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FEATURE ARTICLE
Fractionating Attentional Control Using Event-Related fMRI

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Despite numerous functional neuroimaging and lesion studies of human executive function, the precise neuroanatomical correlates of specific components of attentional control remain controversial. Using a novel approach that focused upon volunteer behavior rather than experimental manipulations, specific components of attentional shifting were fractionated, and their neural correlates differentiated using event-related fMRI. The results demonstrate that the ventrolateral prefrontal cortex is involved in switching attention "between" stimulus dimensions, whereas the posterior parietal cortex mediates changes in stimulus-response mapping. Furthermore, reversals based on negative feedback activated the lateral orbitofrontal cortex, whereas positive feedback modulated activity in the medial orbital frontal cortex. Finally, the dorsolateral prefrontal cortex was active throughout solution search. These findings support the hypothesis that lateral prefrontal, orbital, and parietal areas form a supervisory network that controls the focus of attention and suggests that these regions can be fractionated in terms of their specific contributions.

Keywords: attention, executive function, lateral prefrontal cortex, orbitofrontal cortex, posterior parietal cortex

Introduction

Multiple regions within the human frontal and parietal cortices have been implicated in aspects of attentional control. Broadly speaking, lateral prefrontal and posterior parietal regions have been shown to play roles in higher level "executive" processes, including working memory and attention (for reviews, see Duncan and Owen 2000; Duncan 2001; Miller and Cohen 2001), whereas orbitofrontal regions appear to be preferentially involved in reward-related components of behavioral control (e.g., Rogers and others 1999, 2000; Elliott and others 2000; O'Doherty and others 2001). Advances in event-related fMRI have made the measurement of transient cognitive events feasible by allowing short events with short interstimulus intervals to be estimated independently within a noisy background of other task-related events. Although a number of studies have used this approach to investigate aspects of attentional control, they have invariably confounded multiple discrete cognitive operations within their designs, making it impossible to define the exact contribution made by any particular cortical region (Nagahama and others 1999, 2001). For example, several previous fMRI studies using variants of the wisconsin card sorting test have confounded attentional switches between dimensions with reception of negative feedback, response inhibition, and updating working memory (e.g., Konishi and others 1998). Other studies have used the same stimuli repeatedly to maximize experimenter control, design simplicity, and the generation of sufficient events to estimate the critical event types (e.g., Dove and others 2000; Cools and others 2002). Again, this approach confounds multiple switch components such as response suppression with attended stimulus change and rule change (Cools and others 2002) or stimulus color change with reversal of rule and response (Dove and others 2000). Most importantly, previous studies have focused on experimental manipulations (e.g., experimenter-imposed shifts) rather than volunteer behavior during the scanning session.

In this fMRI study, a novel approach was used in which the responses dictated the pace and order of experimental events. Hence, the focus of attention could be monitored and used to define the events (e.g., attentional shifts), rather than those events being dictated by the experimental design. This approach allowed the volunteers' chosen decision-making strategies and attentional shifts to be functionally and behaviorally examined for the first time. Many stimulus sets were used, each containing stimuli of 2 distinct types (faces and buildings). Switches of attention between stimuli of the same type (intradimensional shifts) and between stimuli of different types (extradimensional shifts) could therefore be modeled. Due to the difficulty of intermixing extradimensional and intradimensional shifts without using unnatural cueing or fixed-order event sequences, previous studies have used blocked designs which allow only limited interpretation of the activation results (e.g., Rogers and others 2000). Here, these transient attentional control functions were intermixed and could therefore be contrasted at the event level in the current trial and error situation. Thus, extra- and intradimensional shifts could be compared directly, effectively isolating the extradimensional component of shifting from other switch-related processes, such as inhibition of the previously relevant response (Nakahara and others 2002). Furthermore, switches of attention could occur both with and without set change, which allowed the reward history of the stimulus set to be manipulated, thereby enabling reward-related switch components to be examined for the first time uncontaminated by other factors in the design. The novel partial feedback paradigm also enabled switch events and feedback events to be modeled separately, allowing regions involved in abstract reward processing and/or the implementation of attentional control to be identified. Finally, less transient functions, such as actively calculating which is the target from within a finite set of possible stimuli by trial and error and making routine responses once the target has been identified, could also be contrasted.

Materials and Methods

Experimental Design

A novel shifting task was designed in which volunteers had to work out which object was the target in a stimulus set consisting of 2 faces and

2 buildings (Fig. 1). The stimulus set was presented as 2 compound stimulus pairs appearing on the left and right of the screen. Both compound stimulus pairs consisted of a face and a building superimposed on top of each other. Each stimulus subtended a visual vertical angle of 6 degrees and a horizontal angle of 6.2 degrees, with a total combined horizontal angle of 15 degrees.

On each trial, the volunteers were required to indicate using a button box which side of the screen they thought the target was located on, and at the point of response, the stimuli were removed from the screen. Every 2nd response, feedback was presented on the screen for 0.6 s, indicating whether the stimulus they had chosen was the target or not. The feedback given was the word "correct" in green if the last 2 responses were both correct. Otherwise, the feedback was the word "incorrect" in red.

After 6 correct responses to the target (i.e., 3 positive feedback events), a change of target occurred. The change was either in the form of a set change, in which new compound stimulus pairs were presented, or in the form of a rule change, in which the set would stay the same and a previous nontarget would become the target. Maximum uncertainty was ensured in both cases, as the new target could be either a stimulus of the same type or a stimulus of the alternative type. As the face–house combinations comprising the compound stimuli were reversed on every trial, it was possible to calculate exactly which stimulus was being attended to by examining consecutive responses.

The partial feedback technique allowed the response events that comprised attentional switch decisions to be modeled separately from those confounding response with feedback.

Before entering the scanner, the volunteers were clearly instructed to keep responding to the correct target until informed that it was no longer the target. Volunteers were also asked to respond "as quickly and accurately as possible." Although it is possible that volunteers could compute the number of trials required to reach criteria and then make anticipatory switches during reversals, the performance data confirm that this never actually happened.

Event Modeling

The event modeling focused on individual types of volunteer response, defined according to the current and previous focuses of attention. There were 5 types of event where the volunteer switched their focus of attention, one non-switchevent, and the responses with positive and negative feedback during solution search and when the target was known were modeled. 1 nonswitch event, and the responses with positive and negative feedback during solution search and when the target was known (Fig. 1).

Two of the switch events related to the period when the volunteer was actively trying to work out which was the target; one was termed "extradimensional" because the focus of attention switched between stimuli of different types (e.g., from a face to a building) and the other "intradimensional" because the focus of attention switched between stimuli of the same type (e.g., from 1 face to another face). Although each of these events involved multiple switch components (e.g., response suppression and attended stimulus change), the only way in which they differed from one another was with respect to the change of attention to stimulus type, so subtraction of one from the other isolated this extradimensional component.

Two additional switch events were defined at the point when the volunteer had correctly identified the previous target and a different stimulus became the new target. In one of these switch events, the stimulus set was changed so the volunteer could not respond to the previous target but had to switch to a target that had not been seen previously. This effectively removed any response suppression component and was called a "set change." In the other switch event, the stimulus set stayed the same but the reward contingency changed. Thus, a negative feedback event to the previous target occurred, and the volunteer was required to shift attention to look for the new target. Because the new target was a previous nontarget and because the previous target was still present (but as a nontarget), this manipulation was termed a "reversal." Although these 2 events had multiple components, subtraction of switching with stimulus set change from switching with reward contingency allowed examination of the reversal aspect of attentional shifting.

The final switch event was the 1st response to the correct target after the volunteer had received positive feedback. At this stage, an important behavioral change occurred as the volunteer stopped trying to work out which was the target (solution search) and began to respond to the stimulus that they now knew to be correct. This switch corresponds to what the volunteer was doing rather than what they were attending to, which remained the same. This event was compared with the otherwise identical subsequent events (the 6th event type), in which the responses were made to the same stimulus again while knowing it was correct on the basis of feedback, and here these are called early and late correct responses. Contrasting these 2 events therefore isolated the goal change component of cognitive control; that is, where the volunteers change their behavioral focus from identifying which stimulus is the target to identifying the location of the known target.

Finally, positive and negative feedback events were compared directly to isolate any components involved specifically in processing the reception of abstract positive and negative rewards.

Regions of Interest

In the fMRI analysis, regions shown previously to have a role in attentional switching were examined.

Regions of interest (ROIs) were defined within the lateral and medial orbitofrontal cortex (OFC), ventral areas of the lateral prefrontal cortex (VLPFC), dorsal areas of the lateral prefrontal cortex (DLPFC), and the posterior parietal cortex (PPC) based on previous studies of executive function.

Multiple regions of OFC have been implicated in reward-based control of behavior (Rogers and others 1999, 2000). Recently, a distinction has been drawn between the lateral and medial surfaces, which are thought to be involved in processing negative and positive reward, respectively (Elliott and others 2000; O'Doherty and others 2001). The coordinates used to define the orbital ROI's in this study were taken from a study by O'Doherty and others (2001) in which a distinct right lateral area was shown to be involved in processing negative reward at reversal of a reward contingency, with a medial orbital region shown to be involved in the reception of positive feedback. Accordingly, bilateral 10-mm-radius spherical ROI's were defined at the reported peak right lateral coordinate, and this coordinate mirrored for the left hemisphere ($X = -36$, $Y = 58$, $Z = -12$) ($X = 36$, $Y = 58$, $Z = -12$). Similarly, the mean coordinates of the medial orbital activation were used to define a 10-mm spherical ROI at $X = -3$, $Y = 37$, $Z = -21$.

Both the VLPFC and the DLPFC have been implicated in a wide variety of tasks requiring attention, but the exact roles played by these regions in attentional shifting is unclear. Ten-millimeter ROI's were defined bilaterally in the DLPFC and the VLPFC, based upon averaged coordinates taken from an analysis, in which multiple and diverse parametrically varied cognitive tasks requiring attention were compared (Duncan and Owen 2000). Mean coordinates were at $X = -38$, $Y = 30$, $Z = 22$ and $X = 38$, $Y = 30$, $Z = 22$ for the DLPFC and $X = -39$, $Y = 20$, $Z = 2$ and $X = 39$, $Y = 20$, $Z = 2$ for the VLPFC.

Finally, PPC activity has typically been observed in association with lateral prefrontal activity, and mean coordinates were again taken from Duncan and Owen (2000) to define bilateral 10-mm spherical ROI's for this region $X = -31$, $Y = -53$, $Z = 40$ and $X = 34$, $Y = -52$, $Z = 41$.

Imaging Acquisition

A total of 16 volunteers were scanned at the Wolfson Brain Imaging Centre using a 3-T Bruker Medspec scanner (Bruker s300, Ettingen, Germany) with 21 slices (4 mm slices with 1 mm interslice gap) per image and a time repetition of 1.1 s and in-plane resolution of 3.125 × 3.125 mm. A total of 850 T_2-weighted echo-planar images, depicting blood oxygen level–dependent contrast were acquired per run, and the 1st 18 were discarded to avoid T_1-equilibrium effects. Images were slice time acquisition corrected, reoriented, subject motion corrected, geometrically undistorted using phase maps (Cusack and others 2003), spatially normalized to the standard Montreal Neurological Institute echo-planar imaging template, smoothed with an 8-mm full-width at half-maximum Gaussian kernel, and modeled using statistical parametric mapping 2 (Wellcome Department of Cognitive Neurology). The time series were high pass filtered. The hemodynamic response was modeled to the stimulus onsets and durations. For switch events durations were

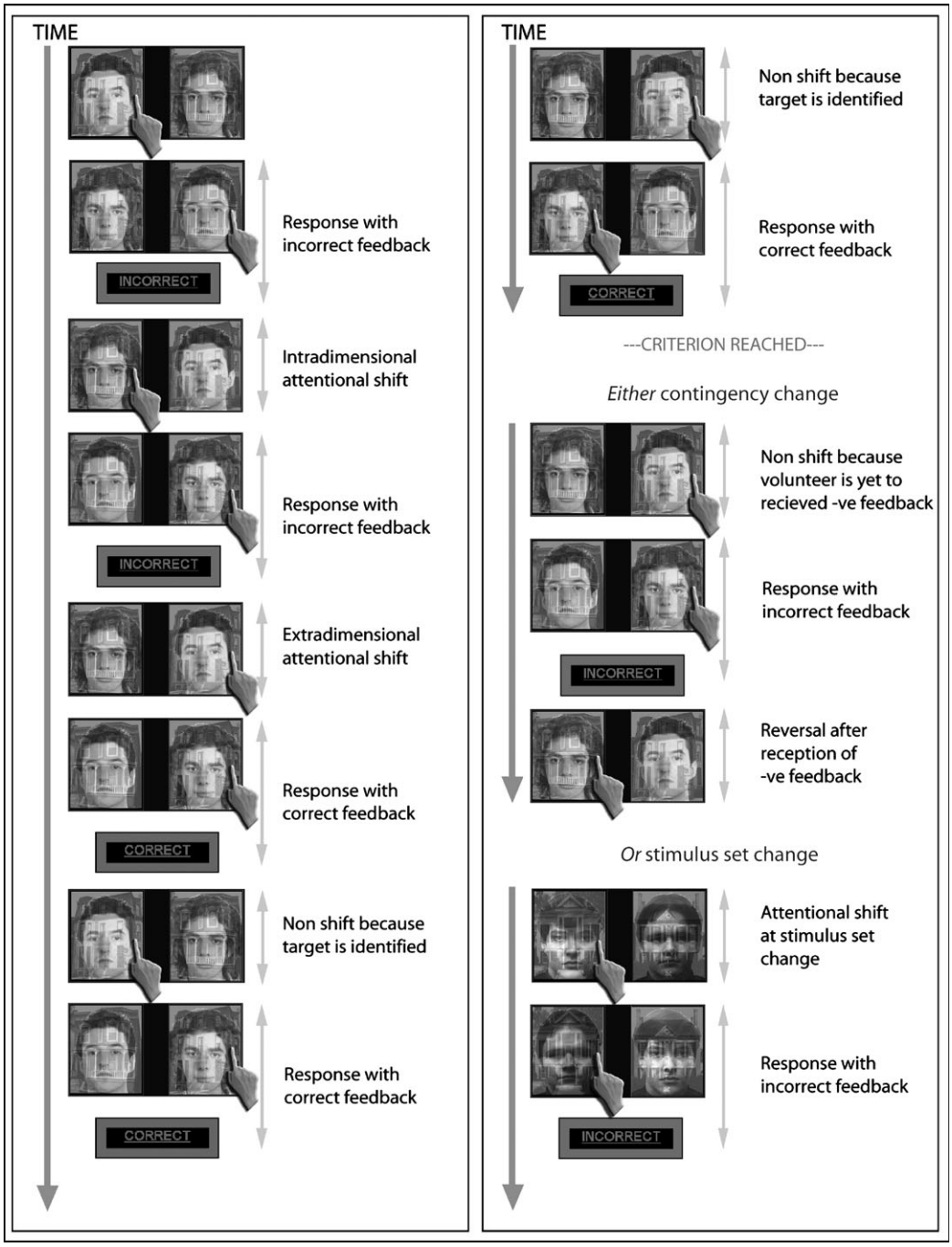

Figure 1. Illustrates a typical series of trials. The volunteer must work out by trial and error which of the 2 faces and 2 buildings is the target item. In this example, the volunteer initially chooses the face in the left superimposed face–building pair and so indicates left with the button box. When the response is made, the stimuli are removed from the screen and reappear after a short interval rearranged with the chosen face on the right of the screen superimposed on the other building; the volunteer therefore indicates right. Because the face–building combinations swap from 1 trial to the next, the program can compute which item was selected and because (in this example) it is not the target, negative feedback is given. Subsequently, the stimuli reappear on the screen, and the volunteer selects the other face (intradimensional shift). Following the 2nd response, negative feedback is given and the volunteer switches to select the building on the right of the screen (extradimensional shift). Following the 2nd response to the building, positive feedback is given because the volunteer has correctly identified the target item. When the stimuli reappear on the screen, the volunteer responds to the same building as they now know that it is the target (early correct response). They receive positive feedback on the 2nd response and so continue to select the same building (late correct response). After responding correctly again they receive positive feedback and have now reached the criteria of 6 correct responses in a row. One of the 2 things then happens; a new stimulus set is presented, in which case the volunteer starts searching for the new target (set change). Alternatively, the reward contingency changes, in which case the volunteer responds twice more to the same building (because they have no way of knowing that anything has changed) before receiving negative feedback. They must then inhibit their responses to the recently rewarded target stimulus and start trying to identify which of the other 3 possible items has become the target (reversal). It is important to note that the extradimensional and intradimensional shift events, along with the feedback, do not always occur in the sequence shown because the order in which the stimuli are tested is determined entirely by the choices made by the volunteers.

up until the time of response at which stage the stimuli were removed from the screen, whereas for feedback events durations were up until the point of removal of the feedback from the screen. The contrasts of interest were extracted, and the con images for the critical contrasts exported and analyzed in a higher level group random-effects analysis. ROIs were then modeled for this higher level analysis using the Marseille Boîte A Region d'Intérét (MarsBars) toolbox (Brett and others 2002). These higher level group analyses were also explored unconstrained for the whole brain in statistical parametric mapping 2 with false discovery rate correction at $P = 0.05$.

The experimental acquisition consisted of 2 15-min runs. As the timing was response driven, the number of switches completed varied for each volunteer. The interstimulus interval was randomly jittered from 0.6 to 1.6 s. Volunteers also underwent a prescanner training session to ensure that they understood and were capable of performing the task. Responses were made using the 1st and 2nd fingers of the right hand on a button box. Response times and the number of errors were recorded throughout the experimental acquisition.

Results

The behavioral data were examined in 2 different ways. Errors were measured, but importantly, only related to the overall difficulty in identifying which stimulus was the target for the different experimenter-controlled manipulations (i.e., for each type of target change). By contrast, the actual fMRI events modeled were defined according to the individual volunteer responses and therefore, can only be compared in relation with their associated response times.

The effects of the 4 types of target change were compared by analyzing the number of errors committed before correct target identification using a 2 × 2 multiway repeated-measures analysis of variance (ANOVA) in Statistical Package for the Social Sciences (SPSS). The 1st factor was dimension change (where the target changed between or within stimulus dimension). The 2nd factor was reversal (whether the target changed with reward contingency change or stimulus set change). There were significant main effects for both reward change ($F_{1,16}$ = 39.0, $P < 0.001$) and stimulus dimension change ($F_{1,16} = 8.7$, $P = 0.01$) with no significant interaction (see, Fig. 2).

Response times were compared for the individual event types that were modeled in the fMRI analysis to give an indication of their comparative difficulty. Volunteers were slower when they decided to move their attention between rather than within stimulus dimensions ($t_{15} = 2.98$, $P = 0.009$) and slower when moving attention between dimensions than when routinely responding to the known target (late correct responses) ($t_{15} = 6.985$, $P < 0.001$).

Shifts of attention due to set change were compared with those due to reward contingency change. Indirect to the error data described above (where more errors were made in the blocks following reward contingency change), the results revealed a significantly greater response time for the set change condition ($t_{15} = 2.74$, $P = 0.015$).

Response times were also compared for the early (i.e., that following the 1st positive feedback event) and late (i.e., subsequent correct responses) ones. The early correct response was found to be significantly slower than the late correct response ($t_{15} = 2.24$, $P = 0.041$).

Finally, there was no significant difference in response times for the events modeled with positive and negative feedback.

The average number of targets correctly identified by the volunteers was 55, with the maximum being 68 and the lowest being 29. The total number of each type of event varied between individuals; the averages were as follows: 34 extra-dimensional shifts, 39 intradimensional shifts, 32 set changes, 24 reversals, 166 positive feedback events, 97 negative feedback events, 58 early correct responses, and 116 late correct responses. Volunteers also underwent a prescanner training session to ensure that they understood and were capable of performing the task.

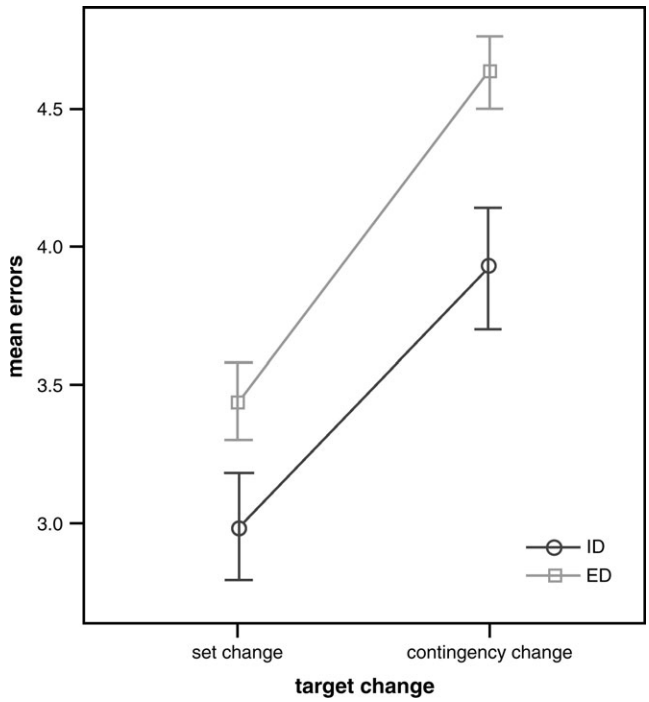

Figure 2. Illustrates the effects on the number of errors made while searching for the target when within and between dimension shifts are required and when the change in target is cued by reward contingency change and stimulus set change. Significantly more errors were made for both extradimensional shifting and reversal at contingency change at $P < 0.01$.

In the event-related fMRI analysis, to isolate the neural correlates of solution search, all events where the target was known (early and late correct responses, and feedback events while the target was known) were subtracted from all events where the volunteer was actively trying to work out the target (extradimensional and intradimensional shifts, reversals, set change, and feedback events during solution search). In the ROI analyses, significant activity at the corrected threshold (corrected for multiple ROI's) was observed in the left and right DLPFC, the left and right VLPFC, the left and right PPC, and the left and right lateral OFC. The medial OFC was significantly deactivated (Fig. 3 and Table 1).

Shifts in the focus of attention between stimulus types (extradimensional shifts) were then compared with shifts within stimulus type (intradimensional shifts). Significant activation was observed only in the VLPFC at the corrected threshold (Fig. 4 and Table 1).

A further contrast was then carried out to determine whether the VLPFC activity observed in the comparison of the extradimensional and the intradimensional shift was a modulation of a significant switch-related activity already present in the intradimensional switch or a novel activation related to shifting the focus of attention between dimensions. Accordingly, nonswitch-related activations were subtracted from the intradimensional shift events using the late nonswitch condition, when the volunteer knew which was the target. No significant

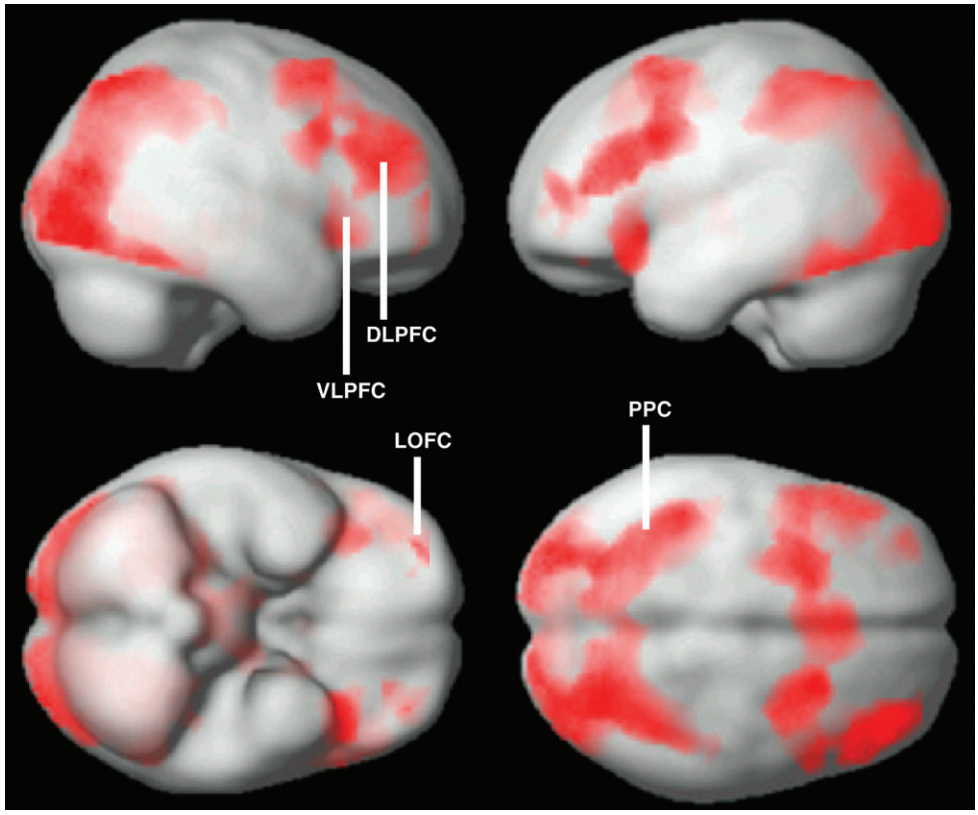

Figure 3. Contrasts all events for the period of time during which the volunteer was working out the target minus those when the target was known FDR corrected for the whole brain mass at $P = 0.01$.

activity in the VLPFC was observed at the corrected threshold. However, the DLPFC and PPC were significantly activated bilaterally (Table 1).

The next contrast compared shifts in attentional focus due to reward contingency change with those due to stimulus set change to examine the reversal component of attentional shifting. Significant activity was observed bilaterally in the PPC and in the lateral OFC (Fig. 4 and Table 1). When the set change event was compared with baseline, the lateral OFC and PPC regions were dissociated. Specifically, the PPC was significantly activated bilaterally in the shift at stimulus set change (left: $t = 5.07$, $P < 0.001$; right: $t = 6.43$, $P < 0.001$), whereas the lateral OFC was not (left: $t = 2.38$, $P = 0.1$; right: $t = 2.02$, $P = 0.2$). To determine whether this apparent difference between the lateral OFC and the PPC was significant, the mean activity in these regions was collapsed across hemisphere and examined at the single subject level in a 2 × 2 repeated-measures ANOVA in SPSS (ROI × condition). A significant main effect of reversal versus shift was observed ($F_{31,1} = 41.7$, $P < 0.001$) with no main effect for PPC versus lateral OFC ROI ($F_{31,1} = 1.31$, $P = 0.3$). There was an interaction of these 2 dimensions ($F_{31,1} = 6.67$, $P < 0.05$) such that for the shift at stimulus set change, the PPC was more active than the lateral OFC ($t = 2.04$, $P < 0.05$). Conversely, in shift at reward contingency change there was no significant difference ($t = 0.941$, $P = 0.4$).

It is important to note that although the contrast of shifts of attentional focus due to reward contingency change with those due to stimulus set change allows the examination of reversal-related activity, the 2 conditions also differ with respect to the absence or presence of novel stimuli, respectively. However, there was no difference in the lateral OFC response in the contrast between stimulus set change and baseline, confirming that activity in this region is dependent on the previous reward history, as suggested in the reversal versus set change contrast.

In a further contrast, the 1st response after the volunteer had learned what the target was based on positive feedback was compared with those responses that followed. These conditions were identical in every respect, except that the 1st response corresponded to the stage at which the volunteer stopped working out which was the target thus isolating the moment at which solution search ended. Significant activity was observed in the left and right DLPFC, the left VLPFC, the left and right PPC, and the right lateral OFC. Activity in the right VLPFC and left lateral OFC followed the same direction but did not achieve statistical significance at the corrected threshold (Table 1).

Subtraction of events involving negative feedback from those involving positive feedback yielded medial OFC activity (Fig. 5 and Table 1). This occurred even when the analysis included only those trials before the volunteer knew which was the correct stimulus on the basis of prior positive feedback ($t = 4.65$, $P = 0.001$). The reverse contrast was found to activate left and right DLPFC and right PPC with the left PPC showing the same direction as the right, but at below the corrected threshold (Table 1).

All of the contrasts described above were also examined using an unconstrained whole brain analysis FDR corrected at $P = 0.05$ to ensure that the ROI analysis had indeed identified the main regions of significant activity for each comparison. Although space limitations do not permit a comprehensive review of the

Table 1

The results for the group ROI's analysis with P values corrected for multiple comparisons

Contrast	ROI	z	Significance (corrected)	Nearest whole brain analysis peak			*t*	Significance (FDR corrected)
				X	*Y*	*Z*		
Solution search minus knowing the target	Medial OFC	−3.597	$P = 0.99$					
	Left OFC	**3.238**	$\mathbf{P = 0.02}$	**−26**	**58**	**2**	**4.180**	**0.009**
	Right OFC	**4.312**	$\mathbf{P < 0.01}$	**28**	**56**	**−10**	**4.890**	**0.001**
	Left DLPFC	**5.864**	$\mathbf{P < 0.01}$	**−50**	**24**	**28**	**6.270**	**0.000**
	Right DLPFC	**5.732**	$\mathbf{P < 0.01}$	**40**	**36**	**24**	**8.370**	**0.000**
	Left VLPFC	**4.844**	$\mathbf{P < 0.01}$	**−32**	**22**	**−10**	**6.640**	**0.000**
	Right VLPFC	**5.116**	$\mathbf{P < 0.01}$	**36**	**28**	**−6**	**6.750**	**0.000**
	Left PPC	**8.306**	$\mathbf{P < 0.01}$	**−30**	**−56**	**48**	**7.990**	**0.000**
	Right PPC	**9.261**	$\mathbf{P < 0.01}$	**22**	**−66**	**50**	**10.590**	**0.000**
Knowing the target minus solution search	**Medial OFC**	**3.597**	$\mathbf{P = 0.01}$	**−4**	**36**	**−4**	**6.070**	**0.004**
	Left OFC	−3.238	$P = 0.98$					
	Right OFC	−4.312	$P = 1.00$					
	Left DLPFC	−5.864	$P = 1.00$					
	Right DLPFC	−5.732	$P = 1.00$					
	Left VLPFC	−4.844	$P = 1.00$					
	Right VLPFC	−5.116	$P = 1.00$					
	Left PPC	−8.306	$P = 1.00$					
	Right PPC	−9.261	$P = 1.00$					
ED minus ID attentional shifts	Medial OFC	0.321	$P = 0.99$					
	Left OFC	0.954	$P = 0.83$					
	Right OFC	0.863	$P = 0.87$					
	Left DLPFC	1.442	$P = 0.55$					
	Right DLPFC	1.817	$P = 0.34$					
	Left VLPFC	**4.007**	$\mathbf{P < 0.01}$	**−38**	**26**	**−2**	**5.430**	**0.040**
	Right VLPFC	**4.459**	$\mathbf{P < 0.01}$	**44**	**18**	**12**	**9.680**	**0.008**
	Left PPC	0.450	$P = 0.97$					
	Right PPC	0.440	$P = 0.97$					
ID shifts minus late correct responses	Medial OFC	−3.269	$P = 1.00$					
	Left OFC	1.202	$P = 0.7$					
	Right OFC	2.351	$P = 0.14$					
	Left DLPFC	**3.500**	$\mathbf{P = 0.01}$	**−50**	**28**	**28**	**4.420**	**0.011**
	Right DLPFC	**3.471**	$\mathbf{P = 0.02}$	**38**	**36**	**26**	**4.930**	**0.007**
	Left VLPFC	2.180	$P = 0.19$					
	Right VLPFC	1.005	$P = 0.8$					
	Left PPC	**6.832**	$\mathbf{P < 0.01}$	**−34**	**−50**	**42**	**6.200**	**0.003**
	Right PPC	**5.538**	$\mathbf{P < 0.01}$	**30**	**−72**	**28**	**11.400**	**0.000**
Reversals at contingency change minus shift at set change	Medial OFC	−1.226	$P = 1.0$					
	Left OFC	**3.346**	$\mathbf{P = 0.02}$	**−32**	**50**	**−6**	**4.850**	**0.050**
	Right OFC	**3.999**	$\mathbf{P < 0.01}$	**42**	**48**	**−16**	**4.850**	**0.050**
	Left DLPFC	1.685	$P = 0.41$					
	Right DLPFC	0.680	$P = 0.93$					
	Left VLPFC	−1.108	$P = 1.0$					
	Right VLPFC	−0.504	$P = 0.10$					
	Left PPC	**4.864**	$\mathbf{P < 0.01}$	**−34**	**−54**	**36**	**9.310**	**0.008**
	Right PPC	**3.247**	$\mathbf{P = 0.02}$	**56**	**−40**	**42**	**5.320**	**0.046**
True minus false feedback	**Medial OFC**	**5.824**	$\mathbf{P < 0.01}$	**8**	**48**	**−12**	**7.730**	**0.008**
	Left OFC	−0.914	$P = 1.00$					
	Right OFC	−1.836	$P = 1.00$					
	Left DLPFC	−2.958	$P = 1.00$					
	Right DLPFC	−3.004	$P = 1.00$					
	Left VLPFC	−1.284	$P = 1.00$					
	Right VLPFC	−1.457	$P = 1.00$					
	Left PPC	−2.202	$P = 1.00$					
	Right PPC	−4.995	$P = 1.00$					
False minus true feedback	Medial OFC	−5.824	$P = 1.00$					
	Left OFC	0.914	$P = 0.85$					
	Right OFC	1.836	$P = 0.33$					
	Left DLPFC	**2.958**	$\mathbf{P = 0.04}$	No peak at $P = 0.05$ FDR corrected for whole brain				
	Right DLPFC	**3.004**	$\mathbf{P = 0.04}$	**40**	**28**	**30**	**7.580**	**0.040**
	Left VLPFC	1.284	$P = 0.65$					
	Right VLPFC	1.457	$P = 0.54$					
	Left PPC	2.202	$P = 0.18$					
	Right PPC	**4.955**	$\mathbf{P < 0.01}$	No peak at $P = 0.05$ FDR corrected for whole brain				
Early minus late correct responses	Medial OFC	0.225	$P = 0.99$					
	Left OFC	2.731	$P = 0.07$	**−36**	**46**	**0**	**4.370**	**0.004**
	Right OFC	**3.857**	$\mathbf{P < 0.01}$	**36**	**52**	**−10**	**5.900**	**0.002**
	Left DLPFC	**3.535**	$\mathbf{P = 0.01}$	**−20**	**26**	**16**	**6.270**	**0.002**
	Right DLPFC	**5.600**	$\mathbf{P < 0.01}$	**34**	**26**	**16**	**7.190**	**0.001**
	Left VLPFC	**2.931**	$\mathbf{P = 0.05}$	**−24**	**32**	**−16**	**5.830**	**0.002**
	Right VLPFC	2.645	$P = 0.08$	**32**	**30**	**−16**	**4.940**	**0.003**
	Left PPC	**3.594**	$\mathbf{P = 0.01}$	**−34**	**−82**	**22**	**5.570**	**0.002**
	Right PPC	**5.448**	$\mathbf{P < 0.01}$	**34**	**−74**	**24**	**6.990**	**0.001**

Note: the nearest peak activations from the whole brain analysis are also included FDR corrected for the whole brain mass. Bold type indicates significant ROI results. ED = extradimensional; ID = intradimensional.

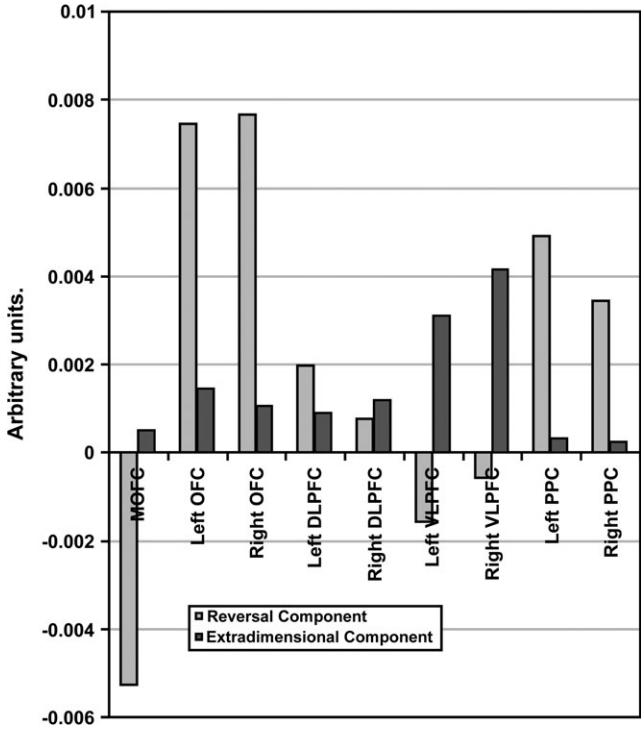

Figure 4. Illustrates a double dissociation between the components of switching at reversal of reward contingency and switching across dimensions; significant activity was observed in the lateral OFC and PPC for the reversal component and in the VLPFC for extradimensional shifting component.

results for all contrasts, the findings broadly support those of the ROI analysis (Table 1). For example, in the comparison of extra- and intradimensional shifts, the largest change in signal intensity was observed in left and right VLPFC (Fig. 6). For the contrast of reversals minus shifts, peaks of activity were observed bilaterally in the PPC and the left and right lateral OFC (Fig. 6). True minus false feedback generated a peak of activity in the medial OFC (Fig. 5), whereas false minus true feedback generated activation in the right DLPFC only.

Discussion

In this study, the DLPFC and VLPFC, medial and lateral OFC, and the PPC were fractionated in terms of their specific contributions to attentional set shifting.

The behavioral data demonstrated that moving attention between stimulus dimensions caused more errors than moving attention between stimuli of the same type and switch trials cued by reward contingency change caused more errors than those cued by stimulus set change. Because all target changes could logically be solved within the same number of trials, these differences must reflect the various strategies employed by the volunteers to solve the task. Volunteer behavior was characterized by a tendency to perseverate to both the previous target and the previous dimension. The main question for the imaging data, therefore, was whether these components of attentional control (i.e., extradimensional shifting and reversal) could be anatomically dissociated.

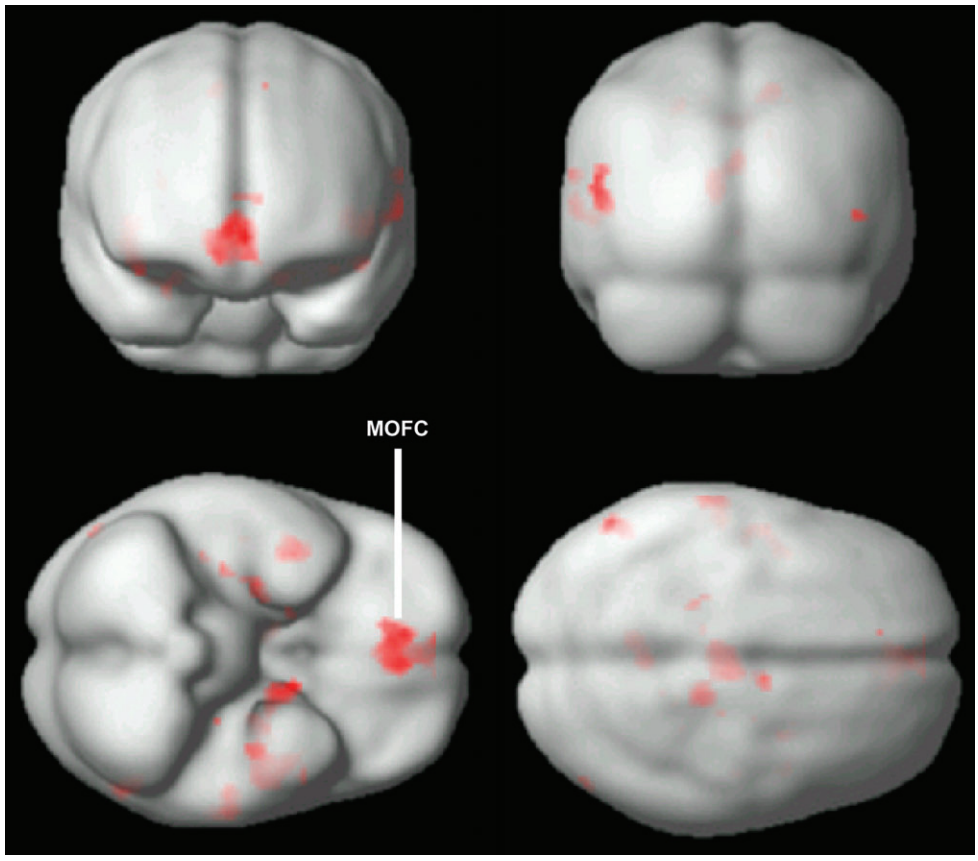

Figure 5. Shows the contrast of responses with true minus false feedback FDR corrected for the whole brain mass at $P = 0.01$. The medial OFC is highly activated in this contrast.

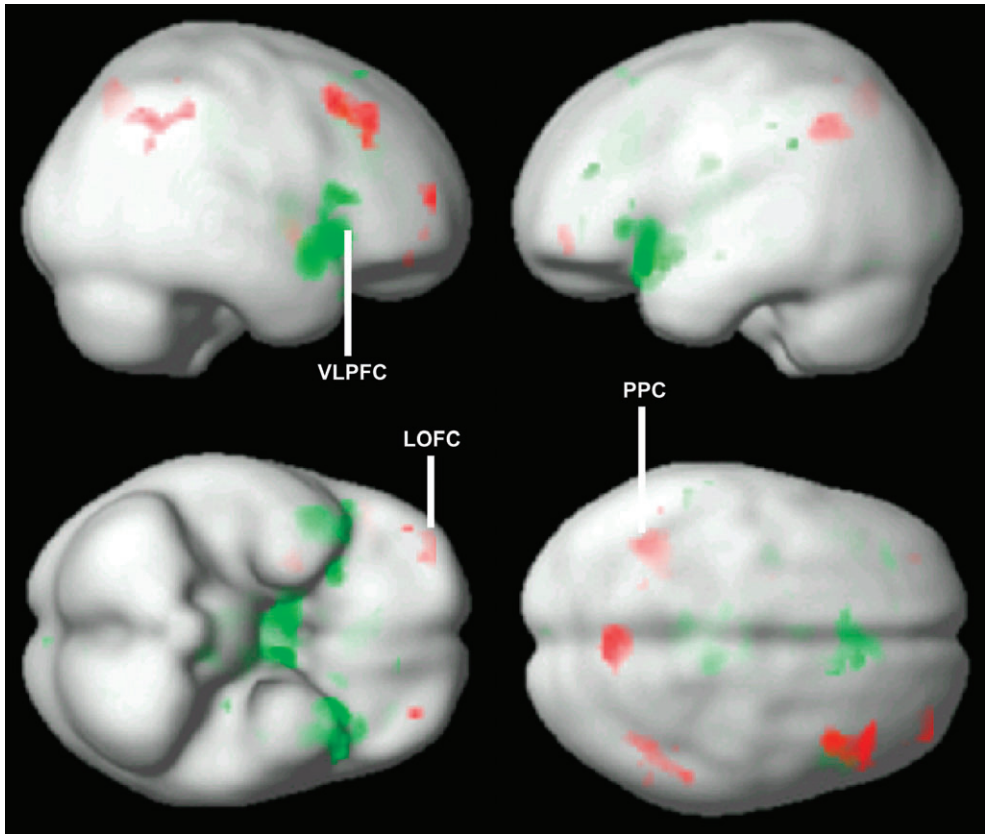

Figure 6. Shows the whole brain analysis for the extradimensional shift component (green), and the reversal component (red) FDR corrected for the whole brain mass at $P = 0.05$. In addition to changes in activity within the defined ROIs changes can be seen within right premotor cortex (reversals) and the anterior cingulate and thalamus (extradimensional shifts).

Previously, Rogers and others (2000) have attempted to address this issue in a block-design positron emission tomography study in which they examined the 1st occurrence of an extradimensional shift and a reversal. Increased activity was observed in DLPFC, but not VLPFC, during extradimensional shifts when compared with intradimensional shifts. However, in that study the activation observed could well have been due to the additional demands of actively working out which dimensions were relevant to the task, rather than the more specific shift of attention between dimensions. In fact, the behavioral data from that study support this suggestion and show that the search period associated with extradimensional shifting was longer than that associated with intradimensional shifting. Unlike Rogers and others (2000), in the current study the same 2 dimensions were used repeatedly in order to identify those regions that are involved in shifting attention between dimensions uncontaminated by those processes that are involved in simply working out which dimensions are relevant to the task, in general.

The choice of faces and buildings in this study was based on previous findings demonstrating that posteriorly these types of stimuli are processed somewhat independently. Building information is processed, to a large extent, in the parahippocampal place area and face information in a network of regions, the most commonly studied of which is the fusiform face area (Kanwisher and others 1997; Epstein and Kanwisher 1998). It was hypothesized, therefore, that switching from faces to buildings and vice versa requires the attentional system to move its focus between information encoded in anatomically distinct areas of posterior neocortex. The results of this experiment clearly demonstrate that it is the VLPFC that plays a central role in this process, not the DLPFC as has previously been suggested (Rogers and others 2000). In fact, Nakahara and others (2002) have reported that the VLPFC is involved in extradimensional shifting in both humans and macaques using a modified version of the wisconsin card sorting test. However, in that study, multiple components were confounded in the set shift leading the authors to interpret the observed VLPFC activity as "related to inhibition of the previous relevant response." The current findings clearly demonstrate that this is not the case as at reversal, where inhibition is maximal, there was no activation in this region compared with either set change or baseline. In addition, this region was not significantly activated when intradimensional shifting was compared with nonshifting. On the basis of the current findings, therefore, we suggest that the observed increase in reaction time for extradimensional shifting reflects the time taken for the VLPFC to bias attentional processing at the "dimensional" (or "categorical") level, a role entirely consistent with its pivotal position at the anterior extent of the ventral stream or "what" pathway (Ungerleider and Mishkin 1982; Petrides and Pandya 1994). A frontal module with similar properties has been proposed recently by O'Reilly and others (2002), although in that computational model this region was defined less specifically as "the lateral prefrontal cortex."

Although a number of important distinctions have been drawn between the functions of the dorsolateral and ventrolateral cortices (Wilson and others 1993; Petrides 1994, 1996;

Owen and others 1996, 1999; Goldman-Rakic 1988; Bor and others 2003), the contribution that each of these regions makes to attentional control has previously been unclear. In part, this is because most studies have confounded multiple possible components of set-shifting behavior. For example, in a study by Cools and others (2002), volunteers were required to shift attention between 2 stimuli based on changes in partial reinforcement contingency. The same stimulus set was used repeatedly and consisted of complex stimuli; hence, reversals, stimulus change, stimulus-response mapping change, and possibly even dimension change were all confounded. In another relevant study (Dove and others 2000), isolation of the multiple components of switching was only achieved by confounding stimulus color change, reversal of rule, and the reversal of response. As predicted from the published literature (e.g., Konishi and others 1998; Nagahama and others 1999, 2001; Owen and others 1999; Rogers and others 1999, 2000; Dove and others 2000; Duncan and Owen 2000; Cools and others 2002), in this study, the DLPFC was shown to be generally involved in solution search. However, unlike the other regions examined, the DLPFC did not appear to be involved in a more specific component of the switching task, and it seems likely, therefore, that this region plays a higher level role in attentional control, involving the coordination of search behavior for active solution derivation. This idea concurs well with previous models of DLPFC function which have suggested a role for this region in functions such as "monitoring" within working memory (e.g., Petrides 1994) and the identification of higher order structure (Bor and others 2003), both of which clearly contribute to the processes involved in the identification of solutions to current problems.

Previous studies have suggested that the OFC is involved in reward-related aspects of behavioral control (e.g., Rogers and others 1999, 2000; Zalla and others 2000; Breiter and others 2001), although a specific role in attentional switching has not been described previously. Several recent fMRI studies have, however, provided evidence that the lateral and medial OFC are differentially involved in processing negative and positive rewards, respectively (Elliott and others 2000). For example, O'Doherty and others (2001) identified a right lateral OFC area that was activated during the processing of negative reward at reversal of reward contingency, whereas a medial orbital region was activated during reception of positive feedback.

In this study, the medial OFC was more active only during positive feedback events and therefore appears to play no role in attentional switching itself (although switching due to positive feedback could not be examined as switches at reward contingency change were cued by negative feedback). This concurs fully with the study by O'Doherty and others (2001) in which the same region was found to be active when positive and negative feedback were compared. In contrast, in the current study, the lateral OFC was shown to play a significant role in negative reward, although at the stage of implementation of the switch due to the negative feedback, rather than at the time of feedback itself. This suggests a dissociation of function between the lateral and medial OFC, which goes beyond mere responsiveness to positive or negative feedback. An implementation-based role for the lateral OFC was also suggested by its involvement at the termination of solution search, where the previous feedback was in fact positive. Thus, we suggest that the lateral OFC plays a role in attention that is related to, although more complex than, merely processing negative feedback. This suggestion also accounts for why this region is activated by tasks that require, for example, reward-related decision making (Rogers and others 1999), as well as tasks that involve negative feedback (O'Doherty and others 2001). Importantly, however, such a role would not be consistent with the suggestion that this region is responsible for assessing stimulus-reward values per se (O'Doherty and others 2003), rather than implementing changes of behavior based on those values. Ultimately, the resolution of this issue may require a technique with higher temporal resolution such as magneto-encephalography to determine whether lateral OFC involvement is primarily at the point of the reception of feedback or at the point of the subsequent attentional shift.

The PPC has previously been implicated in a wide variety of cognitive tasks, and in the context of these experiments, it is difficult to untangle its precise function from that of the prefrontal cortex. Typically, the PPC has been thought to be centrally involved, not in the executive component of task switching, but at the level of stimulus-response mapping (Kimberg and others 2000; Miller and Cohen 2001; Rushworth and others 2001; Andersen and Buneo 2003; Corbetta and Shulman 2002; Dreher and Grafman 2003). In line with this, the results here demonstrate that the PPC is most active at reversal, when the old stimulus-response mapping must be overridden and the new one formed. Further, at the switch event when a new stimulus set was presented, a new stimulus-response mapping was also required; during this event the PPC was active, but less so than for reversals. Conversely, when the target was known, the stimulus-response mapping was unchanged, and hence, with repetition of response to the same stimulus, the PPC became less involved in the task.

The finding that reversals and extradimensional shifts preferentially recruit anatomically distinct brain regions fits well with the previous patient literature showing that lateral frontal-lobe damage causes impairments in shifting attention between stimulus dimensions (Owen and others 1993; Pantelis and others 1999), whereas orbitofrontal lesions cause deficits in reward-based learning (Hornak and others 2004). Broadly speaking, they also concur well with studies in the monkey, which have shown that reward-related activity is associated with damage to the orbital surface, whereas lateral frontal lesions preferentially affect extradimensional set-shifting activity (Roberts and others 1992; Dias and others 1996). An important question that remains is precisely what constitutes a "dimension" for the VLPFC: must dimensional information be processed within distinct brain regions (such as the parahippocampal place area and fusiform face area) or would more abstract dimensions such as "lines" and "shapes" produce similar effects, as suggested by the existing literature in non-human primates (e.g., Roberts and others 1992; Dias and others 1996). Further, it remains unclear whether the role that the VLPFC plays at this abstract category level is a general one across all tasks, or does it, as has been suggested recently (Duncan 2001), play a more adaptable role in cognition?

Finally, a frequent confound in the cognitive neuroscience literature is that of general task difficulty (for discussion, see Duncan and Owen 2000). In contrasting 2 events where 1 has a greater response time than the other, or 1 elicits more errors than the other, the question inevitably arises as to whether any activation observed is due to a specific additional component or just the modulation of a general difficulty variable. The results of the current study are not easily explained in terms of general

difficulty because contrasting event types which differed with respect to response times or error rates did not produce consistent patterns of activation in any area of the brain. For example, when extra- and intradimensional shifts were compared, bilateral VLPFC activity was observed, with no change in either the DLPFC or the PPC. In contrast, when intradimensional shifts were compared with nonshifts, changes in DLPFC and PPC were observed with no change in VLPFC. It seems more likely that the different components of attentional shifting examined in this study make varying demands on discrete cognitive processes, which are mediated preferentially by anatomically distinct neural substrates. The novel approach employed here demonstrates that such processes may be dissociated within a single task using event-related fMRI. It seems likely that the same approach could be used to examine, and differentiate between, the attention set-shifting deficits that have been reported in various patient groups (e.g., Owen and others 1991, 1992; Pantelis and others 1999) in order to elucidate more precisely the cognitive and neural mechanisms responsible.

Notes

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