Distinct regions of medial rostral prefrontal cortex supporting social and nonsocial functions

Sam J. Gilbert,[1] Iain D. M. Williamson,[1] Iroise Dumontheil,[1] Jon S. Simons,[1] Christopher D. Frith,[2] and Paul W. Burgess[1]

[1]Institute of Cognitive Neuroscience and Department of Psychology and [2]Wellcome Department of Imaging Neuroscience, Institute of Neurology, University College London, London, UK

While some recent neuroimaging studies have implicated medial rostral prefrontal cortex (MPFC) in 'mentalizing' and self-reflection, others have implicated this region in attention towards perceptual vs self-generated information. In order to reconcile these seemingly contradictory findings, we used fMRI to investigate MPFC activity related to these two functions in a factorial design. Participants performed two separate tasks, each of which alternated between 'stimulus-oriented phases' (SO), where participants attended to task-relevant perceptual information, and 'stimulus-independent phases' (SI), where participants performed the same tasks in the absence of such information. In half of the blocks ('mentalizing condition'), participants were instructed that they were performing these tasks in collaboration with an experimenter; in other blocks ('non-mentalizing condition'), participants were instructed that the experimenter was not involved. In fact, the tasks were identical in these conditions. Neuroimaging data revealed adjacent but clearly distinct regions of activation within MPFC related to (i) mentalizing vs non-mentalizing conditions (relatively caudal/superior) and (ii) SO vs SI attention (relatively rostral/inferior). These results generalized from one task to the other, suggesting a new axis of functional organization within MPFC.

Keywords: area 10; attention; medial prefrontal cortex; mentalizing; theory of mind

Recent studies have pointed to the medial rostral prefrontal cortex (MPFC) as a region of the human brain that plays a crucial role in social cognition (Amodio and Frith, 2006). Functional neuroimaging studies have consistently reported MPFC activation related to mentalizing (Frith and Frith, 2003), i.e. attributing mental states to other agents. Additional studies have reported MPFC activation associated with reflection upon one's own emotions (Lane et al., 1997; Gusnard et al., 2001) and character traits (Johnson et al., 2002; Macrae et al., 2004). It has therefore been proposed that this region 'is engaged when we attend to our own mental states as well as the mental states of others' (Frith and Frith, 2003, 467).

Other studies have suggested a role of MPFC [approximating Brodmann Area (BA) 10] in attentional selection between stimulus-oriented (SO) and stimulus-independent (SI) thought (Burgess et al., 2005). For example, in one study (Gilbert et al., 2005) MPFC activity was consistently observed in three separate tasks whilst participants attended to visually presented information ('SO phases'), compared with when they performed the same tasks 'in their heads' ('SI phases'). This activity was unrelated to task difficulty and a subsequent study ruled out an explanation in terms of task-unrelated thought during SO phases because MPFC

activity was positively related to performance (Gilbert et al., 2006a, b). In addition, potential differences in 'working memory' demands between conditions were unable to explain these results, because greater MPFC activity was observed in the conditions that, if anything, had reduced working memory demands. Consistent with these findings, other studies have reported medial rostral PFC activation in a variety of tasks requiring strong attentional engagement with the external environment. For example, Small et al. (2003) found that activity in this region was associated with deployment of visual attention toward specific regions of space, in a spatial cueing paradigm (Posner, 1980) and Janata et al. (2002) found that activity in medial rostral PFC varied systematically according to the musical key of a melody in an auditory vigilance task.

These results present a paradox. While studies investigating social cognition have suggested that MPFC activity reflects self-referential mental processes, studies investigating attentional selection have suggested a role for MPFC in attention towards perceptual information. A possible resolution of this paradox was suggested by a recent meta-analysis of functional imaging studies that reported activation peaks within BA 10 (Gilbert et al., 2006c). Activation peaks from studies involving mentalizing and self-reflection tasks were significantly caudal to those from studies involving other tasks. Conversely, activation peaks from studies involving multiple-task co-ordination (previously argued to depend upon selection between SO and SI thought; Burgess et al., 2003) were significantly rostral to
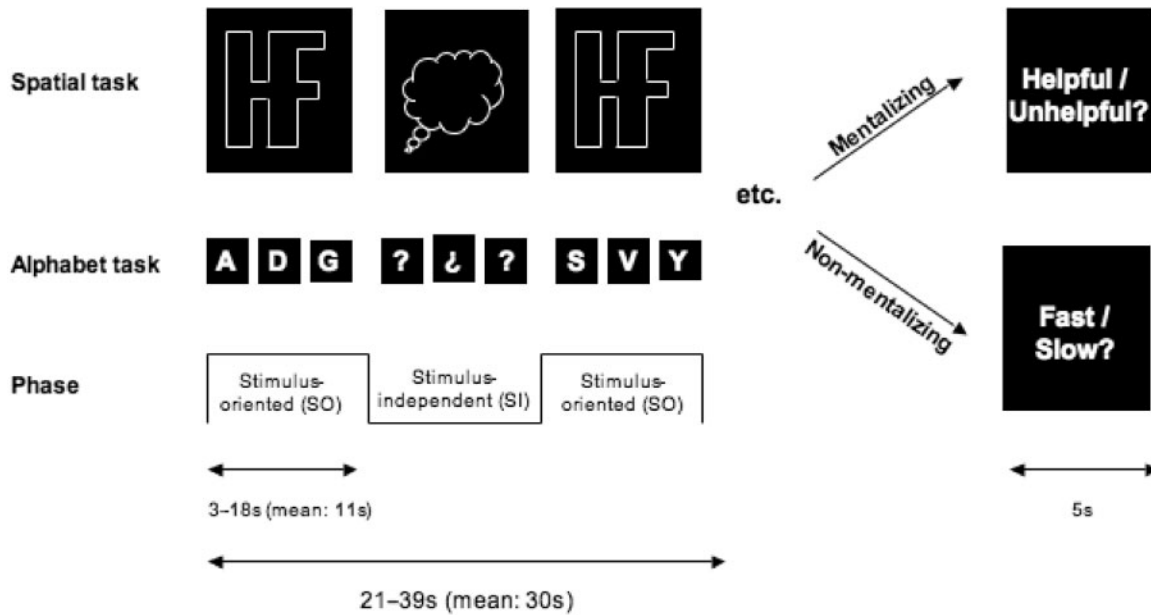
Fig. 1 Schematic illustration of the two behavioral tasks. In the 'spatial' task (SO phase), participants repeatedly pressed one of two response buttons, as if navigating around the edge of a complex shape in a clockwise direction, to indicate whether the next corner would require a left or a right turn. During the SI phase this shape was replaced by a 'thought-bubble' shape and participants were required to imagine the shape that was presented in the SO phase and continue navigating as before. In the 'alphabet' task (SO phase), participants classified upper-case letters of the alphabet according to whether they were composed of straight lines or curves. The stimuli cycled through the alphabet, skipping two letters between each stimulus and the next. In the SI phase the letters were replaced with question marks. Participants mentally continued the sequence and continued classifying letters as before.

those from other studies. This suggests that caudal and rostral MPFC may be preferentially involved in social cognition and attentional selection respectively. However, convincing segregation of function is only given by imaging data for which the two kinds of task have been performed by the same subject in the same experiment. The present study therefore employed a 2×2 factorial design crossing the factors of attentional focus (SO vs SI) and mentalizing (mentalizing vs non-mentalizing).

We investigated two of the three tasks originally studied by Gilbert et al. (2005). In both tasks, participants alternated between SO phases, where visual information was task-relevant, and SI phases, where visual information was no longer informative (Figure 1). The transitions between these phases were cued by changes in the appearance of the visual stimuli, and occurred at unpredictable times. Unlike our earlier study, the tasks in the present study were presented in two conditions: mentalizing and non-mentalizing. In mentalizing blocks, participants were told that they were performing the tasks in collaboration with an experimenter (Gallagher et al., 2002), who was able to control the timing of transitions between the SO and SI phases with a button-press. At the end of these blocks (mean duration: 30 s) participants made a judgment as to whether the experimenter was trying to be helpful or unhelpful in his timing of the transitions in that block. In non-mentalizing blocks, participants were told that the timing of these transitions was randomly chosen by the computer. At the end of these blocks, participants judged whether the transitions between

phases occurred faster or slower than usual. Thus, both types of blocks were matched in that participants saw identical stimuli and made judgments on precisely the same source of information (the timing of switches between SO and SI phases). However, only in the mentalizing blocks were participants required to interpret this information in terms of the mental state of another agent, i.e. to 'mentalize'. In actuality, the timing of SO/SI transitions was randomly selected in all blocks.

METHODS

Participants

There were 16 healthy right-handed participants (mean age: 21, range 18–27; nine female). All were healthy UCL students whose first language was English, with no significant medical history of substance abuse, mental illness, head injury or other neurological condition necessitating hospital admission. All provided written informed consent before participating.

Tasks and procedure

In SO phases of the 'spatial task' (task 2 of the study of Gilbert et al., 2005), participants repeatedly pressed one of two buttons, as if navigating around the edge of a complex shape in a clockwise direction, to indicate whether the next corner would require a left or a right turn. The stimulus presented during this phase was white, approximately $7°$, tall and wide, and shaped similarly to the outlines of the letters H and F placed adjacent to one another, with the vertical line

between them removed (Figure 1). A green arrow at the top-right corner of the shape indicated the position from which to start, at the beginning of each block. Following the first button-press response this arrow was removed. During SI phases, the shape was replaced by a similarly sized white 'thought-bubble' shape; subjects were required to imagine the shape that was presented in the SO phase and continue navigating from their current position.

In SO phases of the 'alphabet task' (task 3 of the study of Gilbert *et al.*, 2005), participants classified capital letters by pressing one of two buttons, according to whether the letter was composed entirely of straight lines, or whether it had any curves. Subsequent letters were presented immediately following each button press, forming a regular sequence that cycled through the alphabet, skipping two letters between each stimulus and the next. Stimuli were presented in white Arial typeface, approximately $1°$ tall and wide. During the SI phase these letters were replaced with alternating question marks and upside-down question marks. Participants were required to mentally continue the sequence from their current position in the alphabet, performing the same classification task for each self-generated letter. The first letter to be presented in each SO phase was the appropriate continuation of the sequence, assuming that the sequence had been correctly maintained during the preceding SI phase.

Each task was performed in two out of four runs in an AABB order counterbalanced across participants. Within each run, participants performed a total of eight blocks, which alternated between mentalizing and non-mentalizing conditions. A different screen background (dark blue or dark red) was used for each condition, counterbalanced across participants. The length of each block varied randomly between 21 s and 39 s (mean: 30 s). In a randomly selected half of blocks ('fast blocks') transitions between the SO and SI phases occurred with a mean rate of every 7.6 s (range 3–18 s). In other blocks ('slow blocks') transitions occurred at a mean rate of every 13.5 s (range: 3–18 s). At the end of each block, there was a 1 s pause, followed by a 5 s period during which participants indicated with a button press whether they believed the experimenter was trying to be helpful or unhelpful (in mentalizing blocks) or whether they believed the SO/SI transitions were faster or slower than average (in non-mentalizing blocks). Following this judgment, there was a 5 s reminder whether transitions were to be controlled by the computer or the experimenter in the following block. There was then a variable pause between 5 and 11 s (mean: 8 s) before the next block began (this is referred to below as the 'stimulus-expectation condition').

Pre-scan training

Participants took part in a pre-scan training session lasting ~40 min. They were first read a cover story explaining that the experiment would sometimes involve collaboration with the experimenter (see Supplementary Material). They were

then trained on each of the two tasks. Following this, they performed one run of six blocks of each task. These runs were identical to the tasks performed in the experimental session, except that transitions between SO and SI phases in mentalizing blocks were controlled by button presses of the experimenter, who sat next to the participant (in accordance with the cover story).

Scanning procedure

A 3T Siemens Allegra head-only system was used to acquire both T1-weighted structural images and T_2^*-weighted echoplanar (EPI) images [64×64; 3×3 mm pixels; echo time (TE), 30 ms] with BOLD contrast. Each volume comprised 36 axial slices (2 mm thick, separated by 1.7 mm, oriented at approximately $10°$ to the AC-PC plane), covering the whole brain. Functional scans were acquired during four sessions, each comprising 174 volumes (lasting ~7 min). Volumes were acquired continuously with an effective repetition time (TR) of 2.34 s per volume. The first six volumes in each session were discarded to allow for T1 equilibration effects. Following the functional scans, a 12-min structural scan was performed.

Data analysis

Behavioral data were analyzed as in the previous study of Gilbert *et al.* (2005). fMRI data were analyzed using SPM5 software (http://www.fil.ion.ucl.ac.uk/spm/software/spm5/). The volumes were realigned, corrected for different slice acquisition times, normalized into 2 mm cubic voxels using the Montreal Neurological Institute (MNI) reference brain using 4th-degree B-spine interpolation, and smoothed with an isotropic 8 mm full-width half-maximum Gaussian kernel.

The volumes acquired during the four sessions were treated as separate time series. For each series, the variance in the BOLD signal was decomposed with a set of regressors in a general linear model (Friston *et al.*, 1995). Separate regressors coded for sustained activity in each of the four main conditions of interest (SO mentalizing, SI mentalizing, SO non-mentalizing, SI non-mentalizing), and the pre-task instruction periods, convolved with a canonical hemodynamic response function. A pair of additional regressors (one for the mentalizing and one for the non-mentalizing condition) indexed the period during which participants made their end-of-block judgments, and a further pair indexed the pause before each run of trials. These regressors, together with the regressors representing residual movement-related artifacts and the mean over scans, comprised the full model for each session. The data and model were high-pass filtered to a cut-off of 1/128 Hz.

Parameter estimates for each regressor were calculated from the least mean squares fit of the model to the data. Effects of interest were assessed in a random effects analysis as follows. Eight contrasts were performed, each contrast individually assessing the variance explained by the

regressors representing each of the four main conditions of interest in the two tasks (i.e. Alphabet SO Non-mentalizing; Alphabet SO Mentalizing; Alphabet SI Non-Mentalizing, etc.). These contrasts were entered into a repeated-measures analysis of variance (ANOVA) using non-sphericity correction (Friston *et al.*, 2002). Appropriate contrasts for effects of interest were conducted at the second level, averaging over the two tasks. Contrasts were thresholded at $P < 0.05$, corrected for multiple comparisons across the whole brain volume (except where stated).

RESULTS

Post-experiment debriefing indicated that no participant was aware that the timing of SO/SI transitions was always random, rather than being under experimenter control during mentalizing blocks, and a pilot study found that participants unanimously described the timing of these switches in terms of the mental state of the experimenter (see Supplementary Material).

Behavioral data: post-block responses

Table 1 shows the mean percentage of 'slow' (*vs* 'fast') responses in non-mentalizing blocks, and the mean percentage of 'unhelpful' (*vs* 'helpful') responses in mentalizing blocks, separately for 'fast blocks' (where transitions between SO and SI phases were relatively rapid) and 'slow blocks' (where such transitions were less frequent). Participants distinguished between fast and slow blocks in both mentalizing [$F(1,15) = 6.0$, $P = 0.027$] and non-mentalizing [$F(1,15) = 9.3$, $P = 0.008$] conditions. In mentalizing conditions, participants were more likely to respond 'helpful' in

Table 1 Post-block responses

	Non-mentalizing blocks (% 'slow' responses)		Mentalizing blocks (% 'unhelpful' responses)	
	Fast blocks	Slow blocks	Fast blocks	Slow blocks
Spatial task	48.4 (8.1)	79.7 (6.6)	43.8 (7.0)	64.1 (7.6)
Alphabet task	50.0 (7.6)	79.7 (6.9)	42.2 (6.3)	56.3 (7.4)

Standard errors are shown in parentheses.

fast *vs* slow blocks (see Supplementary Material). In neither type of block was there a main effect or interaction involving Task [Spatial or Alphabet; $F(1,15) < 2.2$, $P > 0.16$].

Behavioral data: task performance

Behavioral data are presented in Table 2. The two tasks were analyzed separately in 2 (Phase: SO/SI) × 2 (Trial-type: switch, i.e. the trial immediately following a switch between the SO and SI phases *vs* non-switch) × 2 (Mentalizing: mentalizing/non-mentalizing) repeated measures ANOVAs. The Trial-type factor was included because the present experimental design can be seen as a variant on the task-switching paradigm (see Gilbert *et al.*, 2005 for discussion). In the reaction time (RT) data, there was a main effect of Phase in the Alphabet task [$F(1,15) = 139$, $P < 10^{-9}$], with SI trials slower than SO trials, but no significant difference in the Spatial task [$F(1,15) = 1.9$, $P = 0.19$]. In both tasks there was a main effect of Trial-type [$F(1,15) > 16.6$, $P < 0.001$], switch trials being slower than non-switch trials. In addition, there was a significant Phase × Trial-type interaction in both tasks [$F(1,15) > 15.8$, $P < 0.002$]. However, while in the Spatial task this resulted from a greater difference between switch and non-switch trials in SO than SI phases, the interaction resulted from the reverse pattern of results in the Alphabet task. In neither task was there a main effect of Mentalizing, nor any significant interaction involving the Mentalizing factor [$F(1,15) < 1.3$, $P > 0.28$]. Thus, participants performed the two tasks equivalently in the mentalizing and non-mentalizing conditions.

In the error data, the only significant effect was a main effect of Phase in the Alphabet task [$F(1,15) = 14.8$, $P = 0.002$], with more errors being committed in SI than SO phases.

Functional imaging results

Table 3 lists all regions of activation in (i) the contrast of SI *vs* SO conditions, (ii) the contrast of SO *vs* SI conditions conditions, and (iii) the contrast of mentalizing *vs* non-mentalizing conditions.

In the SI > SO contrast, there were significant activations in bilateral insula, left supplementary motor area/cingulate gyrus and premotor cortex, left inferior parietal lobule and

Table 2 Mean reaction time (RT) and error rate in each condition of the two tasks

Task	Phase	Trial type	Non-mentalizing		Mentalizing	
			RT	Error (%)	RT	Error (%)
Spatial	Stimulus-oriented	Non-switch	965 (99)	9.3 (2.0)	993 (95)	9.4 (1.9)
		Switch	1173 (87)	8.6 (2.7)	1252 (80)	12.9 (2.7)
	Stimulus-independent	Non-switch	1116 (114)	11.3 (3.3)	1120 (108)	9.3 (1.9)
		Switch	1161 (111)	11.4 (3.6)	1163 (105)	9.4 (2.7)
Alphabet	Stimulus-oriented	Non-switch	836 (68)	2.6 (0.5)	840 (61)	2.0 (0.5)
		Switch	1075 (66)	3.7 (2.0)	1054 (72)	4.0 (2.1)
	Stimulus-independent	Non-switch	1575 (107)	13.6 (3.3)	1570 (107)	12.0 (3.8)
		Switch	2312 (116)	15.4 (3.1)	2321 (151)	13.3 (4.2)

left medial occipital cortex. In the contrast of non-mentalizing *vs* mentalizing conditions, there were no significant voxels. Importantly, both the SO > SI contrast and the mentalizing > non-mentalizing contrast revealed activation in MPFC. However, consistent with the meta-analysis (Gilbert *et al.*, 2006c), the activation peak associated

Table 3 Regions showing significant differences in BOLD signal between conditions ($P < 0.05$ corrected for whole-brain volume). Brodmann Areas (BAs) are approximate

Region	BA	Hemisphere	x	y	z	Z_{max}	Voxels
Stimulus-Independent > Stimulus-Oriented							
Insula	13	R	34	26	−4	4.8	1
	13	L	−30	22	2	4.8	2
SMA/cingulate gyrus	6/32	L	−6	18	48	6.2	297
Premotor cortex	6	L	−26	8	54	5.4	36
Inferior parietal lobule	40	L	−44	−44	40	5.5	40
Medial occipital cortex	18/19	L	−8	−96	22	4.9	6
Stimulus-Oriented > Stimulus-Independent							
Medial frontal cortex	10	R	−10	68	20	5.0	12
	10/9	R	2	66	26	5.0	9
	10/11	−	0	58	−14	5.1	50
	6	L	−22	−6	74	4.8	1
	6	L	−4	−18	52	5.7	76
Postcentral gyrus	3	L	−40	−20	56	>8	1490
Inferior parietal cortex	40	L	−50	−22	18	5.7	38
Posterior cingulate/precuneus	31	R	4	−52	32	5.6	176
Superior parietal cortex	7	R	30	−56	60	6.7	182
	7	L	−20	−62	60	5.0	9
	7	R	26	−66	52	4.8	6
Lateral occipital cortex	18	R	34	−94	8	>8	4483
	18	L	−32	−94	6	>8	2800
Mentalizing > Non-mentalizing							
Medial frontal cortex	10/9	L	−8	54	30	4.8	2
Temporal pole	21/38	R	48	8	−34	5.2	33

with attentional selection was rostral to the activation peak associated with mentalizing (Figure 2). There was virtually no overlap between the regions of activation for these two contrasts, even at a more liberal threshold of $P < 0.001$ uncorrected (Figure 3). Moreover, analysis of the interaction between the two factors (attentional focus and mentalizing) revealed no active voxels. This interaction was not significant in any of the peak MPFC regions identified in the above contrasts $[F(1,15) < 4.3]$. Thus, there was no evidence for shared processes underlying attentional selection and mentalizing. The results of this last analysis are presented in Figure 4, with results plotted separately for the peak MPFC regions in the two contrasts and the two tasks. In this graph, the 'stimulus-expectation condition' is used as a common reference condition, because it was present in all scans. As shown in the figure, the stimulus-expectation condition was associated with greater signal than any other condition.

In order to test formally for whether the regions activated by these two contrasts were spatially distinct, peak y and z co-ordinates within BA 10 were extracted on a subject-by-subject basis for each contrast, at each sagittal slice between $x = -8$ and $x = +8$ (in this analysis, BA 10 was defined as $y \geq 40$; $-12 \leq z \leq 30$). Analysis of these co-ordinates confirmed that activations associated with attentional selection were significantly rostral to those associated with mentalizing $[y = 59.9 \text{ } vs \text{ } 55.3; F(1,15) = 5.6, P = 0.03]$, as well as being significantly inferior $[z = 6.6 \text{ } vs \text{ } 12.5; F(1,15) = 5.2, P = 0.04;$ Figure 5].

As well as contrasting mentalizing and non-mentalizing conditions during performance of the Alphabet and Spatial tasks, we also compared these conditions during the 5-s period at the end of each block where participants
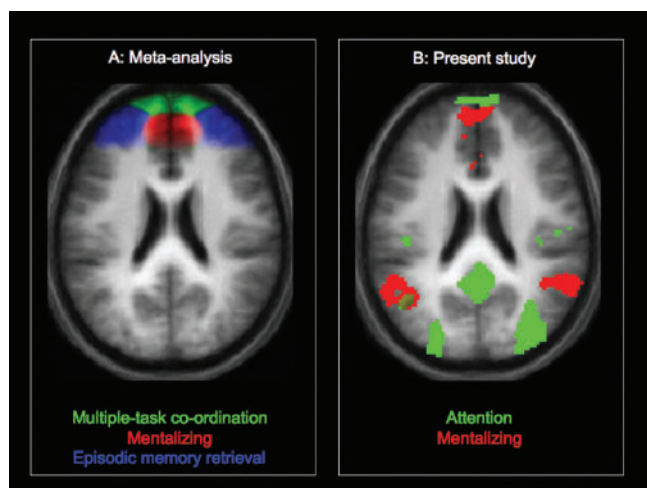

Fig. 2 Panel A: functional subdivision of rostral PFC according to an earlier meta-analysis of functional neuroimaging studies (Gilbert *et al.*, 2006c, adapted from Figure 6). Panel B: regions of activation in the present study for contrasts related to attention (SO > SI, shown in green) and mentalizing (mentalizing > non-mentalizing, shown in red), thresholded at $P < 0.001$ uncorrected. Results are displayed on axial slices ($z = 24$) of the participants' mean normalized structural image.
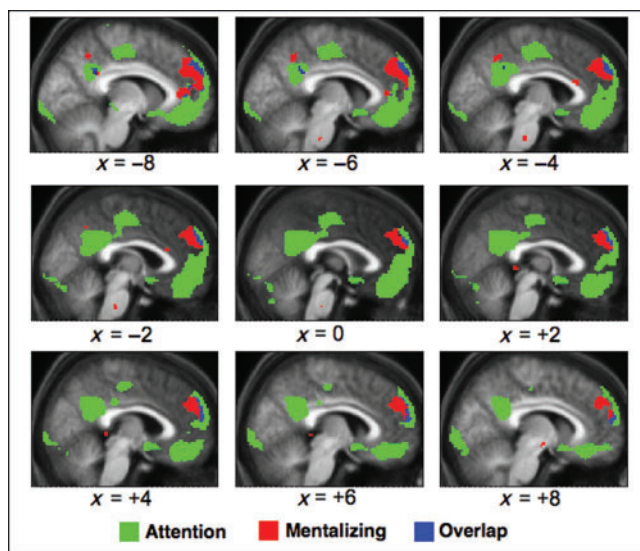

Fig. 3 Regions of activation related to attention (SO > SI, shown in green), mentalizing (mentalizing > non-mentalizing, shown in red), and their overlap (blue). Contrasts were thresholded at $P < 0.001$ uncorrected and plotted on the participants' mean normalized structural image.
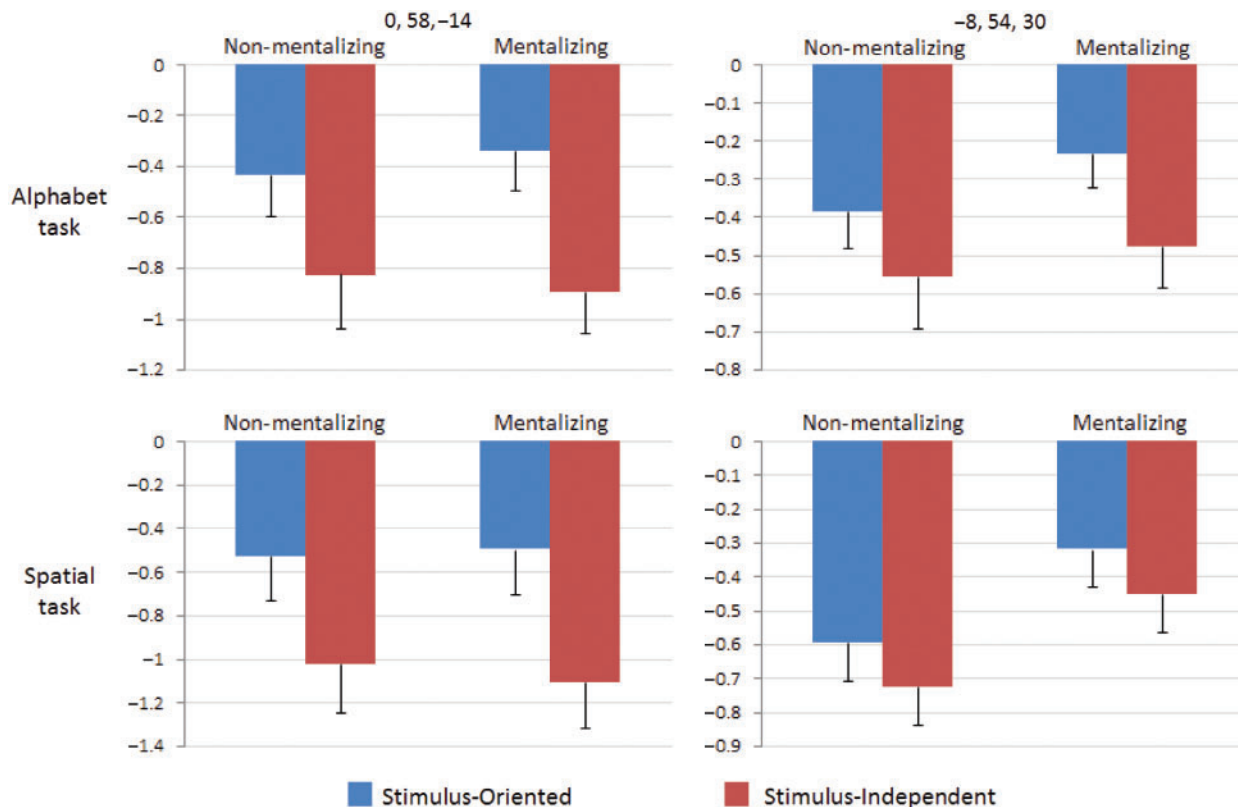
Fig. 4 BOLD signal associated with the four experimental conditions, in each task. Left panel: results from the peak MPFC region identified in the contrast of SO > SI. Right panel: results from the peak MPFC region identified in the contrast of mentalizing > non-mentalizing. Results indicate the mean parameter estimate in each condition from a 6 mm-radius sphere centered on the relevant activation peak. All results are plotted relative to the stimulus-expectation condition, i.e. the period at the beginning of each block before any stimulus is presented. Error bars represent standard errors.
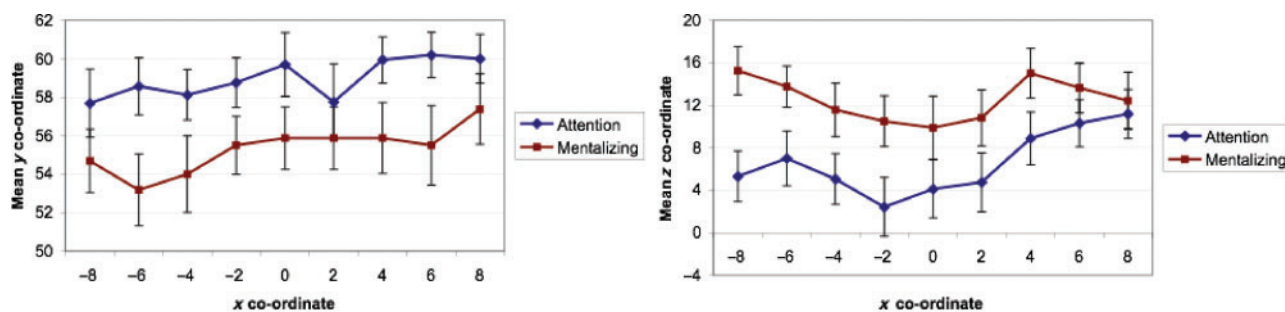

Fig. 5 Mean peak y (left panel) and z (right panel) co-ordinates within BA 10 for the contrasts related to attention (SO > SI) and mentalizing (mentalizing > non-mentalizing), at each sagittal slice between $x = -8$ and $x = +8$. Error bars represent standard errors.

indicated whether the experimenter was being helpful or unhelpful (mentalizing blocks) or whether switches between phases were relatively fast or slow (non-mentalizing blocks). There were no areas of activation at a whole-brain corrected threshold. However, applying a small volume correction to an 8 mm radius sphere centered on the peak MPFC co-ordinate in the contrast between mentalizing and non-mentalizing conditions during task performance (−8, 54, 30), this contrast revealed significant activation in a nearby region of MPFC (−8, 50, 30, 5 voxels, $P = 0.035$ corrected for multiple comparisons across search volume). In addition,

there was significant activation in the original activation peak (−8, 54, 30) at an uncorrected threshold [$t(15) = 2.3$, $P = 0.03$]. Thus, a similar region of MPFC was activated both during task performance, when participants were told that they were performing the task with an experimenter, and also at the end of each block, when participants decided whether the experimenter was being helpful or unhelpful.

In a further set of analyses, we investigated potential differences between the two tasks, by examining interactions between the main experimental factors (Phase: SO/SI; Mentalizing: mentalizing/non-mentalizing) and Task

Table 4 Regions showing significant Task x Phase interactions ($P < 0.05$ corrected for whole-brain volume). Brodmann Areas (BAs) are approximate

Region	BA	Hemisphere	x	y	z	Z_{max}	Voxels
Alphabet (SO > SI) > Spatial (SO > SI)							
Lateral occipito-temporal cortex	37	R	54	−68	−2	7.0	222
	37	L	−50	−70	2	5.0	21
Spatial (SO > SI) > Alphabet (SO > SI)							
Lateral premotor cortex	6	L	−56	−2	46	5.0	15
Superior parietal cortex	7	R	22	−64	60	5.4	28
Lateral occipital cortex	19	R	30	−80	18	6.4	148
Medial occipital cortex	18	R	10	−96	6	7.1	611

Table 5 Mean correlation coefficients between medial rostral PFC contrast estimates

		Alphabet task		Spatial task	
		Attention	Mentalizing	Attention	Mentalizing
Alphabet task	Attention	–	0.11	0.34**	0.03
	Mentalizing		–	0.04	0.17*
Spatial task	Attention			–	−0.11
	Mentalizing				–

*$P < 0.05$. **$P < 0.0005$.

(Alphabet/Spatial). There were no regions showing significant Task × Mentalizing activations, suggesting that the mentalizing manipulation had similar effects in the two tasks. In the Task x Phase analyses (Table 4), several posterior brain regions showed significant activations. There was bilateral activation in lateral occipito-temporal cortex, which showed a greater difference between the SO and SI conditions in the Alphabet task than the Spatial task. The reverse contrast revealed activation in left lateral premotor cortex, right superior parietal cortex and widespread activation in medial and lateral occipital cortex, all of which showed a greater difference between the SO and SI conditions in the Spatial task than the Alphabet task.

It important to note that the Task × Phase interactions failed to reveal any significant voxels in medial prefrontal cortex. In the behavioral data, there was a significant difference in reaction time between SO and SI conditions in the Alphabet task, but not the Spatial task. This resulted in a highly significant Task × Phase interaction [$F(1,15) = 130$; $P < 10^{-9}$]. If differences in BOLD signal between the SO and SI conditions reflected these behavioral differences (e.g. due to the influence of 'task difficulty'), a similar Task × Phase interaction would be expected in the BOLD data. However, even at a threshold of $P < 0.05$ uncorrected, none of the three MPFC regions identified by the SO > SI contrast showed such an interaction. Moreover, even in the Spatial task, where there was no significant difference in reaction time between the SO and SI phases, there was

a significant difference in BOLD signal in all three of these regions [$F(1,15) > 13$, $P < 0.003$]. In neither task was there a significant correlation between behavioral differences between SO and SI conditions and the corresponding BOLD differences in any of these three regions ($|r| < 0.3$, $P > 0.26$). Thus, the present results cannot be explained simply by differences in task difficulty between conditions.

Finally, we analyzed the degree to which signal in medial rostral PFC (defined using the same co-ordinates as above) generalized from one task to the other. For each participant we extracted signal at every voxel within this region for each of the four orthogonal contrasts resulting from the factorial crossing of Task and Contrast (i.e. Alphabet Attention, Alphabet Mentalizing, Spatial Attention, Spatial Mentalizing). Because we were interested in the spatial distribution of responses to each of these contrasts, rather than the overall level of activity, the results for each contrast were normalized so that throughout medial rostral PFC there was a mean response of zero, with standard deviation of one. We then calculated the correlation matrix between responses at each voxel to each of these contrasts, separately for each participant. The resulting correlations were entered into one-sample t-tests to test for consistent results across participants (Table 5). Of the six possible pairwise correlations, only the correlations between the two Attention contrasts and the two Mentalizing contrasts were significantly different from zero. Thus, results from the Attention contrast generalized significantly from one task to the other, as did results from the Mentalizing contrast. However, medial rostral PFC responses did not generalize consistently from the Attention to the Mentalizing contrast, or vice versa, even within the same task.

DISCUSSION

These results confirm a new axis of functional organization within MPFC, with the most rostral part preferentially involved in tasks requiring SO *vs* SI thought, and an adjacent caudal (and superior) region preferentially involved in mentalizing (i.e. reflecting on the mental states of another agent). One consequence of this finding is that there need be no contradiction between functional imaging studies reporting MPFC activation associated with mentalizing/self-reflection (involving attention to self-generated information) and those reporting MPFC activation associated with attention to current perceptual input, because different regions of MPFC were activated by these two types of contrast. In addition, there were no voxels yielding a significant interaction between the attention and mentalizing factors, and the interaction effect was not significant in the peak MPFC regions identified by the main effects. Thus, insofar as any MPFC regions showed an effect of both factors, these effects were additive rather than interactive, suggesting an absence of shared underlying processes (cf. additive factors logic; Sternberg, 1969, 1998. For an application of the additive factors logic to fMRI see

Reynolds *et al.*, 2006). Of course, a wide variety of processes are likely to contribute to mentalizing tasks. Indeed, recent studies have begun to subdivide such processes and provide evidence for distinct neuroanatomical substrates (e.g. Saxe and Powell, 2006). In this context, it is perhaps even more remarkable that there was so little overlap between MPFC regions involved in mentalizing and attentional selection, given that the mentalizing manipulation is likely to have affected a large range of underlying cognitive processes. Before discussing the implications of these findings, we first consider their relationship with (i) potential differences in 'task difficulty' between conditions; (ii) potential differences in 'working memory' demands between conditions; and (iii) the issue of activation 'increases' or 'decreases', compared with a baseline condition.

The finding of increased BOLD signal in medial rostral PFC during SO *vs* SI attention replicates the earlier findings of Gilbert *et al.* (2005, 2006a). This increased activation during SO attention is unlikely merely to reflect differences in task difficulty between SO and SI phases. In common with earlier studies (Gilbert *et al.*, 2005, 2006a), signal change in medial rostral PFC was unrelated to task difficulty, as indexed by RT. In addition, there was a significant behavioral difference between the two phases in only one of the tasks (Alphabet task), yet activity in medial rostral PFC was significantly different between the SO and SI phases both Alphabet and Spatial tasks, and signal change associated with the SO > SI contrast did not differ significantly between the two tasks. Another possibility is that activity in medial rostral PFC reflects demands for rehearsal or maintenance of information (i.e. 'working memory'). However, in the present study increased BOLD signal was observed in SO phases. If anything, these phases had reduced working memory demands, because task-relevant information was perceptually available. Thus, this hypothesis cannot provide a full account of the present results.

In the analysis of BOLD signal associated with the various conditions relative to the 'stimulus expectation condition' (i.e. lying in the scanner with no task apart from waiting for upcoming task-relevant stimuli), all conditions were associated with decreased signal. Although this condition was not matched with the other conditions in terms of stimuli, task or any other factor, these results are consistent with previous demonstrations that low-demand conditions are associated with relatively high signal in MPFC (e.g. McKiernan *et al.*, 2003; Gilbert *et al.*, 2006a). However, the suitability of such low-demand conditions (e.g. 'rest') as a baseline in neuroimaging studies is at present a matter of considerable debate (Morcom and Fletcher, in press). Because psychological processes are so unconstrained in such conditions, it is unclear whether they are best characterized as involving an unusual degree of SI cognition (i.e. 'mind-wandering', e.g. McKiernan *et al.*, 2003), an unusual degree of SO cognition (i.e. watchfulness towards the external environment, e.g. Gilbert *et al.*, 2006a) or a

combination of the two (i.e. 'surveillance of the internal and external environments', Gusnard *et al.*, 2001, 4259). Thus, rather than relying on comparisons with an arbitrary baseline condition, conclusions in the present study were drawn from comparisons between more constrained experimental conditions.

The finding that activation peaks related to mentalizing were caudal to those related to attentional selection fits well with our earlier meta-analysis (Gilbert *et al.*, 2006c), which showed that studies involving mentalizing tended to produce relatively caudal activations within rostral PFC, compared with studies involving other types of task. Thus, the present results confirm that as well as there being cytoarchitectonic differences between relatively rostral and caudal regions within rostral PFC (Carmichael and Price, 1994), there are corresponding functional differences. In addition to variation along a rostral-caudal axis, we also found that activation peaks related to mentalizing were significantly superior to those involving attentional selection, consistent with previous social cognitive neuroscience studies indicating functional variation along this axis (e.g. Mitchell *et al.*, 2006). Patterns of activity generalized significantly from one task to the other, despite differences in stimulus-materials between the two tasks. However, there were no significant associations between patterns of results within either task when different processes (attention-related *vs* mentalizing-related) were compared. Thus, the present results are more consistent with a process-specific model of PFC subdivisions (i.e. the idea that different subregions of PFC support different cognitive functions, regardless of the nature of the stimulus materials) rather than a material-specific model (i.e. the idea that different subregions of PFC support the same fundamental cognitive process operating on different categories of stimulus; see Gilbert *et al.*, 2006c for further discussion). Recent studies have suggested a gradient of functional specialization within prefrontal cortex, with representations becoming increasingly abstract in more rostral regions (e.g. Koechlin *et al.*, 2003; Amodio and Frith, 2006). The present results would be consistent with such an account, in the sense that the most rostral part of MPFC showed activity related to the SO *vs* SI constrast that was not dependent on the particular type of stimulus that was presented, or the specific task being carried out.

One potential interpretation of these results is that the two regions of rostral MPFC identified in the present study both play a role in directing attention towards task-relevant information. However, whereas the most rostral part of MPFC may be preferentially involved in non-social tasks that require biasing of attention towards current perceptual information, the adjacent caudal region may be preferentially involved in social tasks that may require biasing of attention towards other types of information (e.g. emotional information; cf. Lane *et al.*, 1997; Gusnard *et al.*, 2001; Lieberman *et al.*, in press). This view is able to accommodate the wide variety of social and non-social tasks that activate

MPFC (Gilbert *et al.*, 2006c), unlike accounts of MPFC function that focus on social or non-social functions alone. Furthermore, the suggestion that rostral PFC is involved in attentional selection between perceptual and self-generated information may potentially explain the role of this brain region in a wide variety of cognitive domains (Burgess *et al.*, 2005). In particular, situations involving co-ordination of multiple tasks and prospective memory demands may depend critically on the ability to select between attending to incoming perceptual information related to the current task and attending to internally represented intentions (Burgess *et al.*, in press). Such situations present particular difficulties to patients with circumscribed rostral PFC damage (Shallice and Burgess, 1991; Burgess, 2000; Bird *et al.*, 2004).

Aside from rostral PFC, the present study revealed signal change in several other brain regions. In the contrast of SI *vs* SO conditions, activation peaks in the insula, supplementary motor area/cingulate gyrus, premotor cortex and inferior parietal lobule matched closely the activation peaks identified in the study of Gilbert *et al.* (2006a), which also involved a comparison between SO and SI conditions. The analysis of task-specific effects revealed that the SO *vs* SI comparison preferentially activated lateral occipito-temporal cortex in the Alphabet task, consistent with a role of this region in processing letter stimuli (Flowers *et al.*, 2004). In the Spatial task, the SO *vs* SI comparison was associated with other regions of visual cortex (BA 18/19), which may have been involved in perceptual analysis of the shape that participants navigated, along with superior parietal cortex (BA 7), which has previously been implicated in visually guided navigation (e.g. Shelton and Gabrieli, 2002).

In the comparison of SO *vs* SI conditions, significant activation in brain regions outside MPFC corresponded well with the regions implicated in the earlier studies of Gilbert *et al.* (2005, 2006a), including posterior cigulate/precuneus and both superior and inferior regions of lateral parietal cortex. In addition, the present study revealed large occipital activations associated with SO *vs* SI conditions. This may reflect attentional modulation of visual cortical areas, depending on SO *vs* SI conditions. However, since in this study the visual stimuli were not perfectly matched between conditions, these occipital activations may simply reflect differences between the stimuli used in the two conditions (for evidence of attentional modulation of visual cortical areas depending on SO *vs* SI conditions, see Gilbert *et al.*, 2006a). Turning now to the mentalizing *vs* non-mentalizing contrast, the only region showing significant activity besides MPFC was right temporal pole. This region is frequently activated in studies of mentalizing (Frith and Frith, 2003), consistent with its strong anatomical projections with MPFC (Barbas *et al.*, 1999). At an uncorrected threshold, additional activity for the mentalizing *vs* non-mentalizing contrast was observed in bilateral tempero-parietal junction (Figure 2). This fits well with previous studies suggesting an important role of this region in mentalizing (e.g. Saxe and Wexler, 2005). Thus, the present study adds to the growing literature indicating that both mentalizing and selection between SO and SI thoughts are associated with robust, reproducible patterns of activation (Frith and Frith, 2003; Burgess *et al.*, 2005). Indeed, even within the present study, activity associated with mentalizing and attention generalized significantly from one task to another (although there was no significant generalization between these two contrasts themselves). In addition, despite the anatomical proximity of the MPFC regions associated with attention and mentalizing, the present results indicate that these regions can be dissociated within a single experiment (see also Simons *et al.*, in press), as well as on the basis of a statistical trend across a large number of studies (Gilbert *et al.*, 2006c).

SUPPLEMENTARY DATA

Supplementary data are available at *SCAN* online.

Conflict of Interest

None declared.

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