFC corresponded to an increase in neural activity relative to baseline, whereas the difference between self and other in the ventral anterior MPFC corresponded to a lesser decrease in neural activity relative to baseline. (B) Left: parasagittal and axial sections showing activation of the posterior dorsal MPFC when taking a third-person compared to a first-person perspective. Right: mean parameter estimates show that the difference between the third-person and first-person perspectives corresponded to an increase in neural activity relative to baseline.

slightly posterior to the dorsal region of MPFC traditionally associated with mental state attribution (Mitchell et al., 2005b, 2006; Frith & Frith, 2003; Gallagher & Frith, 2003) but has nevertheless been found to be recruited when people judge words that refer to psychological states compared with words referring to body parts (Mitchell, Banaji, & Macrae, 2005a), attempt to form an impression of another person (Mitchell, Macrae, & Banaji, 2004), or attribute mental states (Calarge, Andreasen, & O'Leary, 2003). This region of MPFC may therefore be related to the process of inferring the mental states of others. On the other hand, the inferior parietal cortex (BA 40) has been related to the process of distinguishing one's own from others' perspectives, whether in the domain of perception, emotion, or knowledge (Ruby & Decety, 2001, 2003, 2004). Activation of the left lateral orbitofrontal cortex had previously been observed when subjects take a cognitive versus an emotional perspective

Table 1. Coordinates and *Z* Values for the Main Effect of Judgment Target (Self vs. Other)

	MNI Coordinates				
Brain Region	*x*	*y*	*z*	*Z*	*Voxels*
L and R dMPFC (BA 9)	−10	46	22	5.08[a]	3052
	10	44	24	4.17[b]	
L and R vMPFC (BA 10)	−8	50	−2	4.17[b]	
	12	44	0	4.42[b]	
Anterior cingulate cortex (BA 24/32)	0	35	0	4.14[b]	
Precuneus (BA 7)	−4	−52	44	3.46[b]	22

L = left hemisphere; R = right hemisphere; BA = Brodmann's area; vMPFC = ventral medial prefrontal cortex with z coordinate ≤10 mm; dMPFC = dorsal medial prefrontal cortex with z coordinate >10 mm.

[a]Significant at $p < .05$ corrected for multiple comparisons at the voxel level over the entire volume.

[b]Significant at $p < .05$ corrected for multiple comparisons at the voxel level over small volumes of interest (see Methods section for details).

(Hynes et al., 2006). The same region has also been related to the inhibition of a prepotent semantic response (Collette et al., 2001) and to inhibitory processes necessary for the controlled processing of emotion (Schaefer et al., 2003). The lateral orbitofrontal cortex might therefore be recruited in order to inhibit an automatic tendency to attribute one's own perspective to others when taking a third-person perspective (Samson, Apperly, Kathirgamanathan, & Humphreys, 2005; Ruby & Decety, 2003). Finally, the precuneus and the left temporal pole have also been observed to be activated in earlier perspective-taking studies (Ruby & Decety, 2001, 2003, 2004) and this has been related to imagery, autobiographical memory retrieval and semantic processing (Cabeza & Nyberg, 2000). Activation of these regions might reflect the retrieval of past experiences with the close friend in order to assist with judgments about this person's perspective. Similarly, activation of the visual cortex (in the lingual gyrus) might also be related to autobiographical memory retrieval and in particular to visual imagery components, which play a key role in autobiographical memory (Greenberg & Rubin, 2003). Our finding that response times were slower when judgments were made with a third-person compared to a first-person perspective might reflect the time taken to retrieve additional autobiographical information to assist perspective taking.

To the best of our knowledge, this is the first study demonstrating that self-referential processing and perspective taking yield activation in different regions of the MPFC. Thinking about the self, as compared to another person, resulted in activation of the ventral and dorsal anterior MPFC, whereas adopting another person's perspective, rather than one's own perspective, yielded activation in the dorsal posterior MPFC. Interestingly, the difference between third-person and first-person perspectives in the dorsal posterior MPFC (Figure 1B, right) and the difference between self and other in the dorsal anterior MPFC (Figure 1A, upper right) corresponded to an increase in neural activity relative to baseline, whereas the difference between self and other in the ventral anterior MPFC corresponded to a lesser decrease in activity from baseline (Figure 1A, lower right). Several studies have found that activity in some regions of the MPFC decreases when various cognitive tasks are compared to a resting baseline (McKiernan, Kaufman, Kucera Thompson, & Binder, 2003; Wicker, Ruby, Royet, & Fonlupt, 2003; Gusnard, Akbudak, Shulman, & Raichle, 2001; Mazoyer et al., 2001; Binder et al., 1999; Shulman et al., 1997), and it has been argued that these decreases correspond to the interruption of processes that are part of a default mode of brain function (Gusnard & Raichle, 2001). Our findings regarding differences in neural activity in the ventral anterior MPFC are consistent with these studies and further suggest that one aspect of default processing in this region might be related to the representation of self-knowledge (D'Argembeau et al., 2005).

In a recent review of the literature on self-referential processing, Gillihan and Farah (2005) pointed out that the "other person" that was used as a comparison target in most functional neuroimaging studies was a public figure, so that the observed activations in the MPFC may

Table 2. Coordinates and *Z* Values for the Main Effect of Judgment Perspective (Third Person vs. First Person)

	MNI Coordinates				
Brain Region	*x*	*y*	*z*	*Z*	*Voxels*
L dMPFC (BA 6)	−10	14	62	4.85[a]	260
L lingual gyrus (BA 18)	−8	−86	−6	6.73[a]	1693
L inferior parietal lobe (BA 40)	−54	−54	26	4.42[b]	270
Precuneus (BA 7)	−10	−64	38	3.81[b]	85
L lateral orbitofrontal cortex (BA 10)	−38	62	−2	3.60[b]	13
L temporal pole (BA 20)	−52	−2	−32	3.38[b]	12

L = left hemisphere; R = right hemisphere; BA = Brodmann's area; dMPFC = dorsal medial prefrontal cortex with z coordinate >10 mm.

[a]Significant at $p < .05$ corrected for multiple comparisons at the voxel level over the entire volume.

[b]Significant at $p < .05$ corrected for multiple comparisons at the voxel level over small volumes of interest (see Methods section for details).

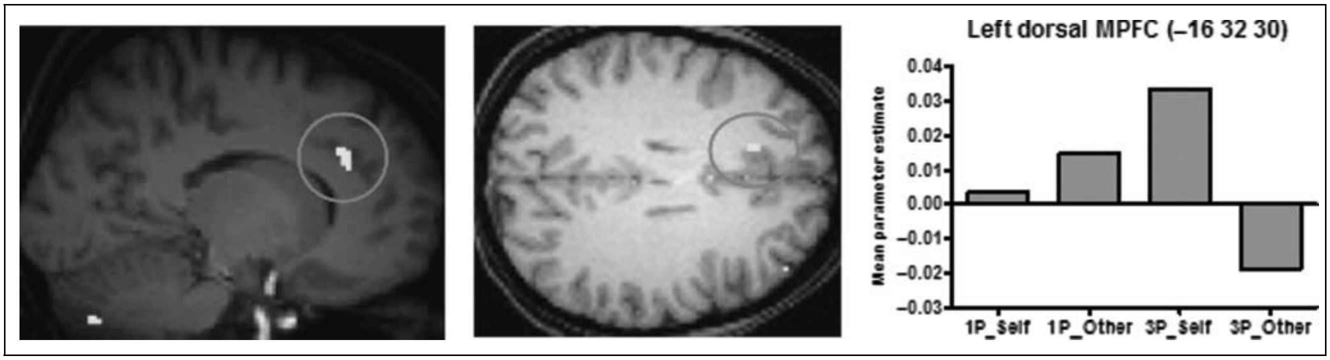

Figure 2. Activation of the left dorsal MPFC for the interaction between judgment target (self vs. other) and perspective (third person vs. first person). Displayed at $p < .005$ uncorrected, on the structural MRI of one participant. Left and middle: parasagittal and axial sections showing activation of the left dorsal MPFC. Right: mean parameter estimates show that the response in the left dorsal MPFC was predominantly evoked by taking a third-person perspective on the self (3P_Self).

reflect differences in the amount of knowledge and/or affective responses rather than a self versus other distinction per se. In this study, we sought to minimize this problem by using a close other as the comparison person and still found activation in the MPFC, both for self-referential processing and perspective taking. In agreement with the present results, a recent study found greater activation in the MPFC for judgments targeting the self versus a close other (Heatherton et al., 2006), but two other studies observed, for the same contrast, prefrontal activations that were more lateral than those usually observed in studies of self-referential processing (Ochsner et al., 2005; Schmitz et al., 2004). The reasons for these inconsistencies remain unclear and deserve further investigation (see Heatherton et al., 2006, for further discussion of potential explanations). With regard to perspective taking, our finding that taking the perspective of a close other activated a dorsal region of MPFC may at first sight seem inconsistent with a recent study by Mitchell et al. (2006). These researchers found that judgments about the mental states of people who are perceived to be similar to versus dissimilar from oneself engaged a ventral region of MPFC, whereas the dorsal MPFC was instead recruited when judging dissimilar rather than similar others. To the extent that a close other is perceived to be relatively similar to oneself, one may have expected to find activation in the ventral rather than dorsal MPFC for perspective taking in the present study. However, it should be noted that, in the present study, judgments about the (similar) other's perspective were compared with judgments concerning one's own perspective, and not with judgments about a dissimilar other as in the study of Mitchell et al. Our third-person versus first-person perspective comparison may thus have subtracted out the neural correlates of simulation processes typically used to understand similar others (i.e., the engagement of the ventral MPFC). Instead, when adopting the other's perspective, participants may have considered dissimilarities between their own and the other's perspectives, and activation of the dorsal MPFC may reflect this process.

Finally, in addition to each dimension being associated with different regions of the MPFC, we found an interaction between self-referential processing and perspective taking in the left dorsal MPFC (BA 9). This region was found to be related to perspective taking (e.g., constructing a mental model of another person's knowledge states) in some earlier studies (Goel, Grafman, Sadato, & Hallett, 1995) and to self-referential processing (e.g., attending to one's own thoughts) in other studies (McGuire, Paulesu, Frackowiak, & Frith, 1996). In our study, the left dorsal MPFC was specifically recruited when the self (vs. other) was considered from a third-person perspective. Although we may have direct knowledge of how a person we are close to views us in the case of some personality traits (e.g., I may know that a friend thinks I am sociable because she told me so explicitly at some point), direct knowledge of the other person's opinion is probably not available for all our personality traits, or may be too coarse for making precise judgments, so that one has to make inferences regarding the other's perspective on oneself. In this process, people primarily use their own self-perceptions (Kenny & DePaulo, 1993), which may then be adjusted by considering any reasons one has for believing that the other person's perception either matches or differs from one's own (Epley et al., 2004; Nickerson, 1999). Evaluating how we are viewed by the other person therefore requires keeping in mind and comparing our own self-knowledge with clues indicating that it might or might not correspond to what the other knows. The function of the dorsal MPFC might precisely be to hold and decouple different representations, such as one's own versus another person's perspective (Frith & Frith, 2003; Gallagher & Frith, 2003). The interaction observed in the present study thus suggests that this decoupling mechanism is recruited to a greater extent when the target of the perspective-taking process is the self rather than another person. This might reflect the need to disengage from one's own perspective to a greater extent when considering the self (versus the other) in order to construct a mental model of how the self might be viewed by others.

In summary, our results show that different regions of the MPFC are related to self-referential processing and perspective taking. The ventral and dorsal anterior MPFC was more activated when reflecting on one's own personality traits than when reflecting on the personality traits of a close friend, suggesting that it plays an important role in representing self-knowledge. By contrast, perspective taking was associated with the posterior dorsal MPFC, which was more activated when taking the perspective of the other person rather than one's own. Finally, the interaction between self-referential processing and perspective taking yielded activation in the left dorsal MPFC. These data support recent hypotheses concerning the critical role of cortical midline structures in self-referential processing (Northoff et al., 2006; Northoff & Bermpohl, 2004) and also suggest that the left dorsal MPFC may specialize in decoupling one's own from other people's perspectives on the self.

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Reprint requests should be sent to Arnaud D'Argembeau, Cyclotron Research Centre, University of Liège, Allée du 6 Août (B30), B-4000 Liège, Belgium, or via e-mail: a.dargembeau@ulg.ac.be.

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