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Cortical areas and the selection of movement: a study with positron emission tomography

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Summary. Regional cerebral blood flow was measured in normal subjects with positron emission tomography (PET) while they performed five different motor tasks. In all tasks they had to moved a joystick on hearing a tone. In the control task they always pushed it forwards (fixed condition), and in four other experimental tasks the subjects had to select between four possible directions of movement. These four tasks differed in the basis for movement selection. A comparison was made between the regional blood flow for the four tasks involving movement selection and the fixed condition in which no selection was required. When selection of a movement was made, significant increases in regional cerebral blood flow were found in the premotor cortex, supplementary motor cortex, and superior parietal association cortex. A comparison was also made between the blood flow maps generated when subjects performed tasks based on internal or external cues. In the tasks with internal cues the subjects could prepare their movement before the trigger stimulus, whereas in the tasks with external cues they could not. There was greater activation in the supplementary motor cortex for the tasks with internal cues. Finally a comparison was made between each of the selection conditions and the fixed condition; the greatest and most widespread changes in regional activity were generated by the task on which the subjects themselves made a random selection between the four movements.

Key words: PET – Blood flow – Movement – Premotor areas – Parietal cortex – Human

Introduction

PET measurements of regional cerebral blood flow (rCBF) have proved a powerful tool for mapping task-induced alterations in neuronal activity in the human brain (Raichle 1987). Focal increases in rCBF have been demonstrated when subjects perform simple motor tasks, and these changes have provided new insights into the functional organization of voluntary movement in man (Roland 1980a, b, 1982; Fox et al. 1985). In a recent study we sought to identify cortical regions associated with the execution of movement by asking our subjects to perform simple movements of the fingers, hand or arm (Colebatch et al. 1990). We found significant increases in rCBF in the contralateral motor cortex irrespective of whether the movements were distal or proximal, and irrespective of whether fine finger movements or whole hand movements were required. We also confirmed that there were increases in rCBF in both premotor cortex and the supplementary motor cortex (SMA) when simple repetitive movements were performed.

In the present study we address the question of the selection of movements. The executive mechanisms must receive instructions from higher areas if they are to execute the movement that is appropriate to the context. Therefore we now describe an experiment in which subjects were asked to select between different movements. Changes in cortical activity associated with selection were monitored by measuring significant increases in rCBF. A comparison was made between tasks on which selection was required and a task in which the subjects made a single movement repetitively.

A similar comparison was made by Roland et al. (1980a) using the ^{133}xenon method to provide a two-dimensional image of the brain. They compared the activation for two tasks, a learned finger sequence and a task in which the subjects repetitively squeezed a spring. In the sequence task the subject had to select between alternative movements, whereas in the second task the movement was always the same. However, as Fox et al. (1985) pointed out, these two tasks were not matched for the rate of movement. Moreover the movements executed were quite different for the two tasks.

In the present study, we matched the rate at which the tasks were performed by requiring that each movement was made when a tone sounded. Furthermore in all the

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conditions the subject had to make similar movements on a joystick.

Four tasks were used in which the subject was required to make a selection between movements on each trial. The tasks differed in the nature of the instructions that told the subject what to do. These four tasks were as follows: 1) the subjects performed according to a previously learned sequence 2) the subjects chose a movement direction at random; 3) the correct movement was specified by which of four tones was presented; 4) the correct movement was the opposite of that specified by each of the tones on the previous task.

In the first two tasks there were no external cues on which the subjects could rely when deciding which movement to make on each trial, and the tasks therefore demanded that the subjects rely on "internal" cues. In the other two tasks the correct movement was specified by external cues. There were two reasons for making this comparison. First, the Bereitschaftspotential can be recorded over the vertex when subjects prepare to make internally generated movements (Deecke 1987). Second, research both on monkeys and on patients has led to the suggestion that the supplementary motor cortex plays an important role in internally generated movements and the premotor cortex in externally cued movements (Goldberg 1985; Passingham 1987).

Methods

Subjects

Eight right handed normal male volunteers aged 21–38 participated in the experiment. The subjects were right handed as measured on the Oldfield (1971) inventory. Informed consent was given by all the subjects, and the procedure was approved by the Research Ethics Committee of the Royal Postgraduate Medical School, Hammersmith Hospital and the Administration of Radioactive Substances Advisory Committee of the DHSS (UK).

PET measurements

The scans were performed using an ECAT 931–08/12 PET scanner (CTI Inc, Knoxville). A head holder was made with thermally molded foam for each subject and the left radial artery was cannulated. Emission PET scans were corrected for the effects of tissue attenuation by corresponding transmission scans obtained with an external 68Ge/68Ga ring source (Spinks et al. 1988). The scanner allowed the simultaneous collection of 15 contiguous planes of data from the brain, resulting in a total axial field of view of 10.5 cm. The spatial resolution after scan reconstruction and filtering (Hanning filter 0.5°/pixel) was $8.5 \times 8.5 \times 7.00$ mm at full width half maximum (FWHM). The set of scans was collected so that the lowest transaxial slice was 20 mm above the orbito-meatal line.

Regional cerebral blood flow was calculated using a dynamic/integral method (Lammertsma et al. 1990). A dynamic sequence of scans was collected during and following the administration of $H_2^{15}O$ by the inhalation of $C^{15}O_2$ for 2 min. The arterial radioactivity was measured every second with an on-line beta probe. The dynamic series of scans was used to correct blood activity for delay and dispersion of the tracer in the radial artery, cannula and external tubing, thus giving a true reflection of tracer delivery to the cerebral tissues. The integral of the tissue radioactivity emitted by the cerebral tissue over the 2 min of inhalation was used with the corrected arterial input function, to calculate rCBF on a pixel by pixel basis. Radioactivity distribution images were thus transformed into quantitative parametric images of cerebral blood flow.

Tasks

Six rCBF measurements were made on each subject at 10–15 min intervals. During scanning the subjects were required to move a joystick with the right hand. There were 4 possible directions: left (L), right (R), forwards (F), backwards (B). The rate of movement was paced by tones presented by a micro-computer every 2 s through an external loudspeaker. There were 4 tones which differed in pitch and quality, and one of them was played before each movement. The order of the tones was randomized by the micro-computer. The subjects performed the tasks with their eyes closed.

Of the 6 scans the first and sixth were constrained in that movement was only permitted in one direction. For scans 2–5 the subjects were required to select one of four movements every two seconds. The conditions differed in the basis on which the subject selected the next movement. In all cases the instructions were learned prior to performance. The tasks in order of scanning were:

1. Fixed: the subjects moved the joystick forwards every two seconds on presentation of a tone.
2. Learned sequence: the subjects performed a sequence of 8 movements of the joystick (F,L,L,R,B,R,B,F). Each movement of the sequence was performed on presentation of a tone; the identity of the tone was not relevant. When the subject had completed the sequence of 8 movements he started at the beginning again. Subjects were trained before the scanning session until they reached the criterion of 80% success; this was usually achieved in 10 sequences.
3. Random: the subjects were asked to move the joystick in any desired direction on presentation of a tone. The only requirement was that there should not be very long sequences of movements in the same direction.
4. Conditional: the subjects moved the joystick in the direction specified by the identity of the tone presented every two seconds. The meaning of each tone was taught to the subjects just prior to the fourth scanning session by moving the subject's hand in the correct direction. Training started with 20–40 presentations of the sounds at a slow rate. Then the subjects were taught at the rate of 1 trial per 2 s to a criterion of 80% correct; this was usually achieved in 100 trials.
5. Opposite: the subjects moved the joystick in the direction opposite to that specified by the tone during the previous condition. The subjects were briefly trained just prior to scanning with execution of 13 trials at the rate of 1 trial every 2 s.
6. Fixed: this was a replication of the first condition.

The experiment was designed so that in all conditions the subjects moved the joystick and heard tones which varied from trial to trial. The difference between the conditions lay in the way subjects selected movements. In all conditions the tones acted as a trigger to tell the subjects *when* to move the joystick; but in conditions 3 and 4 the sounds also instructed subjects *which* movement to make.

Reaction times

Reaction times were measured by a micro-computer. These were the times needed to move the joystick following the presentation of a tone until the joystick touched a microswitch (thus these times include the movement time). These data were analyzed by a one way analysis of variance.

Data analysis

The scans were analyzed on a SUN 3/60 computer with software for image analysis (ANALYZE; Biodynamic Research Unit, Mayo Clinic, Minnesota).

Anatomical localization

Scans were spatially standardised by transformation into a standard coordinate space (Talairach and Tournoux 1988) in order to allow precise anatomical localization of the CBF changes and group analysis of the data.

The position of the intercommissural line (AC–PC) was estimated directly from standard landmarks on the PET images (Friston et al. 1989). The scans were reoriented to lie parallel to the estimated AC–PC line, and then rescaled by linear proportion in the three orthogonal directions to produce a normalized set of 26 images with 7 slices below and 18 above the AC–PC plane, corresponding directly to the sections presented in the atlas of Talairach and Tournoux (1988). Each slice was 4 mm deep. The images were then smoothed with a square filter of length 9 pixels square (18.45×18.45 mm) to increase the signal to noise ratio.

Statistical analysis

A statistical analysis was performed to localize foci in the brain at which there was an increase in rCBF. Decreases in flow were not analyzed. Global changes and differences in cerebral blood flow were first removed by a pixel by pixel analysis of covariance with global CBF as the confounding variable (Friston et al. 1990). This was performed across tasks for all subjects, such that group mean blood flow maps were generated, adjusted to the overall mean blood flow for all subjects in all tasks. The pixel values with associated error variances of each adjusted group mean CBF map were used for further analysis.

Comparisons were then made between the different tasks. Every comparison was thresholded at the $P<0.05$ and $P<0.01$ levels. The statistic was corrected for the effective number of pixels analysed. The correction took account of the number of pixels in the cerebral space and the redundancy imposed by smoothness, as well as the number of comparisons performed. This was achieved by setting a threshold such that the expected number of false positives (a false positive is a contiguous number of suprathreshold pixels) was 0.05 or 0.01 for the whole volume of the data analyzed and the number of a priori comparisons made. This threshold depends upon the smoothness of the statistical map which is estimated from the variance of the gradients and is related to the autocorrelation function. This can be thought of as a means of determining and accounting for the effective number of independent measurements in the images.

The following comparisons were made:

1. All the tasks involving selection of movement (Sequence, Random, Conditional, Opposite) were compared with the two conditions in which only one movement was possible (Fixed). Foci with a significant increase in rCBF were identified and their co-ordinates plotted on horizontal, coronal and lateral views of the brain.
2. The tasks with internal cues were compared with the tasks with external cues. Two comparisons were made. The first compared the two Fixed conditions, Sequence and Random with the tasks Conditional and Opposite; the second compared tasks Sequence and Random with Conditional and Opposite. The Fixed conditions are included in the first comparison; on these conditions the subjects can prepare the movement in advance but they do not have to make a selection in advance. Foci with a significant increase in rCBF were plotted as before.
3. Each of the tasks involving selection of movement (Sequence, Random, Conditional, Opposite) was compared separately with the conditions in which no selection was made (Fixed). Foci with a significant increase in rCBF were plotted as before. The size of the rCBF increases was calculated from the ancova-normalized adjusted group mean maps of rCBF at the pixel of maximum significance of rCBF change, with a region size of 18.45×18.45 mm.

Results

Effect of selection

To test the effect of selection of movement, the 4 Selection conditions were pooled and compared to the two Fixed conditions. Figure 1 plots the significant foci of rCBF increase related to selection of movement. The rCBF increased bilaterally in both the frontal and parietal lobes when subjects were required to select movements. The frontal areas included the premotor cortex, SMA and prefrontal cortex (area 46/9) in both hemispheres. In the parietal lobe the rCBF increased in both hemispheres in the superior parietal association cortex on the lateral and medial surfaces.

Internal versus external cues

Two comparisons were made. The first contrasted the Random, Sequence and Fixed conditions with the Conditional and Opposite tasks; the second contrasted the Random and Sequence tasks with the Conditional and Opposite tasks. For both comparisons there was significantly greater activation of the anterior SMA for the tasks with internal as compared to external cues ($P<0.01$). There was also greater activation for the tasks with internal cues in the right parietal area 40 ($P<0.01$) and the left prefrontal area 9/46 ($P<0.05$).

In two cases the two comparisons gave different results. In the first comparison, which included the Fixed condition, there was a significant increase in rCBF in the posterior part of the SMA ($P<0.01$). In the second comparison, which excluded the Fixed condition, it was possible to distinguish a peak in the left premotor area distinct from the activation in the SMA ($P<0.01$).

Figure 2 shows the mean reaction time for the 8 subjects for each condition. A one way analysis of

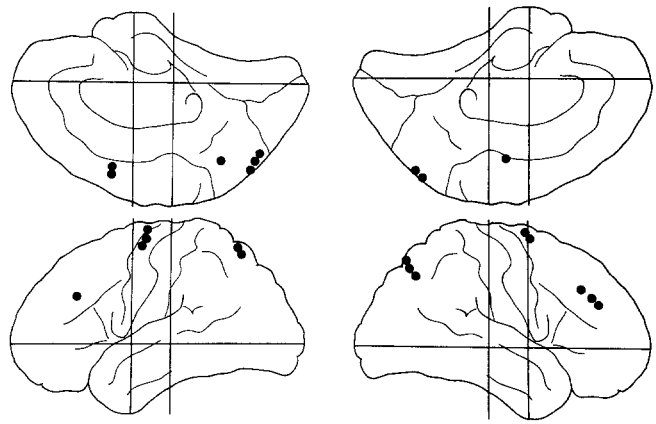

Fig. 1. Location of peaks of maximal significant change in rCBF for the comparison between the 4 selection conditions taken together and the Fixed conditions. The diagram does not give information on the extent of change as only maxima per plane are plotted for each level showing significant change. Outline drawing taken from Talairach and Szikla (1967). Lateral view below, medial above; left hemisphere on left, right hemisphere on right

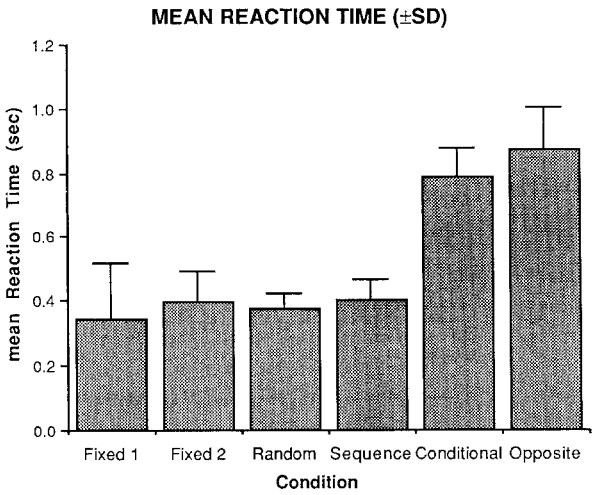

Fig. 2. Mean reaction times with standard deviations for the 4 experimental tasks and the Fixed condition

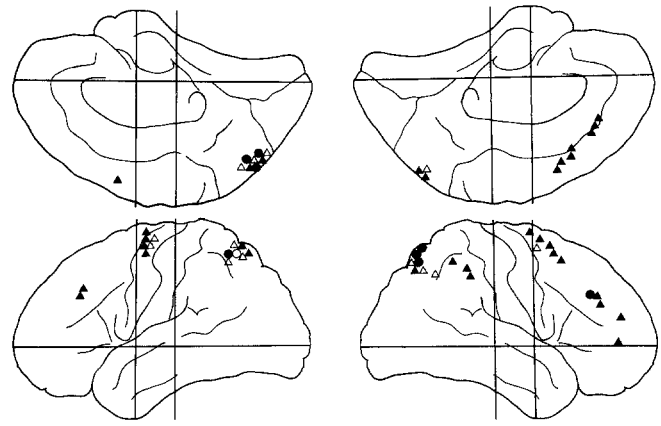

Fig. 3. Location of peaks of maximal significant change in rCBF for comparisons between each of the 4 selection conditions taken separately and the Fixed conditions. The diagram does not give information on the extent of change as only maxima per plane are plotted for each section showing significant change. ▲ = Random, △ = Sequence, ○ = Conditional, ● = Opposite. Lateral view below, medial above; left hemisphere on left, right hemisphere on right

Table 1. Mean normalized rCBF values at pixel coordinates of maximum significance, and percent increases over the fixed condition for each of 4 selection conditions. The coordinates are given in the order x (width), y (anterior-posterior), z (height)

Area	Random	Fixed	%Increase	Coordinates			Sequence	Fixed	%Increase	Coordinates		
				x	y	z						
SMA (6)	51.3[b]	48.5	5.7	2	14	52						
Cingulate sulcus (32)	42.0[a]	39.5	6.3	8	34	32						
Left premotor (6)	48.3[b]	44.7	8.1	−22	− 6	56	47.7[a]	44.9	6.3	−20	−10	60
Right premotor (6)	48.9[b]	44.8	9.1	20	10	56	49.3[a]	46.5	6.0	22	2	56
Left prefrontal (46/9)	43.3[a]	39.6	9.4	−34	32	28						
Right prefrontal (46/9)	43.3[b]	40.3	7.3	34	36	28						
Right prefrontal (10)	42.0[a]	40.0	5.1	26	50	16						
Left superior parietal	41.1[b]	37.4	9.8	−16	−64	52	42.0[b]	38.3	9.5	−16	−62	52
Right superior parietal	39.7[a]	36.9	7.7	22	−68	44	47.7[a]	44.7	6.7	36	−56	40
Medial superior parietal	48.3[b]	44.0	9.6	− 2	−72	44	49.8[b]	46.0	8.3	−10	−72	40
Right inferior parietal (40)	45.3[a]	41.7	8.6	40	−46	48						

	Conditional	Fixed	%Increase	Coordinates			Opposite	Fixed	%Increase	Coordinates		
				x	y	z						
Right prefrontal (46/9)							39.3[a]	36.4	8.0	38	34	28
Left superior parietal	40.4[a]	37.7	7.3	−28	−56	52	40.9[b]	38.2	7.1	−30	−54	52
Right superior parietal							40.1[b]	36.4	10.0	12	−66	52
Medial superior parietal							50.1[b]	47.1	6.2	− 8	−72	40

[a] = $P < 0.05$, [b] = $P < 0.01$

variance revealed a highly significant effect of task ($F = 101.6$, $P < 0.0001$). The reaction times were significantly shorter for each of the internally cued tasks (Fixed, Random, Sequence) than for either of the externally cued tasks (Conditional and Opposite) (Scheffe, $P < 0.01$).

Comparison of the four selection tasks

The foci of maximum significant increase in rCBF are plotted for each anatomical region and for each condition in Fig. 3. The figure shows the foci of most significant change in distinct anatomical regions for each plane separately.

When compared to the Fixed condition, there were significant increases in rCBF in the frontal and parietal lobes and in both hemispheres. The areas are listed in Table 1 with the stereotaxic locations of the pixel of maximum significant change per region.

Table 1 also gives the flow values. These were obtained from the adjusted group mean flow maps, which were normalized by ancova to the global mean for all

subjects and conditions. The overall mean flow over all subjects and all conditions was 35.5 ml/100 ml/min.

In all the comparisons there was no increase in activity in the executive motor cortex because all conditions involved the execution of movements; hence no significant differences were expected.

Frontal lobe

Premotor cortex. Premotor cortex was bilaterally activated in both the Random and Sequence conditions. This activation occurred between 48 and 64 mm above the AC–PC plane. It extended over more planes for the Random than the Sequence condition. The maximal activation lay further forward in the right than the left hemisphere (by 16 mm for the Random condition, and 12 mm for the Sequence condition) (Fig. 3).

Supplementary motor area. When comparisons were made between each task separately and the Fixed condition, the SMA was found to be activated significantly only in the Random condition. Peaks of activity were found on 3 planes on the right (44–52 mm above the AC–PC line), and for 1 plane on the left (56 mm above AC–PC).

Prefrontal cortex. Foci of activation were found in the vicinity of the border of Brodmann areas 9 and 46; these were bilateral for the Random condition and restricted to the right hemisphere for the Opposite condition (24–32 mm above AC–PC). For the Random condition there were additional foci in the right prefrontal area 10 (0 and 16 mm above AC–PC), and also within the anterior part of the cingulate sulcus in the right hemisphere (24–40 mm above AC–PC).

Parietal lobe

The rCBF increased significantly in the left superior parietal association cortex in all four selection conditions. This activation was more extensive for the Random and Sequence conditions (48 to 56 mm above AC–PC) than for the Conditional and Opposite conditions (52 mm above AC–PC). The right superior parietal cortex and the medial parietal cortex was activated in all conditions except for Conditional. Foci were allocated to the medial surface when they fell within 10 mm of the midsaggital line.

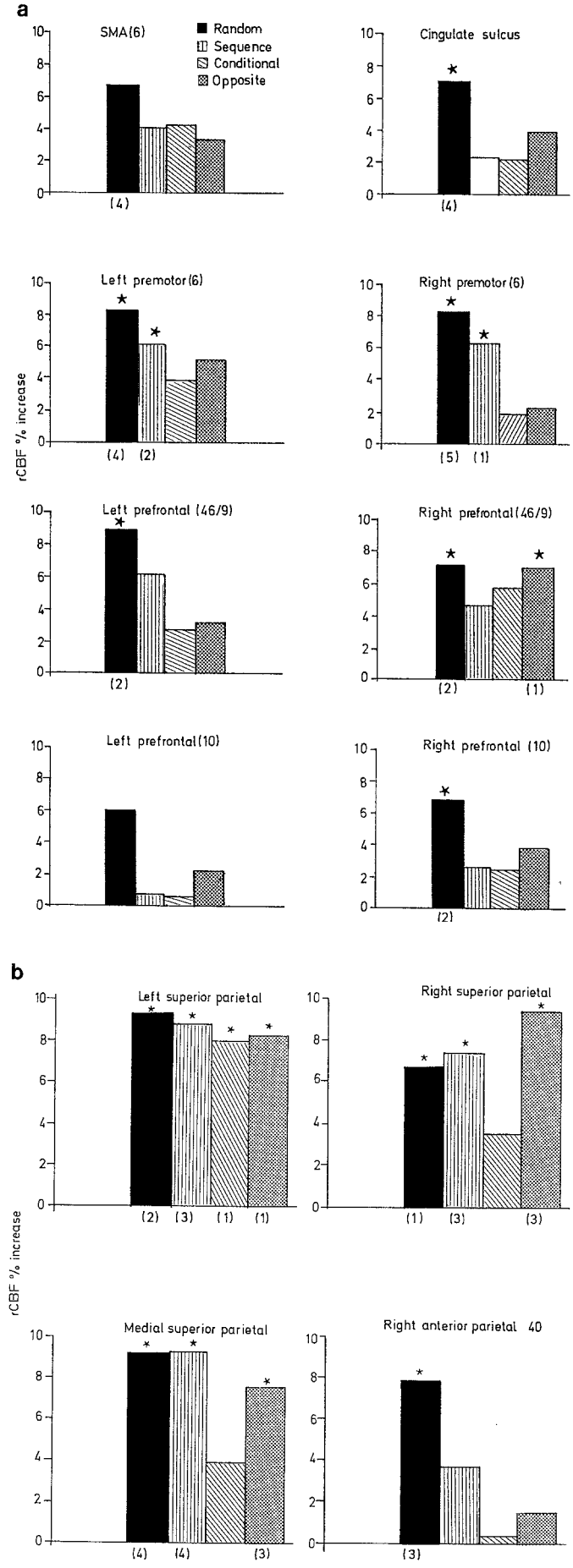

Fig. 4. a Percent rCBF increases in the frontal lobes for the 4 selection conditions taken separately compared to the Fixed condition. Asterisk = foci of statistically significant change in rCBF. Numbers under the abscissa = number of planes in which there is a significant increase. Where there were no planes with a significant increase for a particular condition, the mean rCBF value is taken from the number of planes in which there was a significant increase in other conditions. **b** Percent increases in the parietal lobes for the 4 selection conditions

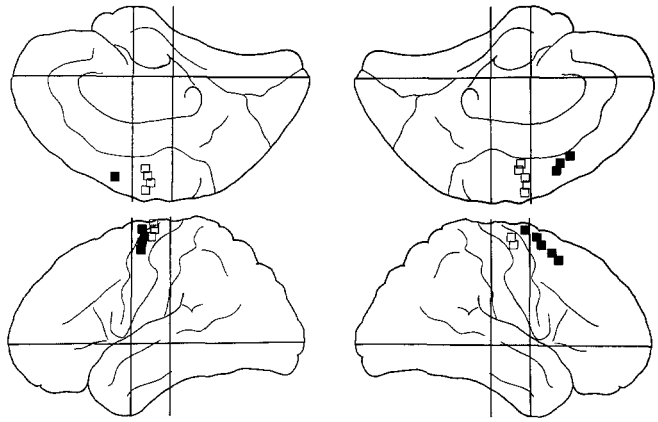

Fig. 5. Location of peaks of maximal significant change of rCBF in premotor cortex and SMA. ■ = peaks for all four conditions taken together in the present study, □ = peaks for all four tasks taken together in study of Colebatch et al. (1990). Some of the points in the premotor cortex lie in the depths of the precentral sulcus; their location is therefore distorted on a lateral view

For the Random condition there was also a significant increase in rCBF in the right inferior parietal association cortex (40–48 mm above AC–PC). This lies in the anterior part labelled 40 by Brodmann (1925) and PF by von Economo and Koskinas (1928).

Figure 4 gives the percentage increases in rCBF for foci of significant change: Fig. 4a presents these for the frontal lobe and Fig. 4b for the parietal lobe. When compared with the Fixed condition the increases in rCBF were of the order of 6–10% whatever the region. The largest increases were seen in the parietal areas. Table 1 gives the mean increases in rCBF over the 8 subjects presented separately for each condition and for every significant region at the pixel of maximum significance.

The location of activity in premotor cortex and the SMA

In a previous experiment, we used the same technique to study the pattern of rCBF increases when subjects performed repetitive movements of the fingers, hand or arm (Colebatch et al. 1990). For these repetitive movements activation was found in both the premotor cortex and the SMA when compared with a resting condition. Fig. 5 shows that the rCBF increases for the selection tasks in the present study were anterior to those related to the simple execution of movements (Colebatch et al. 1990). According to the conventions of Talairach and Tournoux (1988), the anterior-posterior coordinates were as follows: left SMA −8 (motor execution), +10 mm (motor selection); right SMA −4, +17 mm; left premotor −13, +7 mm; right premotor −12, +7 mm. It must be pointed out that in some cases the resolution of the method does not permit a reliable allocation of activity to the SMA in the left or right hemisphere.

Discussion

Little is known of the details of the pathways by which movements are selected and prepared plans are put into action. The executive mechanisms must be directed by higher associative areas that are sensitive to the relevant context. The present experiment uses the PET scanner to measure activity in higher associative areas while human subjects perform movements that are appropriate to the context. The Selection tasks are alike in that on all the subject must choose between alternatives. They differ in whether the movements are guided by an internal or external context.

Selection

Figure 1 compares all the experimental conditions together with the Fixed condition. The figure shows that there were cortical areas in which there was an additional increase in rCBF when the subject had to select between four movements.

It could be argued that these increases in activity occurred because the joystick was moved to the left, right, front and back in the Selection conditions but it was only moved forwards in the Fixed condition. This is unlikely to be the relevant factor as there was no such increase in the sensorimotor cortex when the subjects made the four different movements compared to one.

There were significant increases in rCBF in both the premotor strip, area 6, and in parietal cortex. Furthermore there were significant increases in both the left and the right hemisphere.

Area 6

There is independent evidence that the premotor and supplementary motor cortex play a role in the learned selection of movements. This comes both from lesion experiments and electrophysiological experiments.

After the removal of the premotor area, macaque monkeys are slow to learn or relearn tasks in which they must choose between two movements on the basis of visual cues (Petrides 1982; Passingham 1985). Similarly, after the removal of the SMA, monkeys are very slow to learn a sequence of three movements (Halsband 1987; Passingham 1987). These observations led to the proposal that the premotor areas are concerned with the learned selection of movements (Passingham 1988).

There is electrophysiological evidence that points to the same conclusion. Wise (1989) recorded cells in premotor cortex, and found that over half the cells increased their response as the animals learned which movement to select, given a particular novel pattern. Similarly Mushiake et al. (1990) recorded from the SMA while monkeys performed a learned sequence of three movements. They found that 41% of the cells were more active during a learned sequence than during a control task in which the animal did not have to learn the sequences.

Parietal cortex

There was a significant increase in rCBF in parietal cortex. All loci of significant rCBF increase lay within the superior parietal cortex (Fig. 1).

There is controversy over the cytoarchitecture of the parietal cortex of the human brain. Brodmann (1925) placed both areas 5 and 7 above the intraparietal sulcus. But in a more recent study Eidelberg and Galaburda (1984) agree with von Economo and Koskinas (1928) in giving the label PE to the full extent of the lateral surface of the superior parietal association cortex. In a macaque monkey the area PE on the lateral surface corresponds to Brodmann's area 5.

Area 5 sends a heavy projection to the premotor strip. Medial parietal 5 sends projections to the SMA (Galyon and Strick 1985), and lateral parietal 5 sends them to the dorsal premotor area (Petrides and Pandya 1984). Many cells in area 5 are similar in their pattern of activity to cells in area 6. Seal et al. (1982) describe a subpopulation of cells in area 5 that respond before movement and continue to do so even when the dorsal roots have been cut to deafferent the arm. Crammond and Kalaska (1989) have shown that 83% of these "early" cells fire selectively according to the movement to be made, and continue to do so while the monkey waits before acting. Similar cells are reported by Weinrich et al. (1984) in premotor cortex.

The present experiment suggests that in the human brain also the superior parietal association cortex plays a role in movement. It further points to a contribution to the process by which movements are selected.

Internally generated movement

The supplementary motor area was significantly more active in the tasks requiring the internal generation of movement compared with those that were directed by external cues. However, the data failed to confirm the prediction that the premotor cortex would be more active in the Conditional and Opposite tasks, in which the external cue instructed the subject which movement to make.

The Random and Sequence tasks differ from the Conditional and Opposite tasks in an important respect. Since the subjects were not relying on external cues to indicate which movement to make next, they were able to decide the next movement before the tone triggered the movement. In the Conditional and Opposite tasks, the subjects needed the tone to tell them how to respond. In the one case, the subjects could prepare the next movement while waiting, and in the other case this was not possible. It is also true that in the Fixed condition the subjects knew the correct movement in advance, but during the wait for the next tone there was no selection to make.

The difference between these conditions can be appreciated by considering the reaction times. When subjects could plan the action beforehand the reaction times were quick; this can be seen for the Random and Sequence tasks in Fig. 2. When subjects selected the appropriate movement after hearing the tone, the reaction times were longer; this can be seen for the Conditional and Opposite tasks.

Thus it is possible that the marked activation of the SMA for the Random and Sequence tasks combined reflects activity in the waiting period between trials. In human subjects it is possible to record a Bereitschaftspotential over the vertex when subjects prepare to move (Deecke 1987). In monkeys, many cells in the SMA fire in the second or two before movement, when the animal is deciding when to act (Okano and Tanji 1987; Romo and Schultz 1987); but when the monkey acted in response to a visual signal Okano and Tanji (1987) found only 3 such long lead cells in the SMA. In experiments where monkeys can select their action in advance many cells in the SMA and premotor cortex also fire during the waiting period (Tanji et al. 1980; Weinrich et al. 1984).

Using the word loosely it may be said that set related activity occurs when an animal is "planning" to act. With human subjects, it is possible to examine planning directly by asking them to think about carrying out an action but to refrain from doing so. Roland et al. (1980a) required subjects to carry out a sequence of finger movements, and reported that there was activation in the SMA but not in motor cortex. Fox et al. (1987) asked subjects to imagine opening and closing the hand, and also found activation in the SMA.

In these experiments no movements were executed whereas in the present experiment the effects of execution were removed from the analysis. Our results confirm the role of the SMA in the process by which movements are planned.

Comparison of four tasks

The four Selection tasks were chosen so as to contrast random selection (Random), the retrieval of a movement from a learned sequence (Sequence), retrieval of a learned response to an external cue (Conditional), and the learning of a new response (Opposite). Figures 3 and 4 present the data for the four tasks separately. Fig. 3 shows for each task the peaks for the areas in which there was a significant increase. Fig. 4 gives the values for the percent increase in rCBF.

Parietal cortex

There was a significant increase in rCBF in the left superior parietal cortex for all four tasks (Figs. 3, 4b). However, in the Random condition there was also a significant increase in the anterior part of the inferior parietal cortex. This area was labelled 40 by Brodmann (1925). However, in a more recent study Eidelberg and Galaburda (1984) designate it PF, which in monkeys is equivalent to area 7b.

In the macaque brain there is a full body representation both in area 5 (Pearson and Powell 1985) and in area 7b (Robinson and Burton 1980). Like area 5 area 7b also sends projections to the premotor strip, but they terminate in the ventral part (Petrides and Pandya 1984).

In a study of cells in area 7b in the macaque, Godschalk and Lemon (1989) divided the cells into visual, visuomotor and motor, and subdivide the visuomotor cells into classes Vm and vM according to the strength of the association with visual cues or motor responses. The proportion of motor cells was 33% in parietal 7b and 25.2% in premotor cortex. The proportion of Vm and vM cells were also very similar in the two areas: for Vm cells the values were 30% in parietal cortex and 31.4% in premotor cortex, and for Vm cells the values were 31.0% and 30.7% (Godschalk et al. 1985)

Roland and Seitz (1989) have also reported activity in the superior and medial parietal association cortex when subjects are learning a sequence of finger movements. They also report that there is no longer a significant increase in activity when the task has become overlearned. This may explain the failure of Roland et al. (1982) to find activation of the lateral parietal cortex when subjects performed an overlearned sequence of finger movements.

In an earlier study with ^{133}xenon, Roland et al. (1980b) reported activation of the parietal association cortex when subjects moved their finger, as instructed, in a maze, or when they drew a spiral in the air. Roland et al. (1980b) argued that the crucial distinction between the finger sequence and the maze task is that the movements in the maze were coded spatially. An alternative explanation arises because the subjects had not been overtrained on the maze and spiral tasks, whereas they had been trained for 80 min on the sequence (Roland et al. 1980a, b).

In the present study the subjects moved a joystick in one of four directions, and the task therefore bears a similarity to moving a finger in different directions in a maze. The important factor, however, is that in this study the subjects were only trained for a few minutes. It is implausible that it was because the movements were spatial that parietal cortex was activated, since parietal cortex was also activated in the study of Roland and Seitz (1989) during the early learning of a sequence of finger movements. The results of the present study indicate that the activity is related to the process by which movements are selected.

Premotor cortex

There was a significant increase in both the left and right premotor cortex for the Random and Sequence conditions (Figs. 3, 4a). Roland and Seitz (1989) have also reported that premotor cortex is activated bilaterally when subjects perform a learned sequence of finger movements.

From the experiments on monkeys reviewed earlier (Passingham 1985, 1987; Wise 1989) we expected a significant increase in rCBF in premotor cortex when the subjects performed the Conditional and Opposite tasks. Both are conditional tasks in which the sensory cue specifies the appropriate movement. However, the increase for the Conditional and Opposite tasks was not significant (Fig. 4a).

Figure 5 shows that the area activated in the Random and Sequence conditions lies in anterior premotor cortex. The peaks of significance for the study of Colebatch et al. (1990) tend to lie behind those found in the present study. In the macaque monkey it is possible to detect subdivisions of the premotor cortex on the basis of differences in cytoarchitecture (Matelli et al. 1985; Barbas and Pandya 1987). Pyramidal fibres originate from two sites in the posterior part of the premotor cortex, the spur of the arcuate sulcus and the precentral sulcus (Martino and Strick 1987). It is reasonable to conclude that the anterior foci in premotor cortex may lie in front of the region of the premotor cortex from which there is a pyramidal projection.

Supplementary motor cortex

In the SMA there was a significant increase in rCBF only for the Random condition (Fig. 4a). When compared with the Fixed condition increases in the other three conditions were not significant.

The absence of a significant increase in the Sequence task is puzzling. Roland et al. (1982) and Roland and Seitz (1989) both report a significant increase in rCBF in the SMA when subjects performed a finger sequence. Three hypotheses can be offered. 1) The finger sequence was overlearned whereas the Sequence task in the present study was not. However, Roland and Seitz (1989) report activation of the SMA early in the training of a finger sequence. 2) The Sequence task in the present study involved directional movements whereas the finger sequence required opposition of the fingers. However, the Random task also involves directional movements and yet there is a significant increase for this task in the SMA. 3) The present study was designed to investigate the effects of selection; thus it compared the experimental conditions against a Fixed condition, and not against a Rest condition as in the study by Roland and Seitz (1989).

The location of the area activated in the Random condition was in the anterior part of the SMA (Fig. 5). This is anterior to the area in which there were significant increases when subjects were required to execute finger, hand or shoulder movements (Colebatch et al. 1990). Braak (1976) has described an area in the cingulate sulcus with gigantopyramidal cells, and this lies behind the Vca line (Talairach and Tournoux 1988). In monkeys there are projections through the pyramidal tract from the posterior half, or so, of the SMA, and these are at approximately the same AP level as the pyramidal projections from cingulate cortex (Hutchins et al. 1988). We conclude that the area activated in the Random condition may lie anterior to the area from which pyramidal fibres originate.

Prefrontal cortex

A significant increase in rCBF was found in three subareas of prefrontal cortex. The first is described as area

46/9 because the loci of maximal significant change lie near the borders between these two areas, and it is not possible to make a more precise allocation. In monkeys area 46 is concerned with spatial memory (Goldman-Rakic 1987). It could be argued that in the condition Opposite the capacity to compute an opposite direction of movement puts a premium on spatial memory. However, the same could be said for the Sequence task and yet there was no significant increase in prefrontal rCBF.

A second area was found in the frontal pole, area 10, which showed a significant increase only for the Random condition. The increase was significant in the right hemisphere, and though there was a similar increase in the left hemisphere it failed to reach significance (Fig. 4a).

The third area lies in the cingulate sulcus. Again there was a significant increase only for the Random condition. The maximal change lies in the cingulate sulcus, and we locate it in the lower bank, area 32, though the allocation is tentative given the resolution of our methods. In the study by Colebatch et al. (1990) in which subjects executed finger, hand or shoulder movements and in which comparisons were made with rest, there was significant activity in the cingulate area 24, posterior to the area activated during the Random condition.

Free choice

In the Random condition subjects chose freely which movement to make. Inspection of Fig. 4 shows that in those areas that were activated by other tasks the percent increases in rCBF were greater for the random condition. This is particularly evident for the SMA.

Of the areas activated only during the Random condition one may be of special significance. This is the area along the anterior part of the cingulate sulcus, tentatively identified as area 32.

In patients lesions of the medial wall can produce a disturbance of voluntary movement. Akinesia has been described in patients with surgical removal of medial frontal cortex (Laplane et al. 1977), infarction of the anterior cerebral artery (Damasio and van Hoesen 1983) or a tumour in the SMA (Straub and Siegel 1988). These lesions are not confined to the SMA. The cortical resections and infarctions included the cingulate cortex, and tumours exert pressure effects on other neighbouring cortical areas. In monkeys removal of the SMA disrupts the ability of the animals to perform a simple arbitrary act at their own pace (Passingham et al. 1989). Animals were required to raise their arm to a particular point in space. In the first sessions after surgery, they made few attempts and their attempts were inaccurate. Removal of the cingulate cortex, including area 32, produced the same effect (Stern 1987).

Such self-initiated behaviour can be studied in animals, but animals cannot be asked to carry out acts that are truly voluntary in the sense that various possibilities are considered and an arbitary choice is made. To study the neurology of such behaviour we must resort to human subjects. Our data show that PET provides a means of doing so.

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