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"Willed action": A functional MRI study of the human prefrontal cortex during a sensorimotor task

(positron emission tomography/human brain mapping/dorsolateral prefrontal cortex/verbal fluency/Brodmann areas 6, 8, 9, 24, 32, 45, and 46)

FAHMEED HYDER[†‡], ELIZABETH A. PHELPS[§], CHRISTOPHER J. WIGGINS[¶], KEVIN S. LABAR[§], ANDREW M. BLAMIRE[‖], AND ROBERT G. SHULMAN[†]

Departments of [†]Molecular Biophysics and Biochemistry and [§]Psychology, Yale University, New Haven, CT 06510; [¶]Max-Planck-Institut für neurologische Forschung, Inselstrasse 22–26, 04103 Leipzig, Germany; and [‖]Medical Research Council, John Radcliffe Hospital, Headington, Oxford OX3 9DU, United Kingdom

Contributed by Robert G. Shulman, April 14, 1997

ABSTRACT **Functional MRI (fMRI) was used to examine human brain activity within the dorsolateral prefrontal cortex during a sensorimotor task that had been proposed to require selection between several responses, a cognitive concept termed "willed action" in a positron emission tomography (PET) study by Frith *et al*. [Frith, C. D., Friston, K., Liddle, P. F. & Frackowiak, R. S. J. (1991) *Proc. R. Soc. London Ser. B* 244, 241–246]. We repeated their sensorimotor task, in which the subject chooses to move either of two fingers after a stimulus, by fMRI experiments in a 2.1-T imaging spectrometer. Echo-planar images were acquired from four coronal slices in the prefrontal cortex from nine healthy subjects. Slices were 5 mm thick, centers separated by 7 mm, with nominal in-plane spatial resolution of 9.6 × 5.0 mm^2 for mean data. Our mean results are in agreement with the PET results in that we saw similar bilateral activations. The present results are compared with our previously published fMRI study of a verbal fluency task, which had also been proposed by Frith *et al*. to elicit a "willed action" response. We find a clear separation of activation foci in the left dorsolateral prefrontal cortex for the sensorimotor (Brodmann area 46) and verbal fluency (Brodmann area 45) tasks. Hence, assigning a particular activated region to "willed action" is not supported by the fMRI data when examined closely because identical regions are not activated with different modalities. Similar modality linked activations can be observed in the original PET study but the greater resolution of the fMRI data makes the modality linkages more definite.**

In humans, a wide range of behavior has been attributed to the prefrontal cortex, including working memory (1, 2), planning and execution (3), willed action (4), self-awareness (5), and verb generation (6, 7). Many other experiments have tried to differentiate the specific regions within the prefrontal cortex whose activity is related to these varied behaviors (8). In a recent study, Frith and co-workers (4) utilized positron emission tomography (PET) to localize area(s) of the prefrontal cortex involved in "willed action," a cognitive concept which they identified as being involved in any task that requires the subject to choose between more than one equally appropriate response.

In an attempt to localize prefrontal cortex activity related to "willed action," Frith and co-workers (4) compared two cognitive tasks involving different modalities: a verbal fluency task and a sensorimotor task. For both tasks, they compared two conditions: a baseline condition where the correct response was determined by the stimulus, and a generate condition where the subject had to choose from more than one correct response. The difference between these two conditions was defined as the "willed action" response. It was hypothesized by Frith and co-workers that any common areas of cerebral activation found in the two cognitive tasks would be the result of a "willed action" component, because these two tasks had very few other common characteristics. In both cognitive tasks activation in a large area of the dorsolateral prefrontal cortex was observed, which led Frith and co-workers to conclude that brain activity in this area is due to "willed action" and is independent of the stimulus modality (i.e., verbal or sensorimotor). However, they reported some differences in the hemispheric locations of the dorsolateral prefrontal cortex activations for the two cognitive tasks. Most significantly, brain activity for the verbal fluency task was lateralized to the left hemisphere, whereas the activity for the sensorimotor task was bilateral. Although the coordinates of the reported center of mass (COM) of the large area of activation in the left dorsolateral prefrontal cortex differed slightly between the cognitive tasks, being slightly superior for the sensorimotor task, Frith *et al*. proposed that "willed acts in the two response modalities studied (speaking a word, or lifting a finger) were associated with increased blood flow in the dorsolateral prefrontal cortex (Brodmann area 46)" (4). These differences raise the question as to whether the areas activated by these two different modalities are the same, or whether there are spatial distinctions dependent on the modality of presentation or other task-specific differences.

In the present study, we attempt to address the question of whether these two different "willed action" tasks produce identical areas of activation. Recently, work within this laboratory has examined the verbal fluency task by using functional MRI (fMRI) (9). Coordinates of the activated foci in our verbal fluency fMRI study and the COM of activations reported using PET (4) agreed to within the combined experimental accuracy. To determine if we find similar activations for the other "willed action" task, here we have performed an fMRI study during the sensorimotor task. First, we compare the areas of activation observed in this study to the previous PET findings of the same sensorimotor task (4). For this purpose it was sufficient to acquire data only from the prefrontal cortex. Second, we compare the fMRI activations observed in the sensorimotor task to localized activations from our previously reported fMRI verbal fluency study (9). Finally, we compare and contrast the localized activities observed by both methods during the verbal fluency task (4, 9, 10) and the sensorimotor task (refs. 4 and 11 and the present study), to

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Abbreviations: fMRI, functional MRI; PET, positron emission tomography; EPI, echo-planar imaging; ROI, region of interest; COM, center of mass.

[‡]To whom reprint requests should be addressed at: 126 MRC, 330 Cedar Street, Yale University, New Haven, CT 06510. e-mail: hyder@mrcbs.med.yale.edu.

examine the similarities and/or differences of regional activations for the two "willed action" tasks. We demonstrate that the revealed areas of activation in the left dorsolateral prefrontal cortex from these two different tasks are not the same, and that these differences in localized activity are very likely to be modality and/or cognitive task dependent.

MATERIALS AND METHODS

Subjects. Sixteen right-handed English-speaking subjects (13 males, 3 females) volunteered for this study. Approval was obtained from the Human Investigation Committee of Yale University and all subjects gave informed consent. Subjects were placed supine on a bed. The subject's head was firmly positioned in a foam-rubber holder which minimized movement. All six subjects involved in the previous fMRI verbal fluency study (9) were included in this study.

Experimental Design. In both conditions presented to the subject, an individual trial consisted of a touch on either of the first two fingers of the subject's right hand, followed by a response from the subject. The response given was a movement of either of these fingers, depending on the particular condition. There were two conditions: *Repeat*, the subject would move the same finger as had been touched; and *Random*, the subject would choose which finger to move and the sequence of which finger was touched was random. In the *Baseline* condition, the subject rested with no stimuli. Before each scan sequence was initiated the subject was informed which condition to expect.

MRI. All experiments were carried out on an extensively modified 2.1-T Biospec 1 spectrometer (Bruker Instruments, Billerica, MA), equipped with actively shielded gradient coils (Oxford Magnet Technologies, Oxford, U.K.). A linear birdcage radiofrequency head transceiver coil was used.

To locate the areas of interest in the frontal lobes, an initial set of sagittal anatomical images were collected, positioned about the midline. The anterior and posterior commissures (AC and PC) were identified, and coronal anatomical images were obtained. These coronal images were collected as a set of four slices, the most anterior of which was positioned approximately 3 cm anterior of the AC. The anatomical images were weighted using an inversion-recovery sequence: image matrix = 128 × 128, echo-time (TE) = 17 ms, inversion time (TI) = 750 ms, repetition time (TR) = 2 s, field of view (FOV) = 19 cm, in-plane resolution (x and z in stereotactic space) = 1.50 × 1.50 mm^2. Angiograms were taken of these same coronal slices (image matrix = 256 × 256, TR = 40 ms, TE = 17 ms, FOV = 19 cm, in-plane resolution (x and z in stereotactic space) = 0.75 × 0.75 mm^2; see ref. 12). In all cases, the slice thickness was 5 mm, with a 7-mm slice separation from the center of each slice. The nominal spatial resolutions in the anatomical image and angiogram were 1.50 × 5.00 × 1.50 and 0.75 × 5.00 × 0.75 mm^3, respectively, for individual subject data (x, y, and z in stereotactic space). The superior portion of the dorsolateral prefrontal cortex was shimmed (13) prior to obtaining functional images.

Functional images were obtained for the four coronal slices using an asymmetric spin-echo echo-planar imaging (EPI) sequence (see ref. 14). The parameters for EPI were as follows: image matrix = 32 × 64, TE (spin-echo) = 28 ms, TE (gradient-echo) = 50 ms, TR = 1.36 s per image, slice thickness = 5 mm, slice separation from center to center = 7 mm, and in-plane resolution (x and z in stereotactic space) = 4.8 × 2.5 mm^2. Images were collected as a "run" of 16 images per slice, with dummy scans (4 images per slice) used to establish magnetization steady state. In each run, the subject rested during the first 4 images per slice (*pre-task*), responded to stimuli during the next 8 images per slice (*task*), and rested again during the last 4 images per slice (*post-task*). In each run there were 16 behavioral trials during the *task* phase of the scan sequence. For each condition (i.e., *Repeat*, *Random*, *Baseline*) three runs were collected.

Data Analysis. The data analysis in this study was identical to that in the previous fMRI verbal fluency study (9). Functional images were analyzed off-line on an Silicon Graphics *Indy* workstation (Mountain View, CA) in MATLAB environment (Natick, MA). Movement artifacts were assessed by a COM algorithm using noninterpolated functional images. Briefly, a thresholded image was created such that intensities of all pixels outside the brain were set to zero, whereas the intensities of all pixels inside the brain were not altered. For each data set, the deviations in the COMs of the thresholded images (in x and z directions of a pixel) were plotted against time to reveal the temporal patterns of motion. A data set was discarded from further analysis if the deviation in the COM for any image in a series was greater than 25% of a pixel size [i.e., 1.2 and 0.6 mm for x and z directions in stereotactic space]. This criterion for movement artifact in a series of functional images was based on the time course of image intensity fluctuations in the resting brain (i.e., *Baseline* condition images where there was no stimulus-initiated movement). No attempt was made to correct for physiologic fluctuations in the fMRI data (15).

For each run consisting of 16 images per slice, the mean of the first 4 images per slice, representing basal signal (S), was subtracted from each image within the series, thus producing 16 difference images per slice and revealing task-related signal changes (ΔS). The last 4 images per slice in a run were not used to represent basal signal because the task-related signal changes are sustained sometimes even after the task is completed (e.g., see ref 9). These images were not included in obtaining activation maps. To compare the difference in brain activity between the *Random* and *Repeat* conditions, a t test was calculated using the *task* images from the two conditions, and the activation map defined by the t test comparison was thresholded to exclude pixels that contained purely noise. Each functional image, with an image matrix of 32 × 64 pixels, was then linearly interpolated to an image matrix of 128 × 128 pixels and stretched to overlay onto its anatomical image. The in-plane linear stretch factors (0.31 and 0.60 in x and z, respectively, in stereotactic space) for the functional images were determined from phantom data of a 12-cm-diameter water sphere. Although the functional image was linearly interpolated and stretched to match the anatomical image, which had a spatial resolution of 1.5 × 5.0 × 1.5 mm^3, the nominal spatial resolution in the stretched functional image was still 4.8 × 5.0 × 2.5 mm^3 for individual subject data in stereotactic space.

A linearly warped coregistration method (16, 17) was applied to the pool of data to create mean coronal slice data with respect to standard stereotactic space (18). There were three consecutive coronal slices which covered the same region of the brain and were common to all subjects. For these three coronal slices, each subject's anatomical image was linearly warped to match a standard image, as in the previous fMRI verbal fluency study (9), and mean anatomical images were created. Likewise, for each slice a mean activation map was created. A gaussian filter (1 pixel wide) was applied to each mean activation map, which was then thresholded at $P < 0.005$ to reveal regions of interest (ROIs) that were significant at that level. This particular threshold value was based on the assumption that resting brain should not reveal any "activated" regions in a t-map (i.e., the *Baseline* condition t-map, where there was no stimulus, showed "no activation" at a threshold value of $P < 0.005$). These linearly warped images were then coregistered in standard stereotactic space such that anatomical location of each ROI could be determined with respect to Talairach and Tournoux coordinates (18). The nominal spatial resolution in the mean data was slightly lower than the resolution in individual subject data. The maximum estimate of standard deviation (SD) for the in-plane resolution in the mean data was assumed to be twice the pixel size of individual subject functional data, and the maximum estimate of the SD in slice position in the mean data was evaluated as [(thickness^2

+ separation^2)/2]$^{1/2}$. The nominal spatial resolution for the mean data presented in this study was calculated to be 9.6 × 6.1 × 5.0 mm^3 in stereotactic space. For each ROI in the mean data, the COM was calculated for that mass of tissue, and the Talairach and Tournoux coordinate (18) of the COM for each ROI was obtained for comparisons. We assumed that the Talairach and Tournoux mapping caused no additional uncertainty in resolution positioning of each (16, 17).

RESULTS

Data from 9 of the 16 subjects were assessed to be free of movement artifacts. The fMRI data from these 9 subjects (8 males, 1 female) were used in the analyses. Six subjects (5 males, 1 female) from this group of 9 subjects had participated in the previous fMRI verbal fluency study (see ref. 9). The area of the smallest ROI in the individual subject data was larger than 5.0 × 2.5 mm^2 (i.e., one EPI pixel in stereotactic space). Each ROI was located in regions that were free of large blood vessels, as revealed by angiograms (data not shown) where the in-plane resolution was 0.75 × 0.75 mm^2 (i.e., one angiogram pixel in stereotactic space). Thus, in all cases reported here, the ROIs comprised functionally active tissue and/or a cluster of smaller blood vessels (diameters <0.75 mm).

Image quality in EPI is very susceptible to magnetic field deviations within the field of view (19). For this study, the magnetic field homogeneity was optimal in the superior prefrontal cortex. A two-dimensional calculation of magnetic field mapping of the human head (20) showed that coronal planes at this location of the brain suffer from large magnetic field deviations in the inferior regions (because of air-filled cavities and sinuses), whereas the magnetic field is very homogeneous in the superior parts. Magnetic field mapping with optimal shimming of the human brain at 2.1 T has confirmed these theoretical findings (21). Because of the large magnetic field deviations in the inferior regions of the frontal cortex, either the inferior (7) or the superior (refs. 2 and 9 and present study) portion can be homogeneously shimmed separately, with the automated shimming algorithm (13), for optimal imaging with EPI at 2.1 T (21). Because of the limited shim currents available for the higher-order shims on the whole-body 2.1-T scanner (13), the inferior and superior regions in the frontal cortex could not be homogeneously shimmed together (19, 21).

The image contrast in this fMRI study was R_2^*-weighted (where R_2^* is the apparent transverse relaxation rate of water), which is dependent on small stimulus-initiated fluctuations in the local magnetic field that produce a slight decrease in the measured value of R_2^* (see refs. 14 and 22–24). In each ROI, the positive signal change observed in fMRI with R_2^*-weighting (i.e., $\Delta S/S > 0$ because $\Delta R_2^*/R_2^* < 0$) is a resultant of a small reduction in the volume magnetic susceptibility difference between capillaries and surrounding tissue due to a decrease

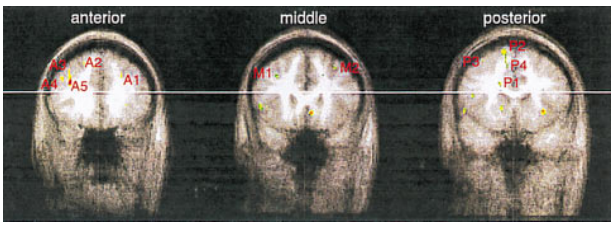

FIG. 1. The mean activation maps (i.e., *t*-maps) overlayed on corresponding mean anatomical images (anterior, middle, and posterior) for *Random* minus *Repeat* (sensorimotor task). The *t*-maps were thresholded at $P < 0.005$ [$t_{0.995}$ (green), $t_{0.996}$ (yellow), $t_{0.997}$ (orange), $t_{0.998}$ (brown), and $t_{0.999}$ (red)]. The Talairach and Tournoux coordinates (18) for the ROIs are listed in Table 1 and depicted in a Talairach and Tournoux coregistered human brain in Fig. 3. Similar activations were observed in *Random* minus *Opposite* (data not shown). The white horizontal lines delineate poorly shimmed regions (see *Results*).

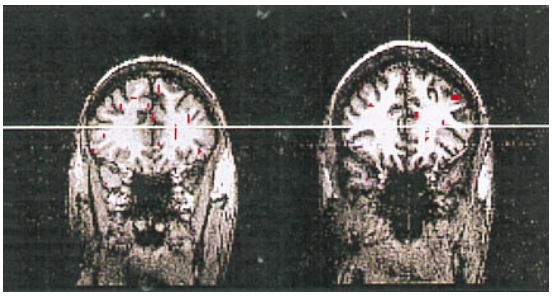

FIG. 2. Comparison of ROIs between individual subjects (*Random* minus *Repeat*; sensorimotor task) in the anterior slice. The thresholding for the individual subject ROIs are $P < 0.01$ (red only). The individual subject ROIs are spatially correlated with the mean ROIs within experimental error. The white horizontal lines delineate poorly shimmed regions (see *Results*).

in the paramagnetic hemoglobin concentration in capillaries caused by an increase in local blood oxygenation fraction. For a fixed volume of tissue, the blood oxygenation fraction is dependent on the coupling between cerebral perfusion and oxygen consumption (22–24). However, non-stimulus-initiated alterations in the measured value of R_2^*, which can occur in poorly shimmed regions (ref. 21; i.e., regions where R_2^* is very large), can lead to "false positives" in the fMRI data. These nonphysiological changes in the measured value of R_2^* within the vicinity of inadequately shimmed regions can result from large quantities of cerebrospinal fluid flowing through ventricles (25), normal brain parenchyma motion (26), and/or unpredictable changes in the volume of air within the cavities below the frontal lobe and the sinuses (27).

The images shown in Fig. 1 are the group mean ($n = 9$) activation maps for the *Random* minus *Repeat* condition (i.e., the "willed action" cognitive element as defined in ref. 4). Since the regions below the white horizontal lines were poorly shimmed, measurements below these lines are unreliable and were not analyzed.

fMRI Sensorimotor Study. The Talairach and Tournoux coordinates (18) of the COM for each ROI for the sensorimotor task are listed in Table 1. Bilateral activation was observed in several areas in the middle frontal gyrus bordering on the superior frontal sulcus (right—A3, A4, A5, M1, and P3; left—A1 and M2). Additional activation was observed in the right superior frontal gyrus (A2, P2) and the right anterior cingulate (P1, P4).

Activations in individual subjects were generally consistent with mean results, although the precise location of an activation within a gyrus varied, as can be seen in the anterior slice for two individual subjects shown in Fig. 2.

Comparison of fMRI and PET Sensorimotor Studies. The Talairach and Tournoux coordinates (18) of the COM for each ROI in the fMRI sensorimotor study and the COMs for the PET sensorimotor study by Frith *et al.* (4) are listed in Table 1 and represented in Fig. 3. It should be noted that the coordinates given for the PET data are for the COMs of

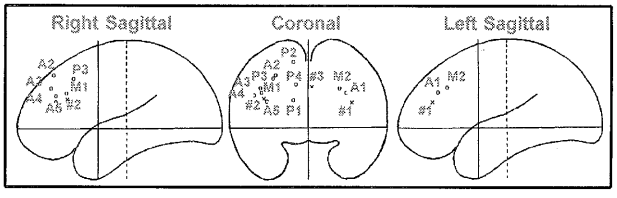

FIG. 3. Comparison of fMRI (present study) and PET (4) activations of the sensorimotor task (*Random* minus *Repeat*) in a Talairach and Tournoux coregistered human brain. The comparison shows that the fMRI ROIs A1 and M1 are analogous to PET COMs nos. 1 and 2, whereas fMRI ROI P4 is close to PET COM no. 3. Refer to Table 1 for Talairach and Tournoux coordinates (18).

Table 1. Activations for the sensorimotor task in Talairach and Tournoux coordinates (18) in mm (*Random* minus *Repeat*)

		x	*y*	*z*	Location
			fMRI (present study)		
ROI					
A1		−30	+35	+28	Middle frontal gyrus (Brodmann area 9/46)
A2		+26	+38	+44	Superior frontal gyrus/superior frontal sulcus (Brodmann area 8)
A3		+38	+40	+33	Middle frontal gyrus (Brodmann area 9)
A4		+43	+36	+27	Middle frontal gyrus (Brodmann area 9/46)
A5		+33	+36	+22	Inferior frontal sulcus/middle frontal gyrus (Brodmann area 8)
M1		+37	+27	+29	Middle frontal gyrus (Brodmann area 46)
M2		−25	+27	+33	Middle frontal gyrus (Brodmann area 9/46)
P1		+12	+16	+23	Cingulate sulcus (Brodmann area 24)
P2		+12	+22	+55	Superior frontal gyrus (Brodmann area 6)
P3		+28	+21	+41	Middle frontal gyrus (Brodmann area 8)
P4		+10	+19	+36	Cingulate sulcus/gyrus (Brodmann area 32)
			PET (Frith *et al.*; ref. 4)		
COM	ROI match				
1	(A1)	−35 (−30)	+39 (+35)	+21 (+28)	Brodmann area 9/46 (Brodmann area 9/46)
2	(M1)	+35 (+37)	+26 (+27)	+24 (+29)	Brodmann area 9/45 (Brodmann area 46)
3	(P4)	−3 (+10)	+16 (+19)	+34 (+36)	Brodmann area 32 (Brodmann area 32)

Each ROI and COM is shown in Fig. 3. In the lower portion of the table, the ROI match (fMRI ROIs from above) are shown in parentheses with the COMs of the PET study of Frith *et al.* (4). Similar fMRI activations were observed in *Random* minus *Opposite* (data not shown).

extended activations. The spatial resolutions of mean data obtained by PET and fMRI were approximately similar in stereotactic space (i.e., $\approx 10 \times 10 \times 10$ mm^3 and $\approx 10 \times 6 \times 5$ mm^3, respectively). Nonetheless, the agreement between the Talairach and Tournoux coordinates (18) for certain fMRI and PET activations is excellent.

In the left hemisphere, the Talairach and Tournoux coordinates (18) for fMRI ROI A1 are very close to the coordinates for PET COM no. 1. The fMRI ROI M2 is most likely a posterior and superior extension of this same activation. Frith *et al.* (4) identified this region as the left dorsolateral prefrontal cortex, although in our data it is more precisely located in the middle frontal gyrus on the border of the superior frontal sulcus.

In the right hemisphere, the Talairach and Tournoux coordinates (18) for fMRI ROI M1 are the closest to PET COM no. 2. The anterior fMRI activations A3, A4, and A5 and the posterior activation, P3, are also within the region of PET COM no. 2. Frith *et al.* (4) identified this region as the right dorsolateral prefrontal cortex, and we identify it more precisely as the bottom of the superior frontal sulcus in the middle frontal gyrus. Additional activation observed by fMRI in the superior frontal gyrus in the right hemisphere (A2 and P2) is slightly beyond the PET COM no. 2.

The Talairach and Tournoux coordinates (18) of the PET COM no. 3, the anterior cingulate activation reported by Frith *et al.* (4), coincides quite well with fMRI ROI P4, while P1 also falls within the extended cingulate activation.

Comparison of fMRI Sensorimotor and Verbal Fluency Studies. Recent work from this laboratory (9) examined the verbal fluency "willed action" task studied by Frith *et al.* (4), a verbal task which had been designed to be cognitively "analogous" to the sensorimotor task. This verbal task can be described briefly as follows: In the *Repeat* condition, the subject responded to a series of cued words by repeating them (e.g., *man*–MAN, *file*–FILE), whereas in the *Generate* condition, the subject generated different words beginning with a letter when cued (e.g., *R*, RABBIT, RAISE). The difference between these conditions was defined as the "willed action" response by Frith *et al.* (4), as the response for the *Repeat* condition is entirely determined by the stimulus, whereas the *Generate* condition involves the selection of an appropriate response. Table 2 lists the Talairach and Tournoux coordinates (*Generate* minus *Repeat*) of the COM for each ROI in the fMRI verbal fluency study (9).

A comparison of activations in the fMRI sensorimotor and verbal fluency studies (see Tables 1 and 2) illustrates several differences. First, the verbal fluency task produced no activation in the right hemisphere. Second, the left dorsolateral prefrontal cortical activations are in different brain regions for the two cognitive tasks. In the verbal fluency task, there were two activations in the left hemisphere: the first was located in the inferior frontal gyrus, and the second on the border of the superior frontal gyrus in the superior frontal sulcus. In contrast, the left dorsolateral prefrontal cortical activation for the sensorimotor task is located between the two verbal fluency activation foci in the middle frontal gyrus. Finally, there was anterior cingulate activation reported in both the verbal fluency and sensorimotor tasks. The cingulate activation was

Table 2. Activations for the verbal fluency task in Talairach and Tournoux coordinates (18) in mm (*Generate* minus *Repeat*)

		x	*y*	*z*	Location
			fMRI (Phelps *et al.*; ref. 9)		
ROI					
A1		−19	+38	+46	Superior frontal gyrus/superior frontal sulcus (Brodmann area 8)
M1		−23	+28	+44	Middle frontal gyrus/superior frontal sulcus (Brodmann area 8)
M2		−46	+24	+18	Inferior frontal gyrus (Brodmann area 45)
P1		−4	+20	+40	Cingulate gyrus/sulcus (Brodmann area 32)
P2		+4	+17	+27	Cingulate sulcus (Brodmann area 24)
P3		−12	+17	+27	Cingulate sulcus (Brodmann area 24)
			PET (Frith *et al.*; ref. 4)		
COM	ROI match				
1	(M2)	−43 (−46)	+29 (+24)	+20 (+18)	Brodmann area 45/46 (Brodmann area 45)
2	(P2)	+4 (+4)	+23 (+17)	+36 (+27)	Brodmann area 32 (Brodmann area 24)

In the lower portion of the table, the ROI match (ROIs from above) are shown in parentheses with the COMs of the PET study of Frith *et al.* (4).

Table 3. Vectorial comparison (Δ, in mm) of left dorsolateral prefrontal activations observed in "willed action" tasks

	PET (SM) COM no. 1	fMRI (VF) ROI M2	fMRI (SM) ROI A1
PET (VF) COM no. 1	12.8	6.2	—
PET (SM) COM no. 1	—	—	9.4
fMRI (VF) ROI M2	—	—	22.3

The vectorial comparison is defined as the difference between two coordinates: $\Delta = [(x_1 - x_2)^2 + (y_1 - y_2)^2 + (z_1 - z_2)^2]^{1/2}$. Refer to Tables 1 and 2 for actual coordinates of sensorimotor and verbal fluency activations, respectively. A Δ value of >10 mm indicates that the two coordinates are significantly different, whereas a Δ value of <10 mm indicates that the two coordinates are similar (see *Results*). Since the largest uncertainty for the spatial resolutions in the PET and fMRI data was ≈10 mm in stereotactic space (see *Results*), two coordinates greater than 10 mm apart were considered to be significantly different from each other. SM, sensorimotor; VF, verbal fluency.

observed in the right hemisphere for the sensorimotor task and bilaterally for the verbal fluency task.

Vectorial Comparison of Dorsolateral Prefrontal Activations Observed in "Willed Action" Tasks. The superior portion of the frontal sulcus in the left hemisphere has been identified as the region in the left dorsolateral prefrontal cortex that is activated during both of the "willed action" tasks (4). The activations observed in this region by PET and fMRI are COM no. 1 (PET-sensorimotor, see Table 1), COM no. 1 (PET-verbal fluency, see Table 2), ROI A1 (fMRI-sensorimotor, see Table 1), and ROI M2 (fMRI-verbal fluency, see Table 2), respectively. Table 3 shows the quantitative vectorial comparison amongst these four Talairach and Tournoux coordinates (18). Since the largest uncertainty for the spatial resolutions in the PET and fMRI data was ≈10 mm in stereotactic space (see above), two Talairach and Tournoux coordinates (18) greater than 10 mm apart were considered to be significantly different from each other. For the two "willed action" tasks, the PET and fMRI measurements agree within 9.4 mm and 6.2 mm for the sensorimotor and verbal fluency tasks, respectively. However, the difference between the specific regions that are activated during the sensorimotor and verbal fluency tasks is quite significant. This difference between localized activities observed during the two "willed action" tasks is 12.8 mm and 22.3 mm measured by PET and fMRI, respectively.

DISCUSSION

In the present fMRI study, we address the question of whether two different "willed action" tasks produce identical areas of activation as proposed initially by Frith and co-workers (4). In both of our fMRI studies, it was adequate to acquire data predominantly from the prefrontal cortex, since that was the area of interest analyzed by Frith and co-workers (4). In the current study, we used identical acquisition/analysis procedures as in our previous verbal fluency fMRI study (9). All of the subjects in the verbal fluency fMRI study participated in the present sensorimotor fMRI study.

Our previous verbal fluency fMRI study (9) confirmed the PET findings of the verbal fluency task (see Table 2), while the present fMRI study agrees with the PET sensorimotor task, including the bilateral nature of its sensorimotor activity (see Table 1 and Fig. 3). The general agreement between coordinates of activation foci obtained by fMRI and PET for the same task(s) (see Tables 1 and 2) indicates that both methods measure similar cerebral vascular responses (28). For these two "willed action" tasks, we also find activation of the anterior cingulate as in the PET study (4). This activation has been reported for a variety of tasks in which the generation of response is somewhat difficult and requires attention (e.g., refs. 4, 6, 29, and 30). In support of this, Raichle *et al.* (10) showed that the magnitude of activation in the anterior cingulate, during a covert verb generation task, decreased with practice.

The results of PET and fMRI "willed action" studies show that two tasks which require the selection of a response, where the response is not completely specified by the stimulus, produce activations in the general area of the dorsolateral prefrontal cortex. However, our fMRI results show that regions are activated within the left dorsolateral prefrontal cortex but that the regions differ between the two "willed action" tasks. The possibility that the differences, which they too reported between the activation foci for the sensorimotor and verbal fluency tasks, might be modality specific was raised and dismissed by Frith *et al.* (4). This conclusion bears reexamination in view of our more detailed fMRI studies.

To examine this conclusion, we concentrate on activation of the left dorsolateral prefrontal cortex for the two cognitive tasks, since obvious differences in the right hemispheric activation were observed with both PET and fMRI between the sensorimotor task and the verbal fluency task (see Tables 1 and 2). For both cognitive tasks, there was good agreement between the fMRI and PET foci in the left dorsolateral prefrontal cortex (see Tables 1 and 2). For the verbal fluency task, the PET and fMRI measurements agreed to within 6.2 mm, whereas for the sensorimotor task they agreed to within to 9.4 mm (see Table 3). However, significant differences between the activation foci for sensorimotor and verbal fluency tasks were observed by both PET and fMRI, being 12.8 mm and 22.3 mm, respectively (see Table 3). The larger separation observed in the fMRI sensorimotor study came because the activation was located in the middle frontal gyrus (Brodmann area 9/46), in contrast to the fMRI verbal fluency study, in which it was in the superior frontal gyrus (Brodmann area 45) (see Tables 1 and 2).

Table 4. Dorsolateral prefrontal cortex activations in overt verbal and sensorimotor tasks

Task	*x*	*y*	*z*	Location	Study
Overt verbal					
Verbal fluency	−43	+29	+20	Brodmann area 45/46	PET, Frith *et al.* (4)
Verbal fluency	−46	+24	+18	Brodmann area 45	fMRI, Phelps *et al.* (9)
Verb generation	−43	+28	+13	Brodmann area 45	PET, Raichle *et al.* (10)
Sensorimotor					
Finger movement	−35/+35	+39/+26	+21/+24	Brodmann area 9/46	PET, Frith *et al.* (4)
Finger movement	−30/+37	+35/+27	+28/+29	Brodmann area 9/46	fMRI, present study
Joystick movement	−34/+34	+35/+36	+28/+28	Brodmann area 9/46	PET, Deiber *et al.* (11)

The tasks in the Frith *et al.* (4) study, Phelps *et al.* (9) study, and the present study are the sensorimotor and verbal fluency tasks that have been described in the text in great detail. The task in the Raichle *et al.* (10) study is a verb-generation task, whereas the task in the Deiber *et al.* (11) study is a random joystick movement task.

If a correlation is to be made from these data it suggests modality-linked prefrontal activations. Raichle *et al.* (10) reported left hemispheric activation in Brodmann area 45 during an overt verb generation task (see Table 4), and this activation focus agrees very well with the overt verbal fluency activation coordinates of our previous fMRI study (9) and the original PET study (4). Table 4 also lists the bilateral coordinates of activations detected in Brodmann area 9/46 during a joystick movement (sensorimotor) task (11), along with the coordinates of activations observed during the finger movement (sensorimotor) task of our present fMRI study and the original PET study (4), and it is clear that these locations are very similar. When the left hemispheric activation of the sensorimotor task of Deiber *et al.* (11) is compared with the left hemispheric activation of the overt verb generation task of Raichle *et al.* (10), the modality-specific spatial distinction between the foci is demonstrated once again, since the activation observed during the verbal task is somewhat inferior to the activation reported in the sensorimotor task.

These results demonstrate a strong correlation between left dorsolateral prefrontal cortex activation and modality. While the fMRI data agree with the PET data, the fMRI data have resulted in a slightly larger separation between activation foci in the left hemisphere between verbal fluency and sensorimotor tasks than that observed in the PET studies, thereby solidifying the differences observed previously by PET.

In view of these results, the concept of "willed action" being an identical cognitive component in the verbal fluency and sensorimotor tasks must be revised. For "willed action" to be a novel cognitive component which distinguishes it from the general belief that the prefrontal cortex supports "executive function" (8), the minimum requirement is that *identical* regions are activated by different modalities. If different activated regions are observed with tasks of different modalities, it is not possible to assume that they are caused by cognitive components that are independent of modality. In support of this, a verbal study by Kapur *et al.* (31) demonstrated that the activation observed in the types of verbal tasks discussed here is not linked to the response selection or "willed action" but depends on the semantic nature of the verbal task. This supports the interpretation that the different activated regions of the left dorsolateral prefrontal cortex are linked to verbal processing (i.e., modality).

In the subtraction method of human brain functional imaging used in these experiments, a cognitive difference is hypothesized to exist between a test condition and its control, and a difference image obtained between the two conditions is considered to reflect activity linked to a particular cognitive task. However, this inference may not be justified, because other cognitive functions which have been overlooked and which were not controlled may also be responsible for the difference image (32). This weakness of this inference is a limitation of the subtraction method in interpreting data. Frith and co-workers (4) compared the difference images of two modality-differing cognitive tasks to see whether "willed action" was a common cognitive element in both. This type of intertask comparison was a stronger test of the assignment than either task alone would provide. Since now we see that in both the PET and the fMRI data the verbal fluency and sensorimotor tasks activate significantly different regions of the brain, the notion of "willed action" being the common cognitive element in the two cognitive tasks must be abandoned.

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