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Regional cerebral blood flow changes in human brain related to ipsilateral and contralateral complex hand movements – a PET study

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Abstract

The purpose of this study was to investigate the cortical motor areas activated in relation to unilateral complex hand movements of either hand, and the motor area related to motor skill learning. Regional cerebral blood flow (rCBF) was measured in eight right-handed healthy male volunteers using positron emission tomography during a two-ball-rotation task using the right hand, the same task using the left hand and two control tasks. In the two-ball-rotation tasks, subjects were required to rotate the same two iron balls either with the right or left hand. In the control task, they were required to hold two balls in each hand without movement. The primary motor area, premotor area and cerebellum were activated bilaterally with each unilateral hand movement. In contrast, the supplementary motor area proper was activated only by contralateral hand movements. In addition, we found a positive correlation between the rCBF to the premotor area and the degree of improvement in skill during motor task training. The results indicate that complex hand movements are organized bilaterally in the primary motor areas, premotor areas and cerebellum, that functional asymmetry in the motor cortices is not evident during complex finger movements, and that the premotor area may play an important role in motor skill learning.

Keywords: cerebral blood flow, functional asymmetry, motor areas, motor skill learning, positron emission tomography

Introduction

Handedness and hemispheric dominance are basic aspects of human motor function. The concept of left hemisphere motor dominance in right-handed individuals for controlling cognitive-motor tasks was originally derived from the description of apraxia by Liepmann (1905). Many investigators have reported clinical evidence consistent with Liepmann's argument (see Haaland & Harrington, 1996 for review).

Recent developments in brain imaging techniques have allowed the functional asymmetry of the cortical motor control system to be investigated by studies specifically aimed at comparison of cortical activation during simple sequential thumb-to-finger movements of the right and left hands (Kawashima *et al*., 1993, 1997; Kim *et al*., 1993). Differences in the cortical mechanisms underlying simple and complex finger movements have been suggested by many investigators. In the human brain, functional roles of the supplementary motor and premotor areas in complex sequential finger movements have been demonstrated by brain imaging studies (Roland *et al*., 1980; Seitz *et al*., 1991; Shibasaki *et al*., 1993; Sadato *et al*., 1996). However, little is known about the asymmetry of cortical function during complex finger movements.

In the present study, in order to shed light on this question, we compared cortical activation during complex finger movements of the left and right hands by measuring changes in regional cerebral blood flow (rCBF) using positron emission tomography (PET). In addition, since the performance of complex motor tasks requires motor skill learning, we addressed the question of whether there are specific cortical structures in the human brain that may be responsible for the learning of motor skills during motor task training.

Materials and methods

Subjects

Eight healthy male volunteers (aged 20–24 years) participated in the study. None had any signs or history of medical or neurological disease, and all demonstrated normal results for magnetic resonance imaging (MRI) of the brain. All subjects were strongly right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971). Written informed consent was obtained from each subject in accordance with the guidelines approved by Fukui Medical University and the Declaration of Human Rights, Helsinki, 1975.

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Prior to PET experiments, a catheter was placed into the right brachial vein of each subject for tracer administration. Individual stereotaxic fixation helmets were worn during the PET measurements. A high resolution MRI scan (1.5 T) of the brain was also performed for each volunteer on a separate occasion.

PET measurements

The PET scans were performed using a General Electric Advance tomograph (GE/Yokogawa Medical System, Tokyo, Japan) with the interslice septa retracted. The physical characteristics of this scanner have been described in detail by De Grado *et al*. (1994) and Lewellen *et al*. (1996). It acquires 35 slices with an interslice spacing of 4.25 mm. In the three-dimensional mode, oblique sinograms were obtained with a maximum cross-coincidence of +11 rings. A 10 min transmission scan was performed using two rotating Ge-68 sources for attenuation correction. CBF images were generated by summing the activity during the 60 s period following the first detection of an increase in cerebral radioactivity after an intravenous bolus injection of 10 mCi of ^{15}O-labelled water (Sadato *et al*., 1997). The images were reconstructed with the Kinahan–Rogers reconstruction algorithm (Kinahan & Rogers, 1989). Hanning filters were employed, giving transaxial and axial resolutions of 6 and 10 mm (full-width at half-maximum), respectively. The use of wide filters here was to increase signal to noise ratio in the PET images, and to account for anatomical differences in the subjects and interindividual differences in activation patterns (Friston *et al*., 1991). The field of view and pixel size of the reconstructed images were 256 mm and 2 mm, respectively. No arterial blood sampling was performed, and thus the images were those of tissue activity.

Task procedures

Each subject was placed comfortably in the supine position in the scanner, a darkened and quiet room, for the duration of the study, and asked to hold two iron balls in each hand with their eyes closed throughout the study. The iron balls had a smooth surface, were 450 mm in diameter and weighted 140 g.

All subjects performed the following three tasks: (i) a two-ball-rotation task with the right hand; (ii) a two-ball-rotation task with the left hand; and (iii) a control task. None had previous experience of similar motor tasks. In the control task, subjects were asked to hold two iron balls in each hand without movement, with the arms in a resting position. An auditory stimulus, a beep tone, was presented once every second during the control task. We obtained two PET scans for the control task, one at the beginning and the other at the end of the study. The right hand task was always followed by the left hand task. For the latter, each subject performed seven successive trial sessions (Fig. 1) starting 10 min after completion of the first PET scan for the control task. In the first trial, auditory cue beep tone signals were presented once every second. Subjects were instructed to rotate the two balls around each other with their right hand once the auditory cue had been given. Subjects held two balls in the hand contralateral to the moving hand, without movement. The first trial continued for 100 s. After a 60 s intertrial interval, the subjects were asked to rotate the two balls with their right hand as fast as possible without any auditory cues (second trial). An intertrial interval of 360 s was incorporated before the third trial. The instructions and cues, as well as the time course, for the third, fifth and seventh trials were the same as those for the first trial, and those for the fourth and sixth trials were the same as those for the second trial (Fig. 1). The seventh trial was started at the time of the bolus injection, and with the performance of the PET scan. The left hand task was started 10 min after the right hand task, using the same schedule.

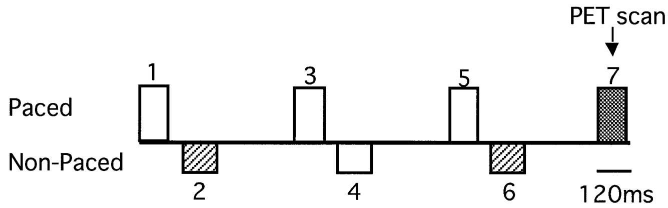

FIG. 1. Schematic diagram of the time course of the training. A PET scan was performed for each subject during the seventh trial. During the odd-numbered trials, subjects were asked to rotate the two iron balls around each other in their hands once a second when the auditory cue was given. During the even-numbered trials, subjects were asked to rotate the balls as fast as possible. A skill improvement ratio (see Materials and methods) was calculated on the basis of their performance during the second and sixth trials.

All subjects were trained to avoid the movement of muscles that were not required for the task. A video recording was made of the entire study for subsequent analysis of each subject's performance. From these recordings, the mean speed (revolutions per minute: r.p.m.) of ball rotation was calculated for each trial. For further analysis, we calculated a skill improvement ratio for each hand task for each subject as follows:

$$SIR = (T6 - T2)/T2$$

where T6 and T2 indicate the mean speed of the ball rotation during the sixth and second trial, respectively. Electromyograms (EMG) of the extensor digitorum and flexor carpi ulnaris muscles were also recorded with surface electrodes during the PET measurements. Because we used surface electrodes, the possibility of coactivation of the other extremity, especially of the deeper muscles, cannot be ruled out. Eye movements were not monitored in the present study.

PET data analysis

In the present study, the standard anatomical structures of the computerized brain atlas of Roland *et al*. (1994) were fitted interactively into each subject's MRI using both linear and non-linear parameters. These parameters were subsequently used to transform each subject's PET and MRI images into the standard atlas form. Anatomically standardized PET images were smoothed with a three-dimensional Gaussian filter of 4 mm width, then globally normalized to whole brain tissue counts of 100 counts/voxel. Subtraction pictures of the control task from each hand task were then made, as well as of tasks from one another, on a voxel by voxel basis, for each subject. In order to eliminate the possible effects of habituation (Grafton *et al*., 1992), counterbalancing of the order of the control task across subjects was performed for this calculation, i.e. the control images obtained at the beginning of the study were used for four subjects, and those obtained at the end of the study for the other four subjects**.** Finally, mean and variance pictures as well as descriptive Student's *t*-pictures were calculated. In the present study, voxels with *t*-values over 5.41 ($P < 0.001$; after Bonferroni correction for multiple comparisons with a control) were considered to represent regions with a significant change in rCBF. Then, each activation was superimposed onto the average reformatted MRI of the same eight subjects participating in the study. Precise anatomical localization of activation in each subtraction condition was made in relation to the mean reformatted MRI. In addition, correlation coefficients between skill improvement ratios and rCBF during each task at points of maximal difference in significant activations were calculated.

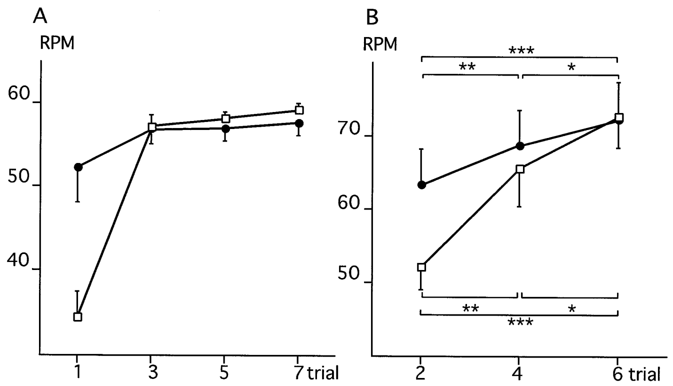

FIG. 2. Mean speeds of ball rotation. Odd-numbered and even-numbered trials are shown in (A) and (B), respectively. Speed is indicated in revolutions per minute (r.p.m.). Filled circles and open squares represent mean speeds during the right and left hand movements, respectively. Bars indicate standard errors of the mean. *: $P < 0.05$, **: $P < 0.01$, ***: $P < 0.001$ (paired *t*-test).

Results

Task performance

Data for the mean speeds of ball rotation during each trial are summarized in Fig. 2. In the auditory-cued movement trials (Fig. 1A), the subjects were able to synchronize their hand movements with auditory signals after the third trial. In the first and second trials, the mean speeds of ball rotation were significantly faster for the left than for the right hand task ($P < 0.005$ and $P < 0.01$, respectively, paired *t*-test). During the PET measurements (seventh trials), the differences in the speed of ball rotation calculated for the right and left hand tasks were not significant. In the trials in which the subjects were asked to rotate the balls as fast as possible (Fig. 2B), the mean speed of ball rotation showed a statistically significant increase with each trial (see Fig. 2B). The mean (SEM) skill improvement ratios for the right and left hand tasks were 40.3 (5.7) and 15.6 (3.5), respectively, showing a statistically significant difference ($P < 0.005$, paired *t*-test).

We did not observe any phasic EMG activity, in the hand contralateral to the moving hand, in relation to hand movements.

PET activation

Table 1 summarizes the data for Talairach coordinates (Talairach & Tournoux, 1988) and *t*-values of peak activation for significant activations during each hand movement task minus the control image.

Complex right hand (Fig. 3) and left hand (Fig. 4) movements were associated with increases in rCBF bilaterally in the sensori-motor areas and cerebellum when compared with the control. Several activation foci were identified within these sensori-motor activation clusters. During movements of the right hand, the left sensori-motor cluster consisted of activation foci in the anterior bank of the central sulcus, the posterior bank of the precentral sulcus, the anterior bank of the postcentral sulcus and the intraparietal sulcus (Fig. 3). During movements of the left hand, the same activation foci, located in the anterior bank of the central sulcus, the posterior bank of the precentral sulcus and the anterior bank of the postcentral sulcus were identified in the activation cluster (Fig. 4). In the right hemisphere, the left hand movements activated a field consisting of activation foci in the anterior bank of the central sulcus, in the posterior bank of the precentral sulcus and in the anterior bank of the postcentral sulcus (Fig. 4). During the right hand movements, activation foci located in the same anterior bank of the central sulcus and in the posterior bank of the precentral sulcus were identified in an activation cluster (Fig. 3).

Primary motor area

A significant increase in rCBF was observed bilaterally in the anterior bank of the central sulcus, i.e. in the primary motor area (Kawashima *et al*., 1994), during unilateral movements of each hand when compared with the control. Larger increases in rCBF were observed in the contralateral hemisphere than in the ipsilateral hemisphere ($P < 0.001$) for tasks with either hand. During movements of the right hand, increases in rCBF in the left primary motor area were also significant when compared with those during movements of the left hand ($P < 0.001$). The same was the case the other way round during movements of the left hand ($P < 0.001$).

Premotor area

Each hand movement activated the cortex lining surrounding the precentral sulci of both hemispheres when compared with control (Figs 3 and 4). These cortices are located in the dorsal premotor area (Kawashima *et al*., 1994). All activation foci were located in the posterior bank of the precentral sulcus. With movement of either hand, increases in rCBF in the contralateral premotor area were significantly higher than in the ipsilateral premotor area ($P < 0.001$), during movements of the right hand, increases in rCBF in the left premotor area were significant when compared with that during movements of the left hand ($P < 0.001$), and also during movements of the left hand, the rCBF increase in the right premotor area was significant when compared with that during movements of the right hand ($P < 0.001$).

During movements of the right hand, a field in the ventral part of the precentral gyrus in the premotor area of the right hemisphere was activated (Table 1). During movements of the left hand, no significant activation was observed in the ventral premotor area.

Supplementary motor area (SMA)

During movements of the right hand, activation was found only in the contralateral (left) SMA (Fig. 3). Since these activation foci were located caudal to a perpendicular line crossing the anterior commissure, we refer to this area as the SMA proper (Picard & Strick, 1996), no increase in rCBF was observed in the right SMA proper. The movements of the left hand also significantly activated the contralateral (right) SMA proper (Fig. 4), in this case, the left SMA proper also showed an increase in rCBF, but this did not attain statistical significance.

Somatosensory area

With each hand movement, an increase in rCBF was observed bilaterally in the postcentral gyrus. Activation foci were located in the anterior lip of the postcentral sulcus of each hemisphere. In the left hemisphere, the same field was activated during movement of either hand. A larger increase in rCBF was observed in the left hemisphere during movements of the right hand than during movements of the left hand ($P < 0.001$). In the right hemisphere, areas of activation during right and left hand movements overlapped (Figs 3 and 4), however, activation foci were identified in different locations (Table 1).

Cerebellum

During movements of the right hand, both the anterior lobule and cerebellar vermis were bilaterally activated (Fig. 3), these areas in the right hemisphere were also significantly activated compared with that during movements of the left hand ($P < 0.001$). During movements of the left hand, the same areas were activated (Fig. 4)

TABLE 1. Significant activations in unilateral complex movements

Structure	Stereotaxic coordinates (X, Y, Z)	Right-hand			Left-hand		
		t	%	vol	*t*	%	vol
Left hemisphere							
Primary motor*	40, –26, 54	16.3	38.6	2078 [a]	9.6	9.2	519 [b]
Premotor (dorsal)*	34, –18, 62	12.5	39.4	2078 [a]	7.6	13.9	519 [b]
SMA	4, –12, 54	10.7	37.0	170	—		
Postcentral*	52, –24, 42	22.5	19.2	2078 [a]	11.9	8.2	88
Intraparietal*	30, –34, 48	19.1	34.1	2078 [a]	—		
Talamus	20, –16, 3	10.4	10.5	30	9.8	9.2	36
Cerebellum**	14, –52, –18	9.0	12.0	146	23.3	25.0	519
Cerebellum	24, –50, –24	9.0	11.0	36	7.7	19.8	37
Right hemisphere							
Primary motor**	–32, –28, 56	6.7	9.2	252 [c]	20.6	30.4	1263 [d]
Premotor (dorsal)**	–30, –23, 60	6.2	7.3	252 [c]	11.1	26.6	1263 [d]
Premotor (ventral)	–52, 0, 36	7.3	7.0	30	—		
SMA**	–4, –14, 56	—			11.9	10.8	178
Postcentral**	–31, –29, 52	—			18.3	28.2	1263 [d]
Postcentral	–52, –28, 42	10.5	9.1	252 [c]	—		
Postcentral	–44, –32, 30	9.1	10.5	37	—		
Intraparietal	–42, –36, 46	—			14.5	16.7	1263 [d]
Cerebellum*	–10, –52, –20	13.1	12.4	777 [e]	—		
Cerebellum*	–28, –46, –24	19.4	17.5	777 [e]	7.6	9.2	35

Talairach coordinates, (X, Y, Z) are in millimetres corresponding to the atlas of Talairach & Tournoux (1988). Volume of activation is in mm^3. Precise anatomical localization was made of these identified structures by superimposition of the activations onto the mean anatomically standardized MRI. Regions where there was also a significant difference in right hand movements minus left hand movements and vice versa are indicated by * and **, respectively. a–e: Several activation foci were identified within activation clusters (see Results).
SMA: supplementary motor area, vol: volume.

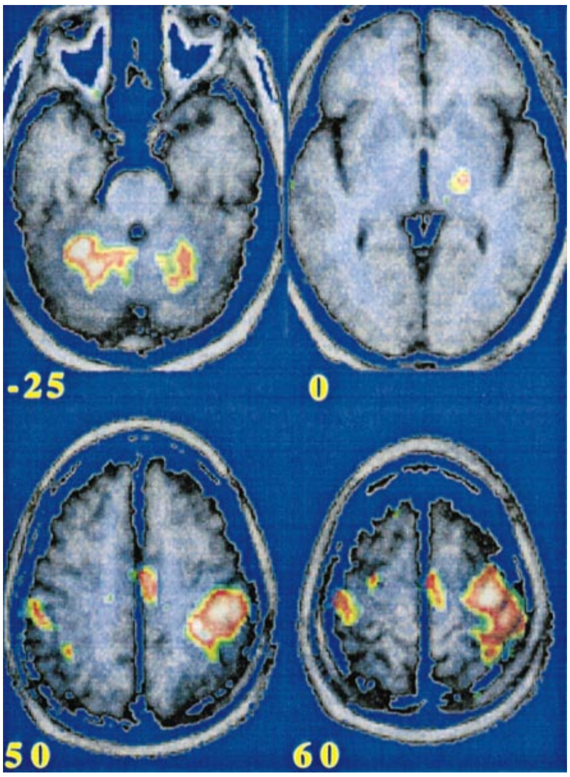

FIG. 3. PET/MRI superimposition. PET data for *t*-values during right finger movements displayed on a colour scale (white > 10, red > 5.41, yellow > 4.79, green > 3.50) superimposed onto the averaged transformed MRI data (grey scale). Images are horizontal sections positioned from –25, 0, 50 and 60 mm above the bicommissural (CA-CP) plane (Talairach & Tournoux, 1988).

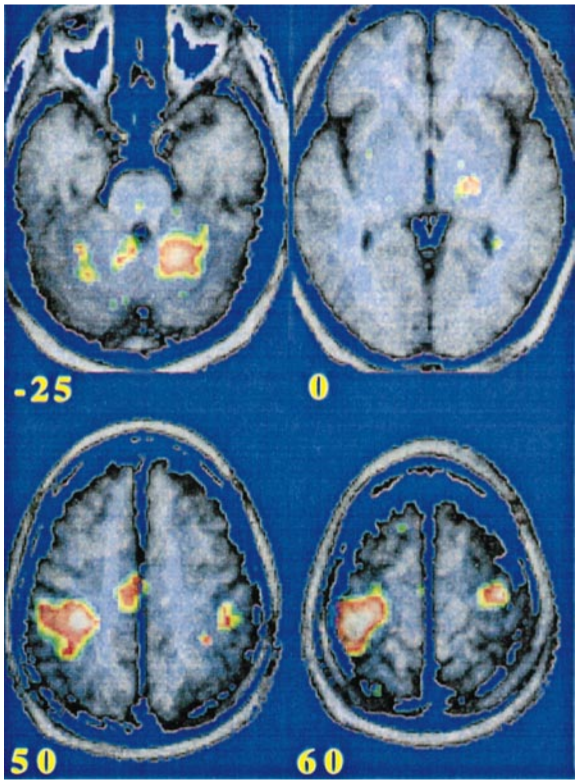

FIG. 4. PET/MRI superimposition. PET data for *t*-values during left finger movements displayed on the same colour scale as for Fig. 3. Images are horizontal sections positioned from –25, 0, 50 and 60 mm above the bicommissural (CA-CP) plane.

in the right hemisphere, however, activation focus was only identified in the anterior lobule. The left cerebellar vermis activation was also significant when compared with the movements of the right hand ($P < 0.001$).

Other regions

In the present study, the contralateral intraparietal cortex and left thalamus were also activated during movement of either hand (Table 1).

Correlation analysis

Statistically significant correlations between skill improvement ratios and the rCBF were observed for the ipsilateral premotor area for movement of either hand, i.e. subjects demonstrating a higher skill improvement ratio showed a higher rCBF in the premotor area of the ipsilateral side. For the left PMA, the correlation between the skill improvement ratio for the left hand and the rCBF during movements of the left or right hand was significant ($r = 0.908$, $P < 0.01$ for the left hand, and $r = 0.718$, $P < 0.05$ for the right hand) (Fig. 5). For the right PMA, the correlation between the skill improvement ratio of the right hand and the rCBF during movements of the right hand was statistically significant ($r = 0.980$, $P < 0.001$) (Fig. 6). The skill improvement ratio for the left hand and the rCBF during movements of the right hand showed positive correlations without statistical significance ($r = 0.483$). Other points of maximal difference in activation did not show any significant correlation.

Discussion

Task performance

In the present study, the mean speed of ball rotation was found to be significantly faster in the left than in the right hand tasks during the first two trials. Because the right hand task was always followed by the left hand task, this difference was probably due to a transfer of motor skills from the right hand to the left (Hicks, 1974). After the third trial, however, no significant differences in the speed of ball rotation were observed.

After the third trial, no significant differences in performance were observed during the auditory cued movements, and the mean speeds of ball rotation during the sixth trial were significantly faster than the speed required to perform auditory cued movements, i.e. 60 r.p.m., suggesting that the learning effect was minimal during the PET scan. However, since mean speeds increased with each trial during which the subjects were asked to rotate the balls as fast as possible, it is difficult to conclude that the subjects had reached an overtrained condition. In the present study, although PET scans were taken after sufficient training and no EMG activity was observed in the muscles of the hand contralateral to the moving hand, the possibility of suppression of movement for the non-moving hand cannot be ruled out.

Functional asymmetry

In the present study, the two-ball-rotation task with either hand activated the primary motor and premotor areas, as well as the cerebellum bilaterally. The magnitude and spatial extent of these activations were more prominent in the contralateral cortical motor areas and ipsilateral cerebellum, and since no significant interhemispheric differences in rCBF change related to contralateral and ipsilateral movements were observed, the existence of functional asymmetry could not be established. Previous human brain imaging studies have, however, indicated functional asymmetry in the activation of the cortical motor areas during unilateral sequential thumb-to-finger movements in right-handed subjects (Kawashima *et al*., 1993; Kim *et al*., 1993) and left-handed subjects (Kawashima *et al*., 1997). The results indicated that the primary motor and premotor areas are involved in the control of ipsilateral movements only when right-handed or left-handed subjects move their non-dominant hand. The difference between asymmetrical activity and symmetrical activity evident in our data, is presumably related to differences in the complexity of the movements. Since the classification of movements as ‘simple’ and ‘complex’ is not absolute, and is sometimes misleading, we think it is necessary to clarify what is meant by the terms simple and complex movements in the present paper, at this point. We categorized movements as ‘simple’ and ‘complex’ as follows: if both elements and sequences of movement had the most basic organization, the movement was considered ‘simple’; and if either elements or sequences were relatively complex, the movement was considered ‘complex’. Therefore, finger movements in the two-ball-rotation task in this study were ‘complex’, because cooperative

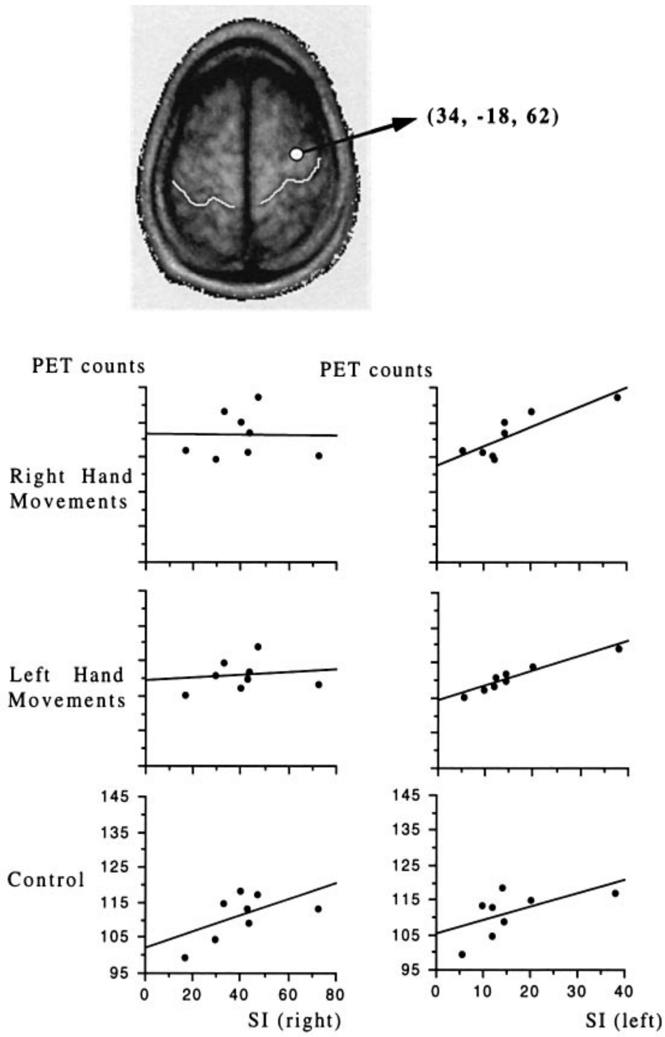

FIG. 5. Regional cerebral blood flow at points of maximal difference in activation of the left premotor area during right hand (top), left hand (middle) and control (bottom) tasks. The location of the focus is indicated at the top left and by x, y and z coordinates (Talairach & Tournoux, 1988). SI is the skill improvement ratio (see Materials and methods). The correlation between the skill improvement ratio and the rCBF during left hand movements is statistically significant ($r = 0.908$, $P < 0.01$).

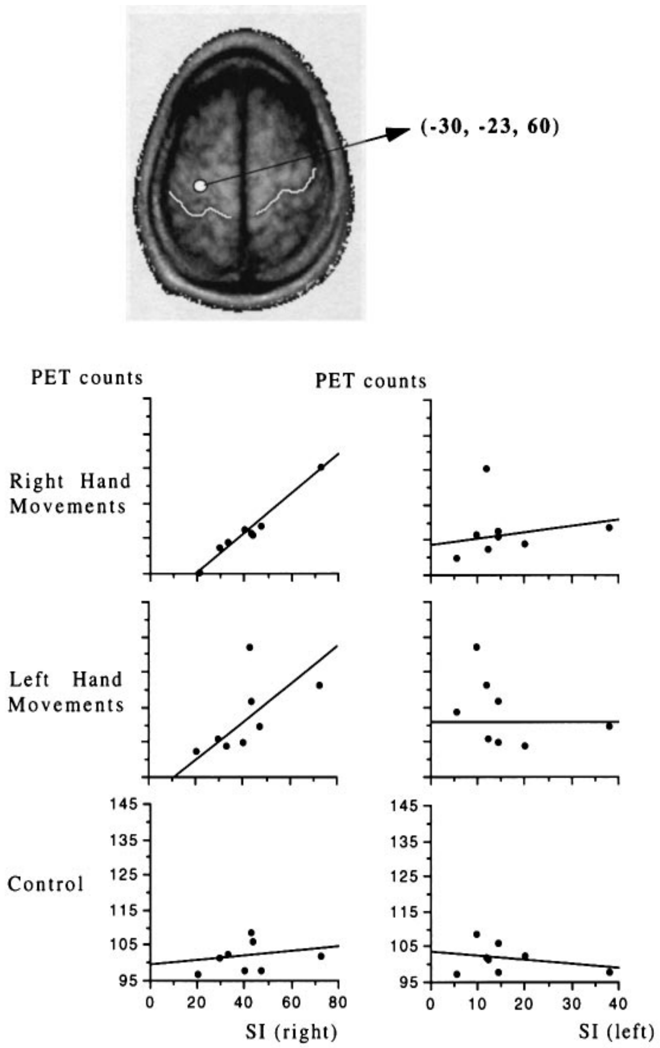

FIG. 6. Regional cerebral blood flow at points of maximal difference in activation of the right premotor area during right hand (top), left hand (middle) and control (bottom) tasks. Other details are the same as for Fig. 5. The correlation between the skill improvement ratio for the right hand task and the rCBF during right hand movements is statistically significant ($r = 0.980$, $P < 0.001$).

movements of the hand muscles were required indicating that the movement element was complex, and sequential thumb-to-finger movements were 'simple' because both elements and sequences of movement were relatively basic. Hence, we conclude that human cortical motor areas are symmetrically organized during complex finger movements but not during simple finger movements. Another possible explanation for this discrepancy may be the right-to-left transfer of motor skills, however, since PET scans were taken after sufficient training, the right-to-left transfer effect at the time of the PET measurements in our study is considered minimal.

In the present study, thalamus activity demonstrated functional asymmetry. Our results are in line with the results of previous PET studies (Seitz & Roland, 1992; Sadato *et al*., 1996) indicating that the left hemisphere of the thalamus is involved in complex motor control. Functional asymmetry of the thalamus has also been suggested by lesion studies in humans (Parkin *et al*., 1994; Kumral *et al*., 1995). For example, Parkin *et al*. (1994) demonstrated that patients with left thalamic lesions had impaired memory for the temporal information necessary for complex sequential finger movements.

Premotor area

In the present study, the cortex surrounding the precentral sulcus, located in the premotor area which directly relates to motor output (Kawashima *et al*., 1994), was bilaterally activated during movement of either hand. In monkeys, the premotor area has been divided into at least two functionally and anatomically distinct parts, i.e. the dorsal premotor area and ventral premotor area (Dum & Strick, 1991). These premotor regions may be equivalent to the dorsal premotor area, since they are located in the dorsal part of the brain. Consistent results have been obtained in previous rCBF studies on right-handed subjects, indicating that the dorsal premotor area is activated bilaterally during complex unilateral hand movements, and that contralateral increases in rCBF are larger than ipsilateral increases (Roland *et al*., 1980; Colebatch *et al*., 1991; Deiber *et al*., 1991; Seitz *et al*., 1991; Jenkins *et al*., 1994; Sadato *et al*. 1996), similar results were obtained in neurophysiological studies of monkeys (Rizzolatti *et al*., 1987; Tanji *et al*., 1988). Furthermore, Sadato *et al*. (1996) found that the right but not the left premotor activity progressively increased with increasing complexity of the movement sequence. Although their observations were limited to dominant (right) hand movements in right handed subjects, they suggested the existence of different roles for the right and left premotor areas in motor control, and that one of the functions of the right premotor area was to store motor sequences in a working memory buffer, the results of previous physiological studies in monkeys, indicating that many neurons are active in the dorsal premotor area bilaterally during complex motor performances, whereas contralateral premotor activity is more marked during simple limb movements (Rizzolatti *et al*., 1987; Tanji *et al*., 1988), may support their idea. In the present case, it was noted that the higher the skill improvement ratio, the higher the rCBF in the ipsilateral premotor area during unilateral complex finger movements, furthermore, while the contralateral premotor activity also showed an increase, a correlation with the subject's skill improvement ratio was less significant. Thus, it seems reasonable to conclude that the ipsilateral dorsal premotor area plays a more significant role in motor skill learning.

SMA

It is of interest to note that SMA activation was found only in the SMA proper, although results of recent PET studies indicate that the SMA proper is activated during simple motor tasks requiring the most basic spatial or temporal organization of movement, and that the pre-SMA is activated during complex tasks which are characterized by additional motor or cognitive demands (see Picard & Strick, 1996 for review). One possible explanation for the activation of the SMA proper in our study is a difference in the level of skill acquisition. The results of recent PET studies on motor sequence learning indicate that the level of activity of the SMA proper increases when learned movements become automatic (Jenkins *et al*., 1994) or improved (Grafton *et al*., 1992, 1995). Another possible explanation is sequence generation. The motor tasks used in the previous PET studies which showed pre-SMA activation (e.g. Roland *et al*., 1980; Seitz *et al*., 1991; Shibasaki *et al*., 1993; Jenkins *et al*., 1994; Grafton *et al*., 1995; Sadato *et al*., 1996) had complex sequences which may require cognitive demands for sequence programming, but relatively simple elements of movement. However, the two-ball-rotation task in the present study required a relatively simple sequence but complex motor elements of movement, and the cognitive demands were minimum.

In the present study, we found activation only in the contralateral SMA to the moving hand. However, the results of some previous PET studies indicate that bilateral SMA activation occurs during unilateral hand movements (Colebatch *et al*., 1991; Deiber *et al*., 1991; Grafton *et al*., 1993; Jenkins *et al*., 1994). In these studies, SMA activation foci were clustered near the midline. On the other hand, the results of some PET studies indicate that SMA activation was found mainly in the contralateral hemisphere during unilateral simple movement tasks of either hand (Kawashima *et al*., 1993, 1997; Matelli *et al*., 1993). We think this discrepancy could also be due to differences in the characteristics of the movements. The complexity of the elements of the movements differ between the two-ball-rotation task used in the present study and the unilateral simple movement tasks used in previous studies, however, the features consistent between these are the relatively simple sequences of movement and the absence of significant cognitive demands. As is often the case, it is difficult to discuss the laterality of the SMA activation because of limited spatial resolution of the PET camera, use of wide filters to smooth PET images and/or insufficient accuracy of the spatial averaging techniques used across the subjects.

Acknowledgements

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Abbreviations

EMG	electromyograms
MRI	magnetic resonance imaging
PET	positron emission tomography
rCBF	regional cerebral blood flow
r.p.m.	revolutions per minutes
SMA	supplementary motor area

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