Involvement of rostral prefrontal cortex in selection between stimulus-oriented and stimulus-independent thought

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Abstract

We used functional magnetic resonance imaging to investigate brain activity while healthy subjects performed three different tasks, each of which alternated between: (i) phases relying on stimulus-oriented thought (i.e. cognitive processes provoked by incoming sensory information); and (ii) phases relying on stimulus-independent thought (i.e. cognitive processes that were not related to any information in the immediate sensory environment). Within each task, the two phases were matched as closely as possible. In all three tasks, lateral rostral prefrontal cortex was transiently activated by a switch between stimulus-oriented and stimulus-independent thought (regardless of the direction of the switch). Medial rostral prefrontal cortex consistently exhibited sustained activity for stimulus-oriented vs. stimulus-independent thought. These results suggest the involvement of rostral prefrontal cortex in selection between stimulus-oriented and stimulus-independent cognitive processes.

Introduction

A basic distinction may be drawn between stimulus-oriented cognitive processes (i.e. cognition provoked by incoming sensory information, or oriented towards something to be experienced through the senses) and stimulus-independent cognitive processes (i.e. cognition that is decoupled from all external stimuli; McGuire *et al*., 1996; Burgess *et al*., 2005a,b). Examples of the former type of process might include inspecting or looking for something; examples of the latter type of process might include imagining an event that is unrelated to one's current sensory environment or novel creative thought. It is important that we are able to select voluntarily between engaging in these two types of process, as the same neural systems may participate in both (e.g. Kosslyn *et al*., 1995; Farah, 2000; O'Craven & Kanwisher, 2000). However, the brain mechanisms involved in this form of selection have not been directly studied.

In the present study we employed functional magnetic resonance imaging (fMRI) to investigate this selection process, using a novel task-switching paradigm. In typical studies of task switching, subjects respond to a sequence of stimuli, alternating between two or more sets of stimulus–response rules (Monsell, 2003). However, in the present study, rather than alternating between stimulus–response rules, subjects alternated between phases where they based their responses on visual information, and phases where they based their responses (using the same task rules) on information that they generated themselves. In other words, subjects alternated between carrying out tasks provoked by stimuli presented to them visually, and doing the same tasks 'in their heads'. In such a design, selection between stimulus-oriented and stimulus-independent cognitive processes may take two forms: (i) sustained biasing of the balance between these two

types of process, depending on the current phase; and (ii) transient processes allowing subjects to switch from one mode to the other at the transitions between phases.

We focused particularly on rostral prefrontal cortex (PFC), approximating Brodmann's area (BA) 10, as previous studies have implicated this region in a wide variety of tasks that could be supposed to involve selection between stimulus-oriented and stimulus-independent thought (see Ramnani & Owen, 2004 for a review). For example, studies of episodic memory retrieval (Simons & Spiers, 2003) may require selection between stimulus-oriented processing of retrieval cues, and stimulus-independent evaluation of the information retrieved. Similarly, evaluating self-referential (Gusnard *et al*., 2001; Johnson *et al*., 2002; Frith & Frith, 2003) or self-generated (Christoff & Gabrieli, 2000) information (i.e. focusing on information that may conflict with incoming sensory information) will depend crucially on this selection process. Paradigms requiring subjects to hold information in mind about one task ('task A'), whilst simultaneously processing stimuli related to a different task ('task B') (e.g. Okuda *et al*., 1998; Koechlin *et al*., 1999; Burgess *et al*., 2001, 2003; Braver & Bongiolatti, 2002; Christoff *et al*., 2003), will also require selection between the stimulus-independent processes related to task A and the stimulus-oriented processes related to task B. Thus, the hypothesis that rostral PFC is involved in selection between stimulus-oriented and stimulus-independent thought may potentially explain its role in a wide variety of cognitive tasks (Burgess *et al*., 2005a,b).

Materials and methods

Subjects

There were 12 healthy right-handed subjects, aged 24–30 years (mean: 26 years; six females). All provided written informed consent before taking part.

Experimental design and procedure

Three separate tasks were investigated. Each task alternated between 'external' and 'internal' phases, which were similar in terms of visual stimuli presented, cognitive operations required and responses produced. However, they differed in that subjects responded on the basis of visually presented information (i.e. stimulus-oriented cognition) during the external phases, and self-generated information (i.e. stimulus-independent cognition) during the internal phases, each phase being cued by the nature of the stimulus (Fig. 1). Between-task differences were maximized in order to obtain a wide sampling of cognitive operations across tasks, and the data were analysed with a conjunction approach (cf. Price & Friston, 1997) so that a region was declared significant for a particular contrast only if it exhibited significant activations for each of the three tasks. Thus, the activations reported below are unlikely to result from task-specific stimuli, cognitive operations, or types of response, as they were observed in all three tasks.

We used a hybrid blocked and event-related design, allowing us to examine both the sustained haemodynamic changes in the brain associated with performing the tasks in one or the other condition, and also the transient changes that occurred when subjects switched from one mode to the other (Visscher *et al.*, 2003). Of course, 'external' phases still required stimulus-independent thought in the sense of the cognitive operations required to perform the tasks. Thus, both external and internal phases required some degree of stimulus-independent thought. However, whereas the external phases additionally required subjects to attend to visually presented information, the internal phases required stimulus-independent thought alone. To ensure that subjects would be likely to withdraw attention from the visual display during the internal phases, we presented potentially distracting visual information during these phases. However, the stimuli presented during the internal phases were sufficiently dissimilar to those presented during the external phases that it was always clear which phase was currently taking place.

Stimuli were projected onto a mirror in direct view of the subjects, who responded by pressing buttons on a response pad with their right hand. There were three tasks. The screen background in all tasks was black. In Task 1, subjects were presented with a white circle, diameter ~2°, with small red vertical marks at the '12 o'clock' and '6 o'clock' positions. During the external phase, a yellow 'clock hand' swept around the circle smoothly in a clockwise direction, passing one of the red marks once per second. Subjects were instructed to press a response button every time the yellow clock hand passed one of the red marks. During the internal phase, the clock hand became purple and turned in an anticlockwise direction, passing one of the red marks every 300 ms. In this phase, subjects were asked to continue pressing the response button at the same rate as they had in the external phase, rather than responding on the basis of the visual display. At a switch between the external and internal phases, the clock hand started from the position of one of the two red marks, chosen randomly.

In Task 2 (external phase) subjects 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, ~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 (see Fig. 1). A red arrow at the top-right corner of the shape indicated the position from which to start, at the beginning of each scanning session. Following the first button-press response this arrow was removed. During the internal phase the shape was replaced by a similarly sized white 'thought-bubble' shape; subjects were asked to imagine the shape that was presented in the

external phase and continue navigating from their current position (see Brooks, 1968 for a related task).

In Task 3 (external phase), subjects classified capital letters by pressing one of three buttons, according to whether the letter was composed entirely of straight lines, entirely of curves, or out of a combination of straight lines and 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, ~1° tall and wide. During the internal phase these letters were replaced with alternating question marks and upside-down question marks. Subjects were asked to mentally continue the sequence from their current position in the alphabet, performing the same classification task for each internally represented letter. The first letter to be presented in each external phase was the appropriate continuation of the sequence, assuming that the sequence had been correctly maintained during the preceding internal phase (see Kosslyn *et al.*, 1985 for a related task).

Within each task, the external and internal phases alternated, each phase lasting between 3 and 54 s (mean: 11 s). Four event types were defined: 'External Switch', marking an internal-to-external phase transition; 'Internal Switch', marking an external-to-internal phase transition; 'External Stay'; and 'Internal Stay'. The latter two 'Stay' events took place during the external and internal phases, respectively, and were accompanied by a displacement of the stimuli by ~1° in a diagonal direction, without the requirement for subjects to shift from one phase to the other. The purpose of these events was to control for the momentary changes in the visual display at the transition points between external and internal phases. The order of the four event types was randomized, with the constraint that each event could be followed only by a 'Stay' event corresponding to the current phase (internal or external), or a 'Switch' event corresponding to the other phase. These two events were selected with 50% probability. For each event, a duration between 3 and 7 s was selected (from a uniform distribution). The subsequent event was triggered by the subject's next response after that interval had elapsed, leading to a mean interval between events of 5.8 s.

Scanning procedure

Subjects were familiarized with the tasks during a practice session lasting ~40 min, immediately before the scanning session. A 3T Siemens Allegra head-only system was used to acquire both T1-weighted structural images and T2*-weighted echoplanar (EPI) images [64×64; 3×3 mm pixels; echo time (TE), 30 ms] with BOLD contrast. Each volume comprised 32 axial slices (3 mm thick, separated by 1.5 mm), covering the whole brain. Functional scans were acquired during six sessions, each comprising 175 volumes (lasting ~6 min). Volumes were acquired continuously with an effective repetition time (TR) of 2.08 s per volume. The first seven volumes in each session were discarded to allow for T1 equilibration effects. Each task was performed for two of the six sessions, in an ABCCBA order counterbalanced across subjects; each session began with an external task phase. Following the functional scans, a 12-min structural scan was performed.

Data analysis

fMRI data were analysed using SPM2 software (http://www.fil.ion.ucl.ac.uk/spm/spm2.html). Volumes were realigned, corrected for different slice acquisition times, normalized into 2-mm cubic voxels
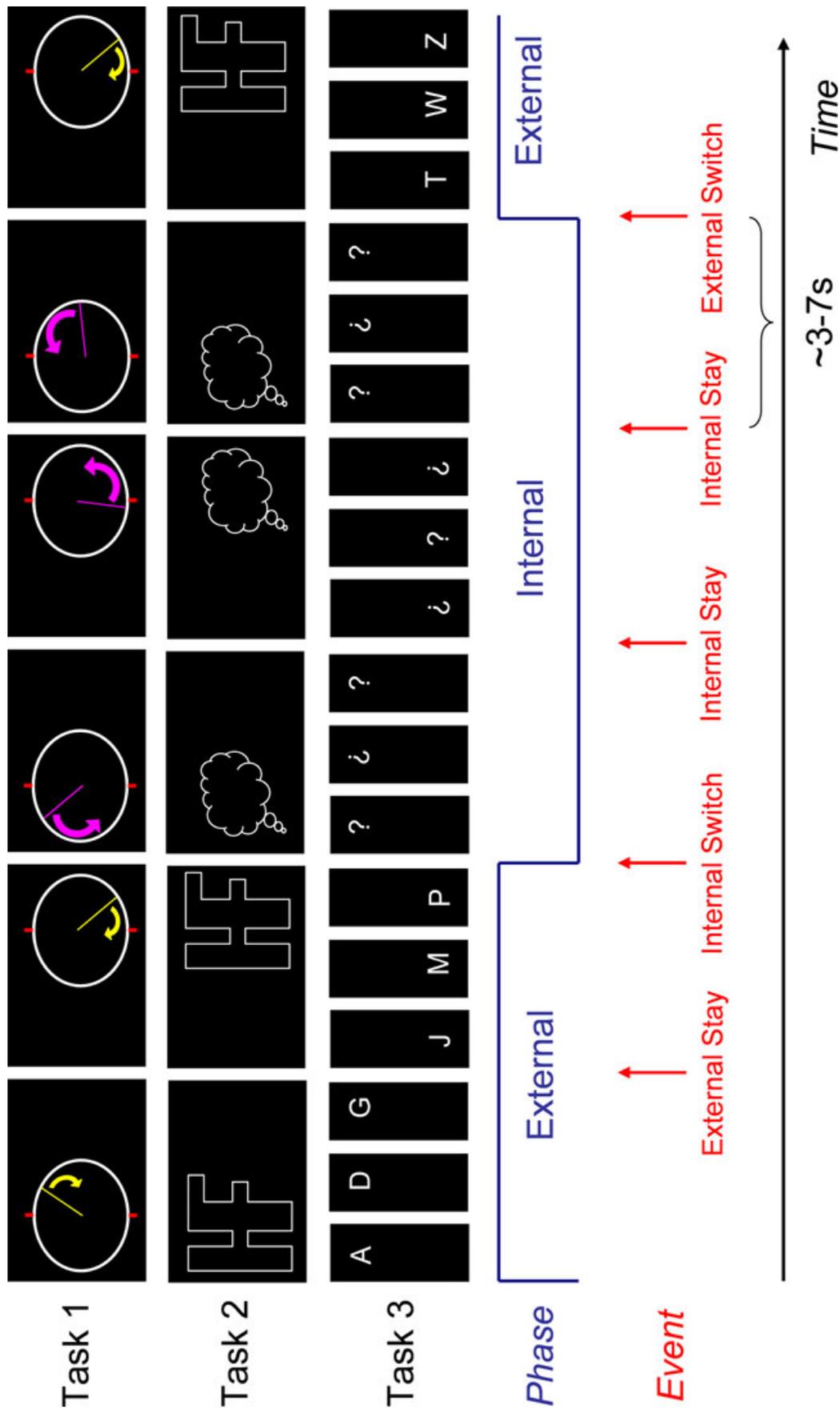
FIG. 1. Schematic representation of the three tasks.

using a standard EPI template based on the Montreal Neurological Institute (MNI) reference brain in Talairach space, and smoothed with an isotropic 8-mm, full-width, half-maximum Gaussian kernel. The volumes acquired during the six 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). Variance was decomposed into components associated both with sustained activity during the internal vs. external phases and transient activity related to the four event types. Because sustained and transient activity was modelled simultaneously, the two types of regressor only accounted for variance unique to each (Visscher *et al.*, 2003). Each event type was modelled with a pair of regressors, constructed by convolving a series of delta functions with a canonical haemodynamic response function (HRF) and the same function delayed by 3 s. The delta functions indexed the occurrence of each event. These regressors modelled event-related responses with two temporal components, referred to as 'early' and 'late' (Henson *et al.*, 2000). Sustained activity was modelled with a single boxcar regressor representing activity sustained throughout the internal phases of each run, convolved with a canonical HRF. These regressors, together with regressors representing residual movement-related artefacts 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. Linear contrasts of parameter estimates were performed separately for each task, averaging across the two sessions. Analyses of the event-related regressors averaged over the early and late components. The three resulting contrasts for each subject, one for each task, were then entered into a repeated-measures ANOVA, using non-sphericity correction (Friston *et al.*, 2002). Statistical parametric maps (SPMs) of the minimum t statistic across the three orthogonalized contrasts were generated; these SPMs were converted into SPMs of the Z statistic via associated P-values. Contrasts were thresholded at $P < 0.05$ corrected for multiple comparisons across the whole brain volume (i.e. each of the three contrasts was independently thresholded at the cube root of this value). Activations falling within BA 10, our *a priori* region of interest, were thresholded at $P < 0.05$ corrected for multiple comparisons across voxels in this region (as defined by the Brodmann map supplied with MRIcro: http://www.mricro.com; Rorden & Brett, 2000; $Z > 3.9$) if they did not survive a whole-brain corrected threshold. In the results below, only clusters of five or more contiguous voxels are reported.

Results

Behavioural data

Reaction times (RTs) outside the range 500–1500 ms in Task 1, and 250–5000 ms in Tasks 2 and 3 were excluded from the following analyses (leading to the exclusion of 2.6% of trials). The mean RTs and error rates for the trial following each of the four event types are presented in Table 1, separately for each of the three tasks. Initially the RT data were analysed in a 3 (Task) $\times 2$ (Phase: External/Internal) $\times 2$ (Switch: Stay/Switch) repeated-measures ANOVA. On average, RTs following Switch events were slower than those following Stay events ($F_{1,11} = 73$; $P < 0.001$), RTs following Internal events were slower than those following External events ($F_{1,11} = 34$; $P < 0.001$), and the difference in RT between Switch and Stay events was greater in the External than Internal phases ($F_{1,11} = 14$; $P < 0.001$). However, each of these effects was significantly modulated by Task

TABLE 1. Mean RTs and error rates for each of the event types, for each task

	External Switch	External Stay	Internal Switch	Internal Stay
Task 1				
RT	1019 ± 8.3	990 ± 4.1	1011 ± 13.5	1000 ± 17.1
Error (%)	0.6 ± 0.6	1.1 ± 0.5	3.9 ± 1.4	5.4 ± 1.7
Task 2				
RT	1590 ± 181	1304 ± 158	1363 ± 153	1466 ± 153
Error (%)	5.7 ± 2.0	4.4 ± 1.9	5.1 ± 1.9	6.8 ± 2.7
Task 3				
RT	1660 ± 140	1041 ± 73	2592 ± 113	2043 ± 142
Error (%)	3.3 ± 1.0	2.4 ± 1.1	3.8 ± 1.1	5.3 ± 2.4

Data are presented as mean ± SEM.

($F_{2,10} > 9$; $P < 0.01$). The effect of Phase was not consistent across tasks, as responses following Internal events were slower than those following External events in Tasks 1 and 3, but faster in Task 2. The effect of Switch and the Phase $\times$ Switch interaction were in the same direction for each task, but differed reliably in magnitude.

In Task 1, a response was counted as 'correct' if it fell within 200 ms of the correct time for that response. In Task 2 it was not possible to assess each response individually for accuracy (as there was no external marker for the subject's position on the edge of the shape), so accuracy was coded by investigating consecutive, overlapping sequences of four responses, to see if they were valid sequences of responses in the task. By chance this procedure should yield 56% accuracy, as only nine of the 16 possible four-response sequences were valid in this task. The proportion of correct responses was significantly greater than this chance level in all conditions ($t_{11} > 13$, $P < 0.001$). Post-error trials were excluded from the analysis of the Internal phases of Task 3, so that an error on one trial was not propagated to subsequent trials. Error data were analysed in a 3 (Task) $\times 2$ (Phase) $\times 2$ (Switch) repeated-measures ANOVA. The only reliable effect was a Task $\times$ Phase interaction ($F_{2,10} = 5$; $P < 0.05$), reflecting a significant difference in accuracy between the two phases in Task 1 ($F_{1,11} = 9$; $P < 0.05$), but not in Tasks 2 or 3 ($F_{1,11} < 2$; $P > 0.3$).

Functional imaging data

First, sustained activity during the internal and external phases was compared. No regions were significantly more active during internal than external phases, in the conjunction across the three tasks. The reverse contrast revealed several regions consistently more active during the external than internal phases, the most significant being a superior rostral medial frontal (hereafter 'rostromedial PFC') region (peak: 0, 64, 26; BA 10, extending superiorly into BA 9). Additional activations were located in more posterior medial frontal regions, parietal cortex, posterior cingulate and cerebellum (Table 2).

Next, we investigated transient activity related to the transitions between the two phases by subtracting activity related to the Stay events from that related to the Switch events. There were activations in bilateral superior parietal cortex (BA 7), right dorsolateral PFC (BA 9/46) and right lateral frontal pole (hereafter 'rostrolateral PFC'; BA 10; see Fig. 2). It should also be noted that similar regions of left dorsolateral and rostrolateral PFC showed significant activations at a more liberal threshold of $P < 0.001$ uncorrected (dorsolateral: -34, 46, 32; extent: 44 voxels; $Z_{max} = 3.87$; rostrolateral: -34, 54, 8; extent: 6 voxels; $Z_{max} = 3.24$), so the present results do not necessarily entail a functional dissociation between left and right prefrontal regions.

TABLE 2. Regions showing significant differences in BOLD signal between conditions

Region	BA	Hemisphere	x	y	z	$P*$	Z_{max}	Voxels (n)
External–Internal (sustained)								
Medial frontal cortex	10/9	–	0	64	26	< 0.001	6.4	102
	10/32	R	8	50	8	0.001	5.7	26
	6	L	−6	−8	74	< 0.001	5.9	50
Medial parietal cortex	7	L	−6	−46	74	0.001	5.8	44
Lateral parietal cortex	7	L	−28	−54	64	0.004	5.5	17
	40	R	52	−54	46	0.02	5.1	17
	7	R	28	−56	58	0.001	5.8	52
Posterior cingulate	23	–	0	−54	18	0.018	5.2	6
Cerebellum	–	–	0	−72	−16	0.003	5.6	13
	–	R	4	−76	−38	0.02	5.1	5
Switch–Stay (transient)								
Frontal pole	10	R	34	60	4	0.029†	4.1	8
Dorsolateral prefrontal cortex	9/46	R	36	46	30	0.007	5.3	11
Lateral parietal cortex	7	R	30	−56	62	< 0.001	6.3	126
	7	L	−38	−56	60	0.001	5.7	32

Coordinates refer to the Montreal Neurological Institute reference brain. BAs are approximate. *Corrected for multiple comparisons across all brain voxels. †Corrected for multiple comparisons across all voxels in BA 10.

A follow-up analysis investigated whether the regions activated by the Switch–Stay contrast were differentially activated by transitions from external to internal phases, vs. transitions in the reverse direction. For each of the four regions listed under 'Switch–Stay' in Table 2, parameter estimates related to the four event types were entered into a 3 (Task) × 2 (Phase: External/Internal) × 2 (Switch: Stay/Switch) repeated-measures ANOVA. In all four regions there was a reliable effect of Switch ($F_{1,10} > 13$, $P < 0.005$). However, neither the Phase × Switch nor the Task × Phase × Switch interaction was significant in any of the regions ($F_{1,10} < 2$, $P > 0.19$). Thus, the results suggest that bilateral superior parietal cortex, right dorsolateral PFC and right rostrolateral PFC are involved in switching between stimulus-oriented and stimulus-independent cognitive processes, regardless of the direction of the switch.

We next investigated whether the difference in results between the rostromedial PFC region (showing a sustained difference in activity between the two phases) and the rostrolateral PFC region (showing transient activation at the point of a switch between the two phases) represents a genuine double dissociation between the roles of these two regions (Shallice, 1988), rather than being a thresholding artefact. The peak signal change associated with each contrast was extracted from the two regions, separately for each task, and entered into a 2 (Region: rostrolateral/rostromedial) × 2 (Contrast: Switch–Stay/External–Internal) repeated-measures ANOVA. The Region × Contrast interaction was reliable in all three tasks ($F_{1,11} > 5.8$; $P < 0.035$ in each task). Moreover, all three were crossover interactions (see Fig. 2C). Thus, the double dissociation was confirmed statistically in all three tasks, and could not be caused by one region being generally more responsive than the other, or by one contrast being generally more likely to elicit signal change than the other.

Finally, we investigated whether the rostrolateral and rostromedial PFC activations in this study could be attributed to task difficulty effects related to differences in RTs and error rates between conditions. First we investigated whether signal change in the rostrolateral PFC region activated by the Switch–Stay contrast mirrored the between-task differences in the behavioural data. The increase in RT for Switch vs. Stay events ranged from 20 ms in Task 1 to 583 ms in Task 3 (Task × Condition interaction: $F_{2,10} = 80$; $P < 0.000001$). However, the corresponding increase in signal in rostrolateral PFC did not differ reliably between tasks ($F_{2,10} = 1$; $P > 0.3$), despite being significant in each ($F_{1,11} > 7$; $P < 0.022$ for each task). Thus, whereas the

magnitude of the RT difference between Switch and Stay events differed ∼30-fold between tasks, the magnitude of the difference in BOLD-signal between Switch and Stay events was relatively constant. It is therefore implausible to suggest that the rostrolateral PFC activation for the Switch–Stay contrast was simply a by-product of the slower RTs for Switch than Stay events. This conclusion was further supported by a re-analysis of the data including additional regressors representing the parametric modulation of each event by RT. In this analysis the subtraction of Switch–Stay was still significant in right rostrolateral PFC (peak: 32, 60, 4; extent: 5 voxels; $Z_{max} = 4.0$). No regions were reliably associated with faster RTs. Slower RTs were associated with activity in a single region of right ventrolateral PFC (peak: 50, 42, −8; extent: 16 voxels; $Z_{max} = 5.8$; BA 47). Even at an extremely liberal threshold of $P < 0.05$ uncorrected, there was no reliable association between RT and activity in the rostrolateral PFC region identified in the original analysis (34, 60, 4).

We next investigated whether the rostromedial PFC activation for the External–Internal contrast could simply reflect the greater 'easiness' of the External phases. The rostromedial PFC signal change associated with this contrast did not differ reliably between tasks ($F_{2,10} < 1$), despite being significant in each ($t_{11} > 3.1$; $P < 0.01$ for each task). However, while the behavioural data in Task 3 suggested that responses in the Internal phases were 967 ms slower than those in External phases, and 2% more error prone, the data in Task 2 suggested that responses in the Internal phases were 33 ms faster than in the External phases, and the difference in error rates between the two phases was below 1%. Thus, the behavioural data varied greatly between tasks, and in at least one task there was no consistent pattern suggesting a difference in difficulty between phases, yet the BOLD signal change associated with the External–Internal contrast did not differ reliably between tasks.

We additionally investigated whether signal change in the rostrolateral and rostromedial PFC regions was reliably correlated with between-subject differences in the behavioural data (i.e. whether subjects showing large behavioural effects showed correspondingly large BOLD signal effects). This analysis was conducted separately for the three tasks. Signal change in the rostromedial PFC region related to the External–Internal contrast was not reliably correlated in any task with either the difference in RTs or in error rates between these two conditions, and nor did these correlations even have a consistent sign across tasks ($−0.50 < r < 0.49$; $P > 0.05$). Similarly,
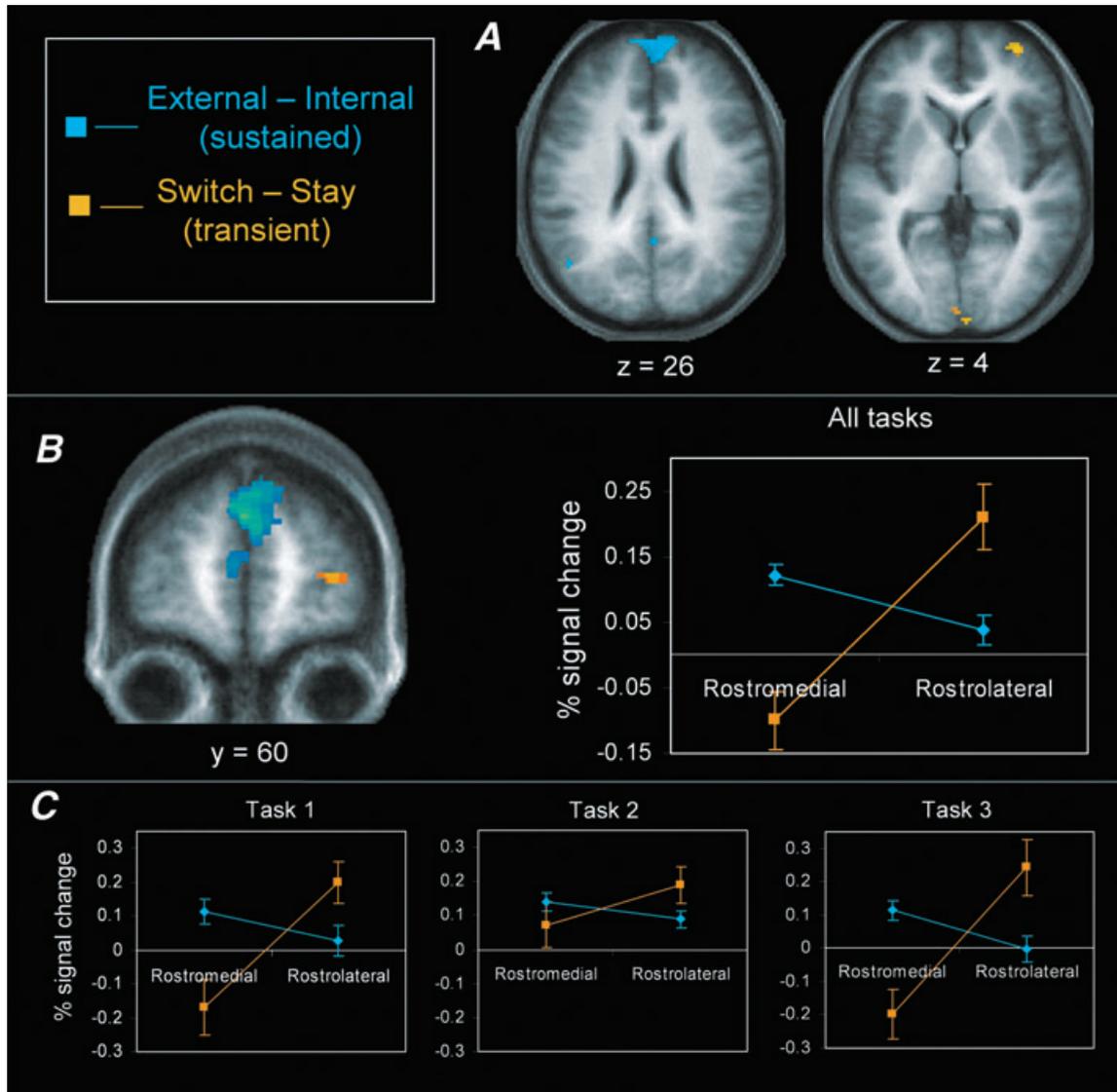
FIG. 2. (A) Areas of activation for the contrasts External–Internal (left) and Switch–Stay (right), plotted separately on axial slices of the averaged normalized structural scan of the 12 subjects. (B) Double dissociation between the rostrolateral and rostromedial PFC regions. Left image shows the two contrasts plotted together on a coronal slice of the mean structural scan. Right graph plots peak signal change related to each contrast in the two regions, averaged across subjects and tasks. (C) Signal change plotted separately for each task. All images follow neurological convention (left∕right not flipped). For illustrative purposes, contrasts were thresholded at $P < 0.0001$ uncorrected, extent threshold: 5 voxels. Note: even at this relatively liberal threshold there were no areas of activation for the contrast of Internal–External. Error bars in graphs show standard errors.

signal change in the rostrolateral PFC region related to the Switch–Stay contrast was not reliably correlated with the difference in RTs or error rates between these two conditions ($-0.35 < r < 0.31$; $P > 0.2$). Thus, it is not possible to attribute the rostrolateral and rostromedial PFC activations in the present study simply to differences in difficulty between conditions, as indexed by RTs and error rates.

Discussion

Consistently, across three quite different tasks, phases that involved both stimulus-oriented and stimulus-independent thought ('external' phases) were associated with sustained activity in rostromedial PFC, compared with phases of the tasks requiring just stimulus-independent thought ('internal' phases). A right rostrolateral PFC region was functionally dissociable from this rostromedial PFC region, consis-

tently showing transient activation at the point of a switch between the internal and external phases. Thus, the results of this study suggest the involvement of rostral PFC in tasks requiring selection between stimulus-oriented and stimulus-independent thought (Burgess *et al.*, 2005a,b), with dissociable roles of lateral and medial subregions (Simons *et al.*, 2005a,b). This functional dissociation is consistent with the existence of cytoarchitectonic variation between lateral and medial regions of human BA 10 (Petrides & Pandya, 1999).

There are three obvious questions one might ask about the pattern of results presented here. This first is whether the results might be due to differences in 'task difficulty' between conditions. The second is whether the results might reflect differences between the internal and external phases in the requirement for rehearsal or maintenance of information (i.e. 'working memory'), or inhibition of conflicting information. The third concerns the degree to which the brain systems

identified here might overlap with those involved in conventional task switching paradigms, involving switching between various sets of stimulus–response mappings, rather than switching between stimulus-oriented and stimulus-independent versions of the same task.

As we have seen, there is little support in the present data for an explanation of rostral PFC activity in terms of the difficulty of the various conditions. Signal change in rostromedial PFC was unrelated to behavioural differences between the internal and external phases, and signal change in rostrolateral PFC was unrelated to the behavioural cost of switching between the two phases. Thus, these activations cannot be attributed simply to task difficulty, as indexed by RTs and error rates. The lack of association between signal change in rostrolateral PFC and the behavioural cost of task switching would be consistent with previous studies suggesting that 'switch costs' may be a poor indicator of the time taken by the control processes responsible for actually implementing a switch of task (Allport et al., 1994; Allport & Wylie, 2000; Altmann, 2002; Gilbert & Shallice, 2002; Yeung & Monsell, 2003; Gilbert, 2005).

An explanation of the present results in terms of different working memory or inhibition demands between the two phases may also be dismissed. There were no reliable activations associated with the internal phases (contrasted with the external phases), even at an uncorrected statistical threshold (Fig. 2). Rather, greater activity was associated with the external phases of the tasks. If anything, these phases had reduced rehearsal or maintenance demands, as task-relevant information was perceptually available, and reduced inhibition demands as this perceptual information, being task-relevant, did not have to be ignored. Thus, it is implausible to suggest that the activations related to the External–Internal subtraction could be a product of differing working memory or inhibition demands between the two phases.

We now turn to the issue of overlap between the brain systems identified here and those involved in conventional task-switching paradigms. The regions that showed transient activity when subjects switched between stimulus-oriented and stimulus-independent thought – right rostrolateral PFC, right dorsolateral PFC and bilateral superior parietal cortex – have all been implicated in previous studies of task switching (e.g. DiGirolamo et al., 2001; Dreher et al., 2002; Braver et al., 2003; see also Rushworth et al., 2002). This suggests some commonality between the processes involved in conventional task-switching paradigms, involving switches between two or more sets of stimulus–response rules (Monsell, 2003), and the processes involved in the present study when subjects switched between stimulus-oriented and stimulus-independent cognitive processes. However, it is not clear from these studies what the critical factor is for eliciting rostral PFC activation, as the majority of studies investigating task switching have not reported rostral PFC activation (e.g. Dove et al., 2000; Kimberg et al., 2000; Sohn et al., 2000; Brass & von Cramon, 2004; Ruge et al., 2005). Furthermore, studies of patients with circumscribed rostral PFC lesions have demonstrated intact performance of tests involving task switching such as the Wisconsin Card Sorting Test (Shallice & Burgess, 1991; Burgess, 2000).

Two recent fMRI studies have shed light on the role of rostrolateral PFC in task switching. In a study by Braver et al. (2003) there were two types of block: 'single-task blocks', where subjects performed the same task on every trial, and 'mixed-task blocks' where trials of two tasks were randomly intermixed. Using a mixed blocked and event-related analysis, Braver et al. (2003) found that dorsolateral PFC and superior parietal regions showed transient activation at the point of a switch between two stimulus–response rules in the mixed-task blocks. By contrast, right rostrolateral PFC showed sustained activation

throughout mixed-task blocks, compared with single-task blocks, without showing transient activity when subjects actually switched between tasks in the mixed-task blocks. One interpretation of these results would be that rostrolateral PFC is involved in the process of co-ordinating an internal representation of the various tasks required with an ongoing sequence of external events, rather than the process of actually switching between task sets. Such a co-ordination process may require frequent switches between executing the stimulus-oriented cognitive processes demanded by the stimuli, and the internally oriented processes that maintain representations of the tasks required, regardless of whether each trial happens to require the same task as the previous trial. This hypothesis is supported by a recent fMRI study of task switching by Forstmann et al. (2005), who found that right rostrolateral PFC was not activated when subjects switched between tasks, but was activated in trials where subjects had to engage in stimulus-independent processing (inferring the appropriate task set from an indirect cue) before executing the stimulus-oriented processes prompted by the experimental stimuli.

Putting together the results of the present study and the results of Braver et al. (2003) and Forstmann et al. (2005), the most parsimonious explanation of the role of rostrolateral PFC in task switching seems to be that this region is activated by switches between stimulus-oriented and stimulus-independent thought, without necessarily being activated by the process of switching from one task set to another (see Pollmann, 2004 for a related suggestion). The critical test of this hypothesis will be to investigate directly whether switching between tasks requiring stimulus-oriented vs. stimulus-independent thought elicits greater activity in rostrolateral PFC than switching between two tasks involving stimulus-oriented (or stimulus-independent) thought alone. It is of course possible that standard task-switching paradigms may at least occasionally elicit a switch between stimulus-oriented and stimulus-independent processing at the point of a switch between tasks (e.g. if subjects need to retrieve the new task rules before switching tasks). Nevertheless, it should be possible for future studies to manipulate the degree to which task transitions require switching between stimulus-oriented and stimulus-independent thought, vs. switching between different sets of stimulus–response mappings, in order to functionally dissociate these two types of task switching. This will be an important topic for further research. The precise role of rostrolateral PFC in switching between stimulus-oriented and stimulus-independent cognition (e.g. whether this brain region is involved in activating the processes one wishes to engage, or in inhibiting the currently active processes) is another matter that requires further investigation.

Turning now to the medial aspects of the rostral PFC, it may appear surprising that rostromedial PFC activation in the present study was greater in the phases requiring stimulus-oriented thought than in the phases requiring stimulus-independent thought alone. Previous studies have implicated this region in a wide variety of tasks involving internally oriented cognitive processes such as attributing unobservable mental states to other agents (Frith & Frith, 2003) or reflecting on one's own emotions (Gusnard et al., 2001). However, these tasks also required subjects to attend to the external environment, perhaps making them more similar to the external phases of the present study than the internal phases. For example, in the study of Gusnard et al. (2001), the task used to induce internally oriented processing required subjects to judge the pleasantness of externally presented photographs, rather than requiring subjects to ignore all externally presented information (as in the internal phases in the present study). Thus, previous studies suggesting an involvement of rostromedial PFC in internally oriented cognitive processes (whilst subjects may also attend to perceptual information) need not be in conflict with the

present results, which demonstrate rostromedial PFC activity associated with performing tasks that involve both stimulus-oriented and stimulus-independent thought (external phases), compared with tasks involving stimulus-independent thought alone (internal phases). This result would be compatible with recent studies suggesting that rostromedial PFC may play a critical role in tasks requiring moment-to-moment perception to be linked with associated cognitive and affective representations (Janata *et al.*, 2002; Koechlin *et al.*, 2002; Small *et al.*, 2003), rather than being exclusively involved in internally oriented cognitive processes.

Several brain regions identified in the present study as being involved in selection between internally and externally driven cognitive processing have been shown previously to exhibit relatively high levels of metabolic activity during conscious rest, compared with their level of activity during various cognitive tasks (Shulman *et al.*, 1997; Raichle *et al.*, 2001). These regions include both lateral and medial rostral PFC, along with other medial frontal and parietal regions, and posterior cingulate cortex. It has therefore been suggested that this network of regions participates in a 'default mode of brain function' when no specific task is instructed (Raichle *et al.*, 2001), involving 'surveillance of the internal and external environments' (Gusnard *et al.*, 2001). The present results are consistent with this model, as such a 'surveillance' process will depend upon continual selection between the various stimulus-independent and stimulus-oriented targets for further cognitive processing, in the absence of any specified task. These results are also consistent with recent theoretical accounts that have focused specifically on the functions of rostral PFC, in terms of processing self-referential (Ruby & Decety, 2001; Johnson *et al.*, 2002; Frith & Frith, 2003) or self-generated (Christoff & Gabrieli, 2000; Christoff *et al.*, 2003; Hunter *et al.*, 2003) information, or in terms of high-level cognitive functions such as establishing linguistic coherence (Ferstl & von Cramon, 2002), cognitive branching (Koechlin *et al.*, 1999), reasoning (Christoff *et al.*, 2001) and the integration of multiple cognitive operations (Braver & Bongiolatti, 2002; Ramnani & Owen, 2004). These accounts provide an important characterization of the types of task, defined in terms of the cognitive functions required, that may rely on processes subserved by rostral PFC. The present study potentially unifies these accounts, providing a simple explanation of the results from these apparently disparate domains. Specifically, the present results suggest that a basic information processing operation – selection between stimulus-independent and stimulus-oriented cognitive processes – could underlie the involvement of rostral PFC in this wide range of cognitive tasks.

A cardinal situation involving selection between stimulus-oriented and stimulus-independent thought is when our ongoing engagement with external stimuli needs to be organized according to previously formed, internally represented intentions (Brandimonte *et al.*, 1996; Duncan *et al.*, 1996). Previous neuroimaging studies of tasks with such requirements (e.g. Okuda *et al.*, 1998; Burgess *et al.*, 2001, 2003) have implicated rostral PFC. Moreover, patients with rostral PFC lesions have been reported to be impaired on such tasks without necessarily being impaired on other tests of executive function (Shallice & Burgess, 1991; Burgess, 2000; Burgess *et al.*, 2000; Goel & Grafman, 2000), although patients with more extensive frontal lobe damage may often show impairments on some of these other tests (e.g. Stuss *et al.*, 2000). The current findings therefore converge with both neuropsychological and neuroimaging investigations to suggest the involvement of rostral PFC in tasks requiring selection between stimulus-oriented and stimulus-independent thought, and establish a dissociation between the roles of lateral and medial subregions (Burgess *et al.*, 2005a,b; Simons *et al.*, 2005a,b).

Abbreviations

BA, Brodmann's area; fMRI, functional magnetic resonance imaging; HRF, haemodynamic response function; PFC, prefrontal cortex; RTs, reaction times; SPMs, statistical parametric maps.

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