Willed action and attention to the selection of action

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Actions are said to be 'willed' if we consciously pay attention to their selection. It has been suggested that they are associated with activations in the dorsal prefrontal cortex (area 46). However, because previous experiments typically used a 'free selection' paradigm to examine this hypothesis, it is unclear whether the results reflected the attention to the selection of action or the freedom of choice allowed by the tasks. In this experiment, we minimized the difference of working memory demand across task conditions by using novel stimuli in each trial. We found that activation in the dorsal prefrontal cortex on a free selection task was not significantly different from that induced by another task that required attention to the selection of action, although the responses were externally specified. This suggests that the dorsal prefrontal cortex is in fact associated with attention to the selection of action, but does not play a unique role in the generation of internally initiated actions. However, the presupplementary motor area (pre-SMA) may subserve this function as activity in this region was found to be tightly associated with the free selection of responses.
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Introduction

It has been proposed that activity in the dorsal prefrontal cortex (area 46) is associated with the selection of 'willed actions'. Frith et al. (1991) used PET to compare cerebral blood flow during tasks in which subjects had to generate pseudo-random finger responses ('willed acts') and tasks in which the responses were externally specified by the experimenter ('routine acts'). The dorsal prefrontal cortex was found to be significantly more activated during the former tasks. This result has proved to be consistent and replicable (Deiber et al., 1991; Jahanshahi et al., 1995; Playford et al., 1992; Spence et al., 1998). Activity has also been reported in the dorsal prefrontal cortex when subjects freely generate words (Frith et al., 1991). Hyder et al. (1997) argue that the peaks for words may differ from the peaks for motor responses, but Buckner et al.

(1995) have shown that not only are there peaks in the ventral prefrontal cortex during word generation, but also in the dorsal prefrontal cortex.

One major problem with the finding that the dorsal prefrontal cortex is activated during willed action is that its interpretation is ambiguous. In the original definition, actions are said to be willed if we consciously pay attention to their selection (Frith et al., 1991); this definition is taken from James (1890). However, in the willed action condition, the subjects had a free choice as to which response to make, and this task has been called the 'free selection' task (Playford et al., 1992). It is unclear therefore whether the activation in the dorsal prefrontal cortex reflects attention to action or the fact that the actions are freely selected.

One reason why the free selection task has been used to test willed action is that when the required response is not fully determined by external parameters (e.g., task instructions and stimuli), one typically has to spend extra mental effort to make a deliberate choice between the different possibilities (Frith et al., 1991). The nonroutine nature of the task means that greater attention must be paid to the selection of action. Thus, the task serves as a reasonable test of willed action as originally defined. However, given this logic, one should also expect other nonroutine tasks that require high attention to the selection of action to be associated with activation in the dorsal prefrontal cortex.

In this study, in addition to a free selection task (FREE, Fig. 1a) and a routine task (ROUTINE, Fig. 1c), we included an extra task condition (SPECIFIED, Fig. 1b). This condition also demanded high attention to the selection of action, but the responses were externally determined. The inclusion of this third condition allowed us to investigate whether the activation in the dorsal prefrontal cortex reflects the general function of attention to the selection of action, or is particularly related to the fact that the responses are freely chosen.

There is a further possible interpretation of the activation reported in the dorsal prefrontal cortex (area 46) when subjects perform a free selection task. It could be argued that the free selection or random response generation task has a high working memory demand, because psychological experiments normally involve many trials, and to generate a sequence of random responses, one has to maintain in memory the responses made in previous trials to avoid excessive repetition of a certain response and thus achieve pseudo randomness (Spence and Frith, 1999). Brodmann's area 46 has long been proposed as the neural substrate

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Available online on ScienceDirect (www.sciencedirect.com.)

a. FREE

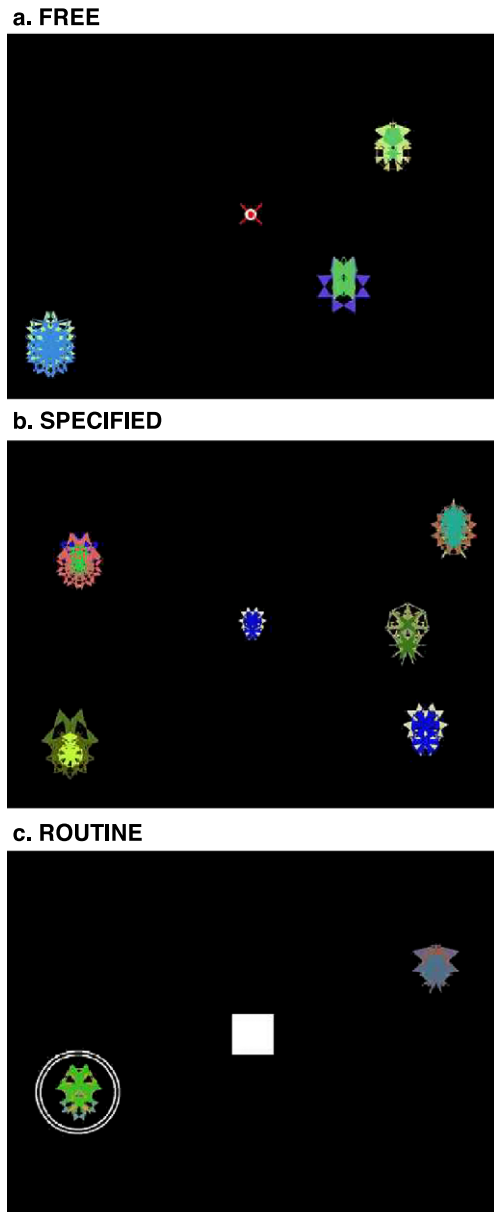**b. SPECIFIED**

c. ROUTINE

Fig. 1. Task conditions (a) FREE: Subjects were required to select one fractal image randomly. (b) SPECIFIED: The fractal image that matches with the cursor image was the correct target, which is located in the lower right corner in this example trial. (c) ROUTINE: The fractal image highlighted by the bright circles was the correct target.

for spatial working memory in macaque monkeys (Goldman-Rakic, 1992, 1995). However, Owen et al. (1998) reported that in humans, this area was also activated on nonspatial working memory tasks. Other evidence for the contribution of area 46 on working memory tasks has been found in humans using functional imaging (Cohen et al., 1997; D'Esposito et al., 1998, 2000; Owen, 1997; Petrides, 2000) as well as transcranial magnetic stimulation studies (Mottaghy et al., 2003; Mull and Seyal, 2001). Thus, the activation in dorsal prefrontal cortex on tasks involving random response generation may be due to the working memory demand.

It could be argued that this issue has been resolved by recent studies involving imaging (Desmond et al., 1998; Nathaniel-James and Frith, 2002) and transcranial magnetic brain stimula-

tion (Hadland et al., 2001). Desmond et al. (1998) asked subjects to complete word stems with varying number of possible completions, and reported that there was greater activation in the dorsal prefrontal cortex for trials with many compared with few possible completions. Because the word stems differed from trial to trial, each trial was independent from the others and there was no need to maintain the previous responses in working memory. Nathaniel-James and Frith (2002) asked subjects to complete sentences and reported greater activation where the sentence encouraged a wide choice rather than a narrow one. However, because the choices were not presented in front of the subjects, it could be argued that in both experiments, the subjects called the various choices into working memory to perform the selection, and the trials with more possible completions therefore induced a higher working memory load and thus higher activations in the dorsal prefrontal cortex.

In a repetitive transcranial magnetic stimulation (rTMS) study, Hadland et al. (2001) explicitly tried to exclude working memory. In their random finger movement generation task, subjects made movement sequence of eight digits and were explicitly instructed not to repeat the same finger movement in each sequence. However, the responses made previously in the same sequence were visually presented to the subjects on the computer screen, thus eliminating the working memory requirement. It was found that rTMS over the dorsal prefrontal cortex prolonged the response time for making randomly generated responses, whether early or late in sequence. However, it could be argued that when the subjects generated the sequence, they prepared the moves before performing the sequence, and that the rTMS interfered with maintenance of those pregenerated moves in working memory.

In the current study, we therefore adopted an event-related design, in which the three task conditions were presented in a pre-randomized order. As the subjects did not know in advance whether the next trial required a free choice, the working memory maintenance load before each trial had to be the same for the three task conditions. To further bypass the problem of working memory, we used novel fractal images as stimuli, and these never appeared on more than one trial for each subject (Fig. 1). The spatial locations and number of targets also varied randomly from trial to trial so as prevent as best we could the use of spatial working memory strategies. The design differs from that of Desmond et al. (1998) and Nathaniel-James and Frith (2002) in that because the fractals were presented on the screen, there was no requirement to load responses into working memory.

Method

Subjects

Nine male and three female healthy volunteers participated in this experiment. All of them were right-handed and were aged 20–39. They all gave informed consent and received a brief MRI safety screening before the experiment.

Tasks

An in-house modified, MRI-compatible, gamepad (i.e., a variant of a joystick) was used in the experiment for the subjects to control a cursor on a computer screen. Subjects were given a very brief (1–2 min) practice session with the gamepad, during which

Table 1
Summary of task condition

	Attentional selection of action	Random response generation
Free	+	+
Specified	+	−
Routine	−	−

they navigated a white square cursor around a blank screen. All of them reported no difficulty in controlling the cursor.

The task instructions were then explained to the subjects. On each trial, two to five target fractal images ($\approx 1.5°$) were presented in random locations on the projector screen ($\approx 18°$), which subjects viewed through inverting mirror spectacles. The cursor image was presented at the center of the screen at the beginning of each trial, and this determined the task in that particular trial. If the cursor was an aiming-cross, the subjects were required to randomly choose a target and then move the cursor over it (FREE condition, Fig. 1a). If the cursor was a small fractal image, the subjects were required to move it over to the target that matched with the cursor in all visual properties except size (SPECIFIED condition, Fig. 1b). The cursor image in this task condition varied from trial to trial, thus making the task nonroutine. If the cursor was a white square, the subjects were required to move it over to the target highlighted by two concentric white circles (ROUTINE condition, Fig. 1c). The same fractal image never appeared in two different trials for each subject.

By varying the number of targets, we could study whether response times increased with the number of targets. Since attention is typically understood as a serial process (Treisman and Gelade, 1980), one should expect that on tasks that require the subject to attend to each of the targets in turn, the response times will increase as the number of possible responses increases. This allowed us to verify that the FREE and the SPECIFIED conditions were attentionally demanding in a way that ROUTINE was not. Table 1 gives a brief summary of the main features of the tasks used.

Subjects were instructed to move the cursor only after they had made the decision of which target to move over to in a particular trial. Once the cursor image overlapped with the target fractal image and stopped moving for 1 s, the trial ended and the targets and cursor image disappeared from the screen. If no choice was successfully made in 5 s from the onset of the trial, the trial also ended automatically. A fixation cross ($\approx 0.8°$) was presented during the intertrial intervals. Stimulus onset asynchrony (SOA; i.e., the temporal difference between the onsets of two consecutive trials) varied systematically from 6 to 12 s to achieve even jittering of event onsets, to maximize the efficiency of the fMRI statistics model (Miezin et al., 2000). The three task conditions were presented in a pre-randomized order throughout the experiment.

A very short 10-trial practice session was then given to make sure that the subjects understood the instructions properly before proceeding into the scanner. In the actual experiment, there were in total 180 trials for each subject, with the three task conditions distributed evenly in numbers. For each condition, one-third of the trials involved two targets, one-third involved three targets, and one-third involved five targets. The experiment lasted for about 27 min for each subject.

Four subjects were randomly selected to perform the same task again outside the scanner about 2 months after the fMRI session. The gamepad, visual angles of stimuli, and timing of trials were the same as in the scanner. Eye movements were measured using an infrared remote eye-tracking device (SensoMotoric Instruments, Teltow, Germany).

Imaging procedures

The fMRI data were acquired in a 3T whole-body MRI scanner (Siemens, Erlangen, Germany) at the Oxford Centre for Functional Magnetic Resonance Imaging of the Brain (FMRIB). A quadrature birdcage head coil was used. Head movements were restrained with foam pads. For each subject, 544 EPI images were acquired continuously with a TR of 3 s and at an image resolution of $3 \times 4 \times 5$ mm. The TE and flip angle were 30 ms and $90°$, respectively. Slices were acquired in axial orientation parallel to the anterior commissure–posterior commissure (AC–PC) line, and they covered the entire brain volume.

Data analysis

Response times (RT) were measured as the difference between the onset of stimuli and the onset of the first cursor movement recorded in a trial. Individual mean response times for the different task conditions were analyzed at the group level (Fig. 2). The eye movement data were analyzed for each of the four subjects using the I-View Data Analysis Software for Windows Version 2.0 (http://www.smi.de/iv/ivsystem.htm). The number of saccades was estimated by counting the number of fixations in different task conditions, as computed by the software.

The fMRI data were analyzed with statistical parametric mapping (Friston et al., 1995), using the SPM99 software (Wellcome Department of Cognitive Neurology, London, UK). The first four scans of an EPI series were excluded from the analysis to minimize T1 relaxation artifacts. A mean image of all scan volumes was created, to which individual volumes were spatially realigned by rigid body transformation. The realigned images were then normalized directly to the Montreal Neurological Institute EPI template, and thus transformed into a standard stereotaxic space and subsampled into a resolution of $2 \times 2 \times 2$ mm. A Gaussian filter of 8-mm full width at half maximum (FWHM) was then applied to smooth the data spatially, to accommodate for anatomical variability across subjects, as well as to satisfy the assumptions of Gaussian random field theory, which was used for correction of multiple comparisons in the analysis (Worsley et al., 1996).
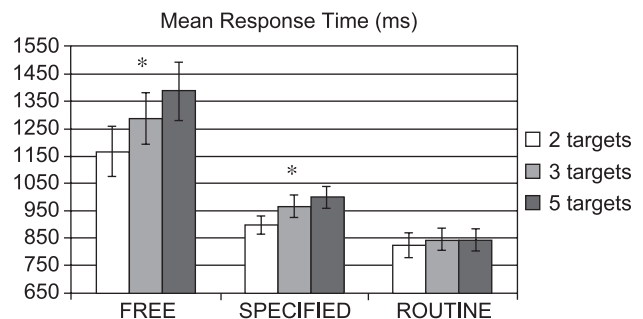

Fig. 2. Mean response times of different task conditions with varying number of targets. In FREE and SPECIFIED, response times were higher when there were more number of targets in a trial. There was no such effect for ROUTINE. The error scale bars represent standard errors.

The time series data at each voxel were then further processed using a high-pass filter with a cutoff of 149 s, so as to remove low frequency drifts that is typically observed in fMRI data. The times series are also temporally smoothed by using a low-pass Gaussian filter of 4 s FWHM. The subject-level statistical analyses were performed using the general linear model (GLM), fitting the time series data with the canonical hemodynamic response function at the relevant event onset time points. The statistical parameter estimates were computed for each task conditions at each voxel of the brain volume. Additionally, the number of targets was also modeled as a parametric modulator for the FREE condition in the design matrix. The following contrast of statistical parameter estimates images were computed for the relevant task condition comparisons for each individual subject: FREE versus ROUTINE, SPECIFIED versus ROUTINE, FREE versus SPECIFIED, and the effect of number of targets in FREE. The group-level random effects analyses were then performed voxel-wise on the images of the 12 subjects. One-sample t tests were performed for all four contrasts, and regression analyses were performed to test if, across subjects, the contrast of parameter estimates for FREE versus SPECIFIED correlated (positively and negatively) with the relevant RT difference.

The resulting images from the random effects analyses were generated at an uncorrected threshold of $P < 0.001$ with an extent threshold of five voxels. They were overlayed onto a high-resolution canonical structural image of a single subject supplied with SPM99 to produce Figs. 3 and 4. Brodmann's area 46 was identified in both hemispheres as regions of interest a priori. Small volume corrections (SVC) were therefore performed in this area, using the coordinates obtained from a previous study (Rowe et al., in preparation). Activations are reported only if they survive a corrected cluster threshold of $P < 0.05$, or contain voxels that are corrected at a small volume or whole brain level at $P < 0.05$.

The adjusted raw data plot for the correlation between BOLD signal differences and RT differences in Fig. 4c was constructed using Russell Poldrack's SPM ROI Toolbox (http://sourceforge.net/projects/spm-toolbox) together with a standard statistical package. This allowed us to inspect the raw data on which the correlations were based, as well as providing a graphical representation so that it is easier to understand. For each subject, the time course of the adjusted raw data of the entire cluster of interest (pre-SMA, 19 voxels) was extracted for all three task conditions using the SPM ROI Toolbox. The difference of BOLD signal between FREE and SPECIFIED in terms of percentage signal change at the 6th second from onset of stimuli was then measured for each subject. This measure was then plotted against the difference of mean RT between FREE and SPECIFIED for each subject. Hence, each dot in the plot represents an individual subject.

Results

Behavioral results

The group averages for the mean response times were 1280.1, 952.9, and 837.1 ms for the FREE, SPECIFIED, and ROUTINE conditions, respectively. The standard deviations were 335.1, 117.1, and 141.5 ms, respectively. The data significantly violated the assumption of homogeneity of covariance (Mauchly sphericity

test, $P < 0.0005$), and therefore the degree of freedom for the ANOVA F test was adjusted using the Greenhouse–Geisser correction method in SPSS version 11.0 (http://www.spss.com/spssbi/spss/). The response times differed significantly across task conditions ($F = 22.375$, $df = 1.063$, 11.144, $P < 0.0005$).

Table 2
fMRI results

Anatomical region	Cluster size (number of voxels)	Peak coordinates (x, y, z)	Z score (at peak)
Free versus routine			
Dorsal prefrontal cortex (area 46) R*	95	36, 44, 32	3.75
Anterior cingulate	1121	−8, 26, 20	4.72
Presupplementary motor area		8, 16, 64	4.13
		−2, 10, 52	4.12
Frontal area 8 R	481	42, 8, 56	4.17
		34, 4, 62	4.11
		46, 4, 38	3.89
Frontal area 8 L	175	−48, 10, 40	3.99
Intraparietal sulcus R	299	34, −60, 38	4.32
		36, −52, 46	4.95
Intraparietal sulcus L	260	−40, −62, 52	4.21
		−42, −50, 50	3.88
		−44, −54, 40	3.60
Lateral cerebellum R	175	40, −62, −30	4.25
		42, −62, −18	3.44
		44, −74, −14	3.27
Lateral cerebellum L	345	−32, −80, −28	4.08
		−38, −80, −16	3.40
		−40, −66, −28	3.40
Specified versus routine			
Dorsal prefrontal cortex (area 46) R*	64	30, 36, 28	3.73
		32, 46, 38	3.64
Intraparietal sulcus L	142	−28, −60, 56	3.99
		−26, −66, 48	3.84
Free versus specified			
Anterior cingulate	213	10, 16, 42	3.86
		−4, 18, 40	3.21
Presupplementary motor area		−4, 12, 54	3.67
Medial parietal cortex	206	6, −72, 44	4.66
Intraparietal sulcus R		26, −66, 36	4.28
		18, −68, 44	3.73
Free: number of targets as parametric modulator			
Striate cortex	1638	10, −98, −6	4.42
Extrastriate cortex		16, −98, 10	4.31
		−14, −82, −22	4.66
Medial parietal cortex	171	−4, −58, 56	4.45
Free versus specified: correlation with RT			
(activation positively correlated to RT differences)			
Superior colliculus L	197	−8, 30, −10	4.43
Superior colliculus R		8, 30, −8	4.40
(activation negatively correlated to RT differences)			
Presupplementary motor area	19	2, 6, 70	5.54

*Does not achieve statistical significance at either a peak voxel or a cluster threshold of $P < 0.05$ (corrected), but contains voxels surviving small volume correction (SVC) with a priori hypothesis at $P < 0.05$.

Dorsal Prefrontal Cotex (Broadmann's area 46)

a. FREE vs ROUTINE
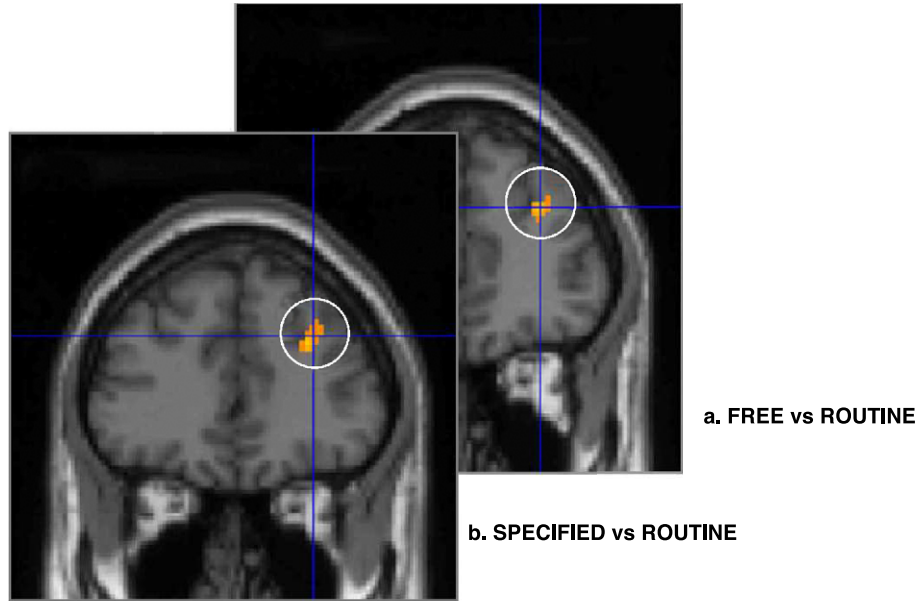
b. SPECIFIED vs ROUTINE

Fig. 3. Dorsal prefrontal cortex: similar activations were found in this region for both (a) FREE versus ROUTINE and (b) SPECIFIED versus ROUTINE.

To test whether the response times were longer for trials with more targets, an ANOVA was performed separately for each condition (with homogeneity of covariance verified in each case). This effect was only found in FREE ($F = 33.588$, $df = 2, 22$, $P <$ 0.0005) and SPECIFIED ($F = 5.690$, $df = 2$, $P = 0.010$), but not in ROUTINE ($F = 0.653$, $df = 2.22$, $P = 0.530$) (see Fig. 1).

The group averages for accuracy were 98.3% for SPECIFIED and 98.8% for ROUTINE; the measure of accuracy is not appli-

Pre-Supplementary Motor Area

a. FREE vs ROUTINE

b. FREE vs SPECIFIED
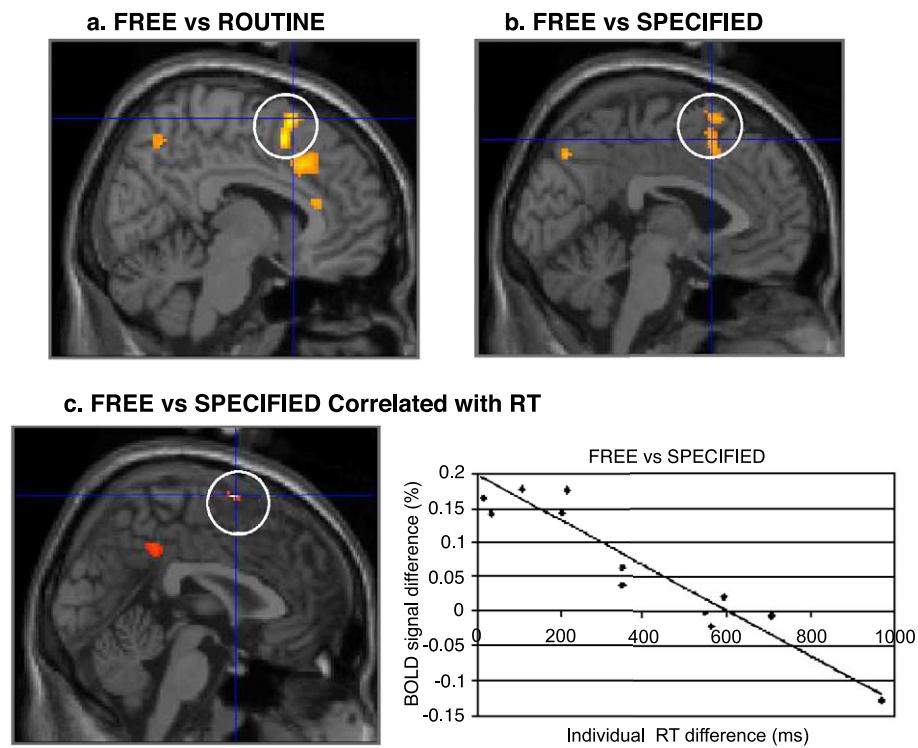

c. FREE vs SPECIFIED Correlated with RT

Fig. 4. Presupplementary motor area: activations were found in both (a) FREE versus ROUTINE and (b) FREE versus SPECIFIED. (c) Activation in this region in FREE versus SPECIFIED also correlated with the relevant response time difference at the group level. Adjusted fMRI data at 6 s from onset of stimuli were plotted against response time data in the graph. Each dot in the plot represents an individual subject.

cable for FREE. A quick inspection of the recorded coordinates for the final cursor positions suggested that these 'errors' were mostly due to a failure to overlap the cursor properly with the target, rather than a failure to identify the correct target. Errors were therefore not considered in the analysis.

Eye movements

Eye movements were measured in four subjects (see Method). The number of saccades made during the response time correlated positively with response times, regardless of the task condition. The Pearson's correlation coefficients for the four subjects were 0.47, 0.85, 0.60, and 0.64, respectively. These correlations were significant for all subjects ($P < 0.0005$ for all four subjects). Inspection of the scatter plots suggested that a linear fit was appropriate for the data for all subjects.

Functional MRI data

These results are summarized in Table 2.

When FREE was compared with ROUTINE, activations were found in the right dorsal prefrontal cortex (Brodmann's area 46; Fig. 3a), anterior cingulate, presupplementary motor area (pre-SMA; Fig. 4a), and bilaterally in frontal area 8, the intraparietal sulcus and lateral cerebellum.

When SPECIFIED was compared with ROUTINE, activations were found in the right dorsal prefrontal cortex (Brodmann's area 46; Fig. 1b) and left intraparietal sulcus.

When FREE was directly compared with SPECIFIED, no significant activation was observed in the dorsal prefrontal cortex, even at the uncorrected threshold of $P < 0.001$. Activations were however found in the anterior cingulate, presupplementary motor area (Fig. 4b), right medial parietal cortex, and right intraparietal sulcus.

We have also tested the effect of the increment of number of targets in FREE, modeling it as a parametric modulator. Activations were found in the striate cortex, extrastriate cortex, and medial parietal cortex, but not in the frontal cortex.

As the behavioral data showed considerable variability in response times in the FREE condition, we performed a regression analysis to look for neural activity that correlated with this variation. We tested the correlation between the subject-level activations in FREE versus SPECIFIED and individual differences in response times between the two conditions. A positive correlation was found for the superior colliculus bilaterally, and a negative correlation was found for the presupplementary motor area (Fig. 4c).

Discussion

As in previous studies, we found activation in the dorsal prefrontal cortex (BA 46) when subjects freely selected between responses (Deiber et al., 1991; Hyder et al., 1997; Jahanshahi et al., 1995; Playford et al., 1992; Spence et al., 1998). The discussion will concentrate on this activation. However, we also discuss the activations on the medial frontal surface because these have also been reported in previous studies involving willed action (Frith et al., 1991; Jahanshahi and Frith, 1998), and rTMS over the medial frontal surface has been shown to interfere with the free generation of responses (Hadland et al., 2001).

Dorsal prefrontal cortex

As in the study by Frith et al. (1991), we found activation in the dorsal prefrontal cortex (BA 46) when we compared a free selection condition with a routine condition. This suggests that this result is robust enough to generalize beyond simple movement or verb generation tasks to the current task in which subjects chose freely between novel fractal images. This was true even though the conditions used in the present study were designed either to eliminate or at least minimize working memory demands.

However, there was also activation in the dorsal prefrontal cortex (BA 46) when we compared SPECIFIED with ROUTINE. Furthermore, the location of the activation was very similar in FREE versus ROUTINE and SPECIFIED versus ROUTINE (Fig. 3). In both FREE and SPECIFIED, the response times increased with the number of targets from which the subjects had to select, but this was not true for ROUTINE. This suggests that FREE and SPECIFIED were attentionally demanding in a way that ROUTINE was not.

There was no significant difference in activation of the dorsal prefrontal cortex for FREE versus SPECIFIED. We carried out a regression analysis to look for brain activations for this comparison that were correlated with individual variation in response times. We did not find any such activation in the dorsal prefrontal cortex. If the activity in dorsal prefrontal cortex had specifically reflected the free selection of responses, we might have expected to find a correlation as we did in the pre-SMA. That we did not do so supports our general conclusion that it is not the freedom of choice that is crucial for activation of the dorsal prefrontal cortex.

However, the activation in the dorsal prefrontal cortex does not simply reflect task difficulty. The response times were longer in FREE than SPECIFIED, but the degree of activation did not differ across the two conditions. Furthermore, in the study by Desmond et al. (1998), activity in this area was greater in the condition in which reaction times were shorter.

There are other imaging studies that have shown activation in the dorsal prefrontal cortex when subjects select between actions even though there are external cues to specify the response. This is true, for example, where there is response conflict on the Eriksen flanker task (Bunge et al., 2002; Cohen et al., 2000) or where there is incompatibility between the stimulus–response mappings (Schumacher and D'Esposito, 2002). Using PET, Petrides et al. (1993) reported that there was a similar level of activation in area 46 when subjects remembered externally ordered number sequences as compared to when they remembered self-generated number sequences. Similarly, Kapur et al. (1994) reported that there was a significant activation in this region in a semantic judgement task where subjects were not generating random responses. Furthermore, Hadland et al. (2001) reported that rTMS over the dorsal prefrontal cortex impaired performance not only when subjects generated novel finger movement sequences but also when they performed the sequences as instructed by external cues but under conditions that made attentional demands. Considered together, the results of the present study add support to the claim that it is possible to find activation in the dorsal prefrontal cortex that reflects attention to the selection of action (Passingham et al., in press). This idea is also similar to the notion of response monitoring as proposed by Petrides et al. (1993), except that here our emphasis is on selection within a single trial instead of a sequence of selections.

Frith (2000) have argued that the activation in the dorsal prefrontal cortex reflects the 'sculpting of the response space', by which he means the selection of 'the set of responses that are suitable for a given task'. He described two PET studies, one using a word generation paradigm (Frith and Friston, in preparation) and the other using a random number generation paradigm (Jahanshahi et al., 2000), in which the degree of activation in the dorsal prefrontal cortex did not change as a function of the rate of response selection. He supposes that if the activity reflected the enhancement of a particular response within the set, the activity should have been greater the more frequently this enhancement occurs. However, on word or random number generation tasks, the subjects might have been remembering their responses to avoid excessive repetition, leading to tonic activation across trials. We suspect that this might have weakened the sensitivity for detecting transient signals in PET.

In the present study, we used event-related fMRI and modeled transient hemodynamic responses time-locked to the selection events, and we also minimized demands on working memory. Instead of testing whether activity in the dorsal prefrontal cortex changed as a function of the rate of response selection, we looked for activation that varied as a function of the number of targets between which the subjects selected. We did not find such activation in the dorsal prefrontal cortex, though there was activity in visual areas that varied with the number of targets. If the activity reflected the inhibition of competing responses, one might have expected it to increase with the number of alternatives. However, if it reflected the enhancement of the final response, as suggested by Passingham et al. (in press), one would not necessarily have to predict a parametric effect. Two previous imaging studies have reported greater activation when there were more possible alternative responses (Desmond et al., 1998; Nathaniel-James and Frith, 2002). In these studies, however, the alternatives had to be recalled from memory, whereas in the present study, the alternatives were presented on the screen. It remains unclear whether activations in the dorsal prefrontal cortex reflect the enhancement of a response set or the enhancement of a selected item within the set. The latter possibility predicts that there will be transient activity associated with the dorsal prefrontal cortex late in the process of selection. This issue could in principal be resolved by future experiments using methods of higher temporal resolution.

Medial frontal cortex

We found activations in the anterior cingulate cortex and presupplementary motor area for the comparison of FREE versus ROUTINE. However, whereas there was no difference in activation in the dorsal prefrontal for FREE and SPECIFIED, there was activation in the anterior cingulate cortex and pre-SMA for FREE versus ROUTINE, but not for SPECIFIED versus ROUTINE.

It has been proposed that the anterior cingulate cortex is responsible for the monitoring of response conflict (Botvinick et al., 1999, 2001; Casey et al., 2000; Cohen et al., 2000; van Veen et al., 2001). In the FREE task, subjects had to decide between equally effective responses, and it could be argued that this induced response conflict. This kind of random response selection has been described as 'underdetermined' (Botvinick et al., 2001). These authors specifically propose that underdetermined responses trigger the conflict monitor and that the activation in the anterior cingulate cortex for underdetermined responses reflects that fact.

The pre-SMA was also activated when FREE was compared with either ROUTINE or SPECIFIED. Moreover, activation in this region was also correlated with the performance of free response selection, providing further evidence that this area is indeed related to free selection per se. This result is intriguing because previous studies have demonstrated that the pre-SMA and SMA are involved in the generation of self-initiated and self-paced actions. Thaler et al. (1995) showed that bilateral lesions of these areas severely impaired the ability of macaque monkeys to generate a simple self-initiated action. This involved raising the arm whenever the monkey decided so as to receive a food reward that was delivered into a food well below. Yet the monkeys could raise their arm when the movement was cued by auditory stimuli. It is also known that a slow negative potential, the readiness potential, or *Bereitschaftspotential*, precedes self-paced movements by as much as about 1 s, as measured by EEG recordings taken over the vertex (Deecke, 1987; Deecke et al., 1969). Recent imaging studies (Cunnington et al., 2002; Jahanshahi et al., 1995; Jenkins et al., 2000; Pedersen et al., 1998; Weilke et al., 2001) have suggested that at least one source of the readiness potential lies in the medial frontal cortex. One can think of performing a self-paced movement task, as in these studies, as generating actions with randomly varying time intervals and freely selecting between these intervals. Interestingly, the readiness potential has also been found to be of higher intensity before randomly selected movements than before externally specified movements (Dirnberger et al., 1998). Given these findings and those of the present study, it is a reasonable hypothesis that the pre-SMA is involved in the endogenous generation of responses when external stimuli do not adequately specify the appropriate action.

There are, however, alternative explanations to consider. The first is that the activity that we ascribe to the pre-SMA might have been in the supplementary eye field (SEF). One might worry that our finding in the medial frontal cortex was due to eye movements made during the selection of the fractal images. Indeed there was activity in the superior colliculus that correlated with response times, and thus the number of eye movements. However, we think it unlikely that the activation in the pre-SMA was due to eye movements. The reason is that the study of Grosbras et al. (1999), as well as other studies they review, shows the SEF to be in general more posterior than the peak in our study. Furthermore, our eye movement data show that subjects in general make more saccades in this experiment when the response time was long. This means that the negative correlation between activation in the presupplementary motor area and response time strongly suggests that the activation in the pre-SMA was not due to eye movements.

The second alternative is that the activity in the pre-SMA merely reflects the monitoring of response conflict. Ullsperger and von Cramon (2001) have suggested that it is the presupplementary motor area, and not the anterior cingulate, that subserves this function. On the other hand, many other studies (Botvinick et al., 1999, 2001; Casey et al., 2000; Cohen et al., 2000; van Veen et al., 2001) have associated activity in the anterior cingulate cortex with the monitoring of conflict. Since response conflict is typically gauged by response times (Eriksen and Eriksen, 1974; Gratton et al., 1992), the negative correlation in our study between activation in the pre-SMA and response time suggests that our result is not due to the monitoring of response conflict. To further resolve the issue, we have specifically compared activation on the Eriksen conflict paradigm and free selection. As reported in abstract form

(Lau et al., in press), we again found activation in the pre-SMA on the free selection task, but we did not find activation here when we compared conflict with no conflict trials.

A final alternative is that the activation in the pre-SMA reflects working memory during free selection. Petit et al. (1998) have reported delay-related activity in the pre-SMA on a working memory task. However, we deliberately set up our task to minimize working memory demands. We used novel stimuli for each trial, which made working memory strategies largely ineffective. Furthermore, the role of the pre-SMA in working memory has so far only been suggested for the maintenance of memory items. However, we used an event-related design in this study and the subjects would not know whether the next trial required free selection or not; thus, any possible maintenance load had to be the same across the three task conditions.

Further evidence that the activation in the pre-SMA may not be related to working memory comes from the rTMS study by Hadland et al. (2001). These authors also used a free selection paradigm that minimized working memory demands. They reported that rTMS over the anterior SMA suggests that the anterior SMA impaired the random generation of sequences, whether it was applied on the second move of the sequence. This was true even though a light indicated the first move that the subject had made.

Conclusions

The notion of 'willed action' to some might seem to be an unfashionable remainder of folk psychology. However, it can be translated into terms that are more congenial to cognitive science, namely attention to the selection of responses. In this experiment, we confirm activation in the dorsal prefrontal cortex (area 46) when subjects perform a free selection task, but show that this is only one example of a task that requires attention to the selection of action. We also found activation here for the SPECIFIED condition. In this condition, the subjects had to inspect each of the targets and vary their response accordingly, whereas in the routine condition, the appropriate target 'popped out' and the response was always the same. The presupplementary motor area, on the other hand, was found to be tightly associated with free selection of responses. Together with previous findings in the literature, we suggest that this area is genuinely involved in the endogenous generation of responses when the responses are underdetermined and there are insufficient environmental constraints.

Acknowledgments

References

2001. Conflict, monitoring and cognitive control. Psychol. Rev. 108, 624–652.

Buckner, R.L., Raichle, M.E., Petersen, S.E., 1995. Dissociation of human prefrontal cortical areas across different speech production tasks and gender groups. J. Neurophysiol. 74, 2163–2173.

Bunge, S.A., Hazeltine, E., Scanlon, M.D., Rosen, A.C., Gabrieli, J.D., 2002. Dissociable contributions of prefrontal and parietal cortices to response selection. NeuroImage 17, 1562–1571.

Casey, B.J., Thomas, K.M., Welsh, T.F., Badgaiyan, R.D., Eccard, C.H., Jennings, J.R., et al., 2000. Dissociation of response conflict, attentional selection, and expectancy with functional magnetic resonance imaging. Proc. Natl. Acad. Sci. U. S. A. 97, 8728–8733.

Cohen, J.D., Perlstein, W.M., Braver, T.S., Nystrom, L.E., Noll, D.C., Jonides, J., et al., 1997. Temporal dynamics of brain activation during a working memory task. Nature 386, 604–608.

Cohen, J.D., Botvinick, M., Carter, C.S., 2000. Anterior cingulate and prefrontal cortex: who's in control? Nat. Neurosci. 3, 421–423.

Cunnington, R., Windischberger, C., Deecke, L., Moser, E., 2002. The preparation and execution of self-initiated and externally-triggered movement: a study of event-related fMRI. NeuroImage 15, 373–385.

Deecke, L., 1987. Bereitschaftspotential as an indicator of movement preparation in supplementary motor area and motor cortex. Ciba Found. Symp. 132, 231–250.

Deecke, L., Scheid, P., Kornhuber, H.H., 1969. Distribution of readiness potential, pre-motion positivity, and motor potential of the human cerebral cortex preceding voluntary finger movements. Exp. Brain Res. 7, 158–168.

Deiber, M.P., Passingham, R.E., Colebatch, J.G., Friston, K.J., Nixon, P.D., Frackowiak, R.S., 1991. Cortical areas and the selection of movement: a study with positron emission tomography. Exp. Brain Res. 84, 393–402.

Desmond, J.E., Gabrieli, J.D., Glover, G.H., 1998. Dissociation of frontal and cerebellar activity in a cognitive task: evidence for a distinction between selection and search. NeuroImage 7, 368–376.

D'Esposito, M., Aguirre, G.K., Zarahn, E., Ballard, D., Shin, R.K., Lease, J., 1998. Functional MRI studies of spatial and nonspatial working memory. Brain Res. Cogn. Brain Res. 7, 1–13.

D'Esposito, M., Postle, B.R., Rypma, B., 2000. Prefrontal cortical contributions to working memory: evidence from event-related fMRI studies. Exp. Brain Res. 133, 3–11.

Dirnberger, G., Fickel, U., Lindinger, G., Lang, W., Jahanshahi, M., 1998. The mode of movement selection. Movement-related cortical potentials prior to freely selected and repetitive movements. Exp. Brain Res. 120, 263–272.

Eriksen, B., Eriksen, C., 1974. Effects of noise letters upon the identification of a target letter in a nonsearch task. Percept. Psychophys., 143–149.

Friston, K., Ashburner, J., Poline, J., Frith, C., Heather, J., Frackowiak, R., 1995. Statistical parametric maps in functional imaging: a general linear approach. Hum. Brain Mapp. 2, 165–189.

Frith, C.D., 2000. The role of dorsolateral prefrontal cortex in the selection of action. In: Monsell, S., Driver, J. (Eds.), Control of Cognitive Processes: Attention and Performance XvIII. MIT Press, Cambridge, pp. 429–565.

Frith, C.D., Friston, K., Liddle, P.F., Frackowiak, R.S., 1991. Willed action and the prefrontal cortex in man: a study with PET. Proc. R. Soc. Lond. B Biol. Sci. 244, 241–246.

Goldman-Rakic, P.S., 1992. Working memory and the mind. Sci. Am. 267, 110–117.

Goldman-Rakic, P.S., 1995. Architecture of the prefrontal cortex and the central executive. Ann. N. Y. Acad. Sci. 769, 71–83.

Gratton, G., Coles, M.G., Donchin, E., 1992. Optimizing the use of information: strategic control of activation of responses. J. Exp. Psychol. Gen. 121, 480–506.

Grosbras, M.H., Lobel, E., Van de Moortele, P.F., LeBihan, D., Berthoz, A., 1999. An anatomical landmark for the supplementary eye fields in human revealed with functional magnetic resonance imaging. Cereb. Cortex 9, 705–711.

Botvinick, M., Nystrom, L.E., Fissell, K., Carter, C.S., Cohen, J.D., 1999. Conflict monitoring versus selection-for-action in anterior cingulate cortex. Nature 402, 179–181.

Botvinick, M.M., Braver, T.S., Barch, D.M., Carter, C.S., Cohen, J.D.,

Hadland, K.A., Rushworth, M.F., Passingham, R.E., Jahanshahi, M., Rothwell, J.C., 2001. Interference with performance of a response selection task that has no working memory component: an rTMS comparison of the dorsolateral prefrontal and medial frontal cortex. J. Cogn. Neurosci. 13, 1097–1108.

Hyder, F., Phelps, E.A., Wiggins, C.J., Labar, K.S., Blamire, A.M., Shulman, R.G., 1997. "Willed action": a functional MRI study of the human prefrontal cortex during a sensorimotor task. Proc. Natl. Acad. Sci. U. S. A. 94, 6989–6994.

Jahanshahi, M., Frith, C.D., 1998. Willed action and its impairments. Cogn. Neuropsychol. 15, 483–533.

Jahanshahi, M., Jenkins, I.H., Brown, R.G., Marsden, C.D., Passingham, R.E., Brooks, D.J., 1995. Self-initiated versus externally triggered movements: I. An investigation using measurement of regional cerebral blood flow with PET and movement-related potentials in normal and Parkinson's disease subjects. Brain 118 (Pt 4), 913–933.

Jahanshahi, M., Dirnberger, G., Fuller, R., Frith, C.D., 2000. The role of the dorsolateral prefrontal cortex in random number generation: a study with positron emission tomography. NeuroImage 12, 713–725.

James, W., 1890. The Principles of Psychology. H. Holt and Company, New York.

Jenkins, I.H., Jahanshahi, M., Jueptner, M., Passingham, R.E., Brooks, D.J., 2000. Self-initiated versus externally triggered movements: II. The effect of movement predictability on regional cerebral blood flow. Brain 123 (Pt 6), 1216–1228.

Kapur, S., Rose, R., Liddle, P.F., Zipursky, R.B., Brown, G.M., Stuss, D., et al., 1994. The role of the left prefrontal cortex in verbal processing: semantic processing or willed action? NeuroReport 5, 2193–2196.

Lau, H.C., Rogers, R.D., Passingham, R.E., in press. Does Medial Frontal Activity on Free Selection Tasks Reflect Conflict Monitoring? NeuroImage (Abstract for OHBM meeting 2003).

Miezin, F.M., Maccotta, L., Ollinger, J.M., Petersen, S.E., Buckner, R.L., 2000. Characterizing the hemodynamic response: effects of presentation rate, sampling procedure, and the possibility of ordering brain activity based on relative timing. NeuroImage 11, 735–759.

Mottaghy, F.M., Gangitano, M., Krause, B.J., Pascual-Leone, A., 2003. Chronometry of parietal and prefrontal activations in verbal working memory revealed by transcranial magnetic stimulation. NeuroImage 18, 565–575.

Mull, B.R., Seyal, M., 2001. Transcranial magnetic stimulation of left prefrontal cortex impairs working memory. Clin. Neurophysiol. 112, 1672–1675.

Nathaniel-James, D.A., Frith, C.D., 2002. The role of the dorsolateral prefrontal cortex: evidence from the effects of contextual constraint in a sentence completion task. NeuroImage 16, 1094–1102.

Owen, A.M., 1997. The functional organization of working memory processes within human lateral frontal cortex: the contribution of functional neuroimaging. Eur. J. Neurosci. 9, 1329–1339.

Owen, A.M., Stern, C.E., Look, R.B., Tracey, I., Rosen, B.R., Petrides, M., 1998. Functional organization of spatial and nonspatial working mem-

ory processing within the human lateral frontal cortex. Proc. Natl. Acad. Sci. U. S. A. 95, 7721–7726.

Passingham, R.E., Rowe, J.B., Sakai, K., in press. Prefrontal Cortex and Attention to Action. In: Humphreys G.W. (Ed.), Attention in Action: Taylor and Francis Group.

Pedersen, J.R., Johannsen, P., Bak, C.K., Kofoed, B., Saermark, K., Gjedde, A., 1998. Origin of human motor readiness field linked to left middle frontal gyrus by MEG and PET. NeuroImage 8, 214–220.

Petit, L., Courtney, S.M., Ungerleider, L.G., Haxby, J.V., 1998. Sustained activity in the medial wall during working memory delays. J. Neurosci. 18, 9429–9437.

Petrides, M., 2000. The role of the mid-dorsolateral prefrontal cortex in working memory. Exp. Brain Res. 133, 44–54.

Petrides, M., Alivisatos, B., Meyer, E., Evans, A.C., 1993. Functional activation of the human frontal cortex during the performance of verbal working memory tasks. Proc. Natl. Acad. Sci. U. S. A. 90, 878–882.

Playford, E.D., Jenkins, I.H., Passingham, R.E., Nutt, J., Frackowiak, R.S., Brooks, D.J., 1992. Impaired mesial frontal and putamen activation in Parkinson's disease: a positron emission tomography study. Ann. Neurol. 32, 151–161.

Schumacher, E.H., D'Esposito, M., 2002. Neural implementation of response selection in humans as revealed by localized effects of stimulus–response compatibility on brain activation. Hum. Brain Mapp. 17, 193–201.

Spence, S., Frith, C.D., 1999. Towards a functional anatomy of volition. In: Libet, B., Freeman, A., Sutherland, K. (Eds.), The Volitional Brain: Towards a Neuroscience of Free Will. Imprint Academic, Exeter, UK.

Spence, S.A., Hirsch, S.R., Brooks, D.J., Grasby, P.M., 1998. Prefrontal cortex activity in people with schizophrenia and control subjects. Evidence from positron emission tomography for remission of 'hypofrontality' with recovery from acute schizophrenia. Br. J. Psychiatry 172, 316–323.

Thaler, D., Chen, Y.C., Nixon, P.D., Stern, C.E., Passingham, R.E., 1995. The functions of the medial premotor cortex. I. Simple learned movements. Exp. Brain Res. 102, 445–460.

Treisman, A.M., Gelade, G., 1980. A feature-integration theory of attention. Cogn. Psychol. 12, 97–136.

Ullsperger, M., von Cramon, D.Y., 2001. Subprocesses of performance monitoring: a dissociation of error processing and response competition revealed by event-related fMRI and ERPs. NeuroImage 14, 1387–1401.

van Veen, V., Cohen, J.D., Botvinick, M.M., Stenger, V.A., Carter, C.S., 2001. Anterior cingulate cortex, conflict monitoring, and levels of processing. NeuroImage 14, 1302–1308.

Weilke, F., Spiegel, S., Boecker, H., von Einsiedel, H.G., Conrad, B., Schwaiger, M., et al., 2001. Time-resolved fMRI of activation patterns in M1 and SMA during complex voluntary movement. J. Neurophysiol. 85, 1858–1863.

Worsley, K., Marrett, S., Neelin, P., Vandal, A., Friston, K., Evans, A., 1996. A unified statistical approach for determining significant signals in images of cerebral activation. Hum. Brain Mapp., 58–73.