Exp Brain Res (1993) 95:172–176

Experimental
Brain Research

Research note

Within-arm somatotopy in human motor areas determined by positron emission tomography imaging of cerebral blood flow

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Received: 15 December 1992 / Accepted: 31 March 1993

Abstract. Within-arm somatotopy was identified in multiple motor areas of six normal human subjects who performed a visuomotor tracking task during positron emission tomography (PET) measurement of relative cerebral blood flow (relCBF). A randomly moving target, presented on a computer monitor, was continuously followed with the index finger (movement at the metacarpophalangeal joint), thumb, fist (movement at the wrist), forearm (movement at the elbow), elbow (movement at the shoulder), and eyes alone (control task) during sequential imaging. Segmental limb movements were associated with relCBF responses in the contralateral motor, supplementary motor, cingulate, and parietal cortex, and in the ipsilateral cerebellum. Localization of responses after stereotaxic transformation into Talairach atlas space, as well as within-subject analysis without anatomic deformations, demonstrated an overlapping somatotopic distribution in the motor cortex, with thumb responses most ventrolateral and shoulder responses most dorsomedial. Proximal limb movements induced relCBF responses of greater magnitude than distal movements. Somatotopy was also identified in the supplementary motor area, with index finger responses dorsal and anterior to shoulder responses. An additional set of somatotopic responses were located in the cingulate cortex, also with finger responses anterior to shoulder responses. Somatotopy was not identified in the anterior cerebellum. The distribution of relCBF responses is concordant with electrophysiologic studies in nonhuman primates that demonstrate a fractured somatotopy on a fine scale and a general somatotopic scheme of the limb on a large scale in multiple discrete motor areas.

Key words: Somatotopy – Motor cortex – Cerebral blood flow – Positron emission tomography – Human

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Introduction

The basic notion of a homuncular representation in the primary motor cortex, with separate areas for arm, leg, face, trunk, and so forth, has stood the test of time and many experimental approaches in a variety of mammalian species including humans (Jackson 1875; Penfield and Boldrey 1938; Sherrington 1906; Woolsey et al. 1952). Evidence suggests that additional motor areas with corticospinal projections are also present in areas such as the mesial agranular frontal cortex or Brodmann area 6. Beginning with the studies of the supplementary motor cortex by Woolsey et al. (1952), it is clear that these additional areas may also be organized in a crude somatotopic representation. Recent studies in nonhuman primates have confirmed the presence of a somatotopic organization in the supplementary motor area (SMA) and also show additional complete homunculi in the cingulate cortex (Dum and Strick 1991; Luppino et al. 1991; Shima et al. 1991). These results in nonhuman primates served as an impetus for us to investigate the somatotopic distribution of neuronal responses of these different cortical motor areas in normal human subjects. Responses were determined with positron emission tomographic (PET) imaging of relative cerebral blood flow (relCBF) as the subjects performed a continuous visuomotor tracking task with different segments of the arm. It was hypothesized that, on the large spatial scale measured with PET, within-limb somatotopy would be preserved in these multiple motor cortical areas.

Materials and methods

Six normal subjects (mean age 24 years) performed a set of six visuomotor tracking tasks with their dominant right arm and hand during PET relCBF imaging, in accordance with the UCLA Human Subjects Protection Committee. A 1-cm target was displayed on a computer monitor in clear view of the subject. The target moved at a fixed rate of 6 cm/s for a random distance and then

Table 1. Location and magnitude of motor somatotopy

Region	Arm segment	Subjects (*n*)	Spatial coordinates for individual analysis						Spatial coordinates for grouped analysis (with stereotaxic transformation)[a]			Magnitude of response (%)	*Z*-score
			X		*Y*		*Z*		*X*	*Y*	*Z*		
			Mean	SD	Mean	SD	Mean	SD					
Motor cortex	Shoulder	4	20	2	−32	4	57	2	22	−24	60	19	5.52
	Elbow	4	24	4	−32	7	55	4	22	−22	60	11	3.45
	Wrist	4	30	4	−27	2	52	5	28	−32	60	13	2.23
	Finger	6	34	8	−25	8	48	3	28	−26	56	11	1.68
	Thumb	2	44		−15		47						
Cingulate motor area	Shoulder	4	5	2	−11	3	40	6	8	−18	44	11	4.57
	Elbow	4	4	2	−8	3	40	8	4	−10	44	7	3.91
	Wrist	4	4	2	−9	5	40	8	14	−10	44	8	2.53
	Finger	6	5	4	1	6	38	5	10	−6	40	7	3.12
	Thumb	2	−2		13		38						
Supplementary motor area	Shoulder	4	3	3	−13	6	50	7					
	Elbow	4	3	2	−9	5	51	6					
	Wrist	4	1	1	−2	8	54	7					
	Finger	6	4	3	−2	6	55	6					
	Thumb	2	2		7		60						
Anterior cerebellum	Shoulder	4	−10	6	−45	7	−11	3	−8	−52	−16	10	2.63
	Elbow	4	−8	7	−47	9	−11	4	−6	−54	−16	13	3.26
	Wrist	4	−9	8	−51	8	−12	5	−8	−56	−16	12	3.01
	Finger	6	−4	13	−50	11	−12	5	−6	−54	−16	11	2.84
	Thumb	2	−15		−48		−15						

X and *Z* coordinates are relative to anterior-posterior commissural line (negative *X* values are right hemisphere) and *Y* coordinates are relative to anterior commissure

[a] Distinct cingulate and supplementary motor area responses could not be identified in the group analysis after stereotaxic transformation

changed to a new random direction. It remained in a 6 × 8 cm window of the monitor and changed direction approximately 200 times per minute. Subjects were instructed to point at the target without actually touching the monitor with the appropriate part of the arm. They were taught to match the direction, speed, and distance of the moving target with a movement of the arm about a specified joint during the acquisition of a relCBF image (Grafton et al. 1991). Each task was performed for 2 min, commensurate with the bolus injection of 50 mCi of radioactive [^{15}O]water. rCBF images were then acquired, as previously described (Grafton et al. 1991). Final image resolution of the Siemens/CTI PET scanner after reconstruction was 1 cm full width at half maximum (FWHM), the contiguous interplane distance was 6.75 mm, and the axial field of view was 10 cm.

During the first scan, four subjects tracked the target by pointing with the index finger alone. The arm and hand were supported on cushions so that only distal limb musculature was required to follow the target. The second and fifth scans were control scans during which the target was tracked only with the eyes. During the third scan, the same four subjects tracked the target by pointing with the first metacarpophalangeal joint, with the hand held lightly in a fist. Movement was at the wrist only. During the fourth scan, the four subjects tracked the target with the distal end of the radius as a "pointer," with the wrist passively flexed; movements were about the elbow alone. During the sixth scan, the four subjects tracked the target by using the elbow as a pointer, with the elbow flexed and the hand placed against the opposite shoulder. Movement in this case was about the shoulder joint. In the remaining two subjects, the first, second, third, and fifth scans were identical to the other four subjects. In the third task the two subjects tracked with the thumb alone. The remaining fourth and sixth tasks in these two subjects were part of a different experiment. In all of the movement conditions the appropriate part of the arm moved freely in the air without touching nearby cushions or the monitor.

Image analysis was performed in two ways. The first was a group analysis in which the scans from all subjects were compiled onto a common stereotaxic map. The methodological details of the stereotaxic transformation of CBF images, adjustment for global CBF, and statistical techniques have all been reported in detail previously (Friston et al. 1990, 1991a,b). In sum, the method yields a statistical parametric map that identifies significant differences between specified conditions. In the current study, each motor task was compared with the two rest conditions to define the local maxima within motor areas. The number of subjects included for each condition in the group analysis are summarized in Table 1. Then, the localization of these maxima were studied to determine whether they followed a consistent homuncular pattern. Final image resolution after stereotaxic transformation was approximately 16 mm FWHM.

Because the grouped method uses spatial smoothing and cortical realignment algorithms that might obscure subtle changes in the location of adjacent responses, a second analysis was also performed on each subject individually, without intersubject averaging. First, any small differences in head position were removed so that all six scans were aligned using an automated digital algorithm (Woods et al. 1993). The accuracy of this coregistration technique is to within 1 pixel element (1.745 mm) in any translational or rotational dimension. Images were simultaneously aligned to the anterior-posterior commissural (AC-PC) line using visually identified landmarks, as previously validated by Friston (Friston et al. 1989). Then, pixel by pixel images of the percentage difference between each movement task and the average of the two controls were

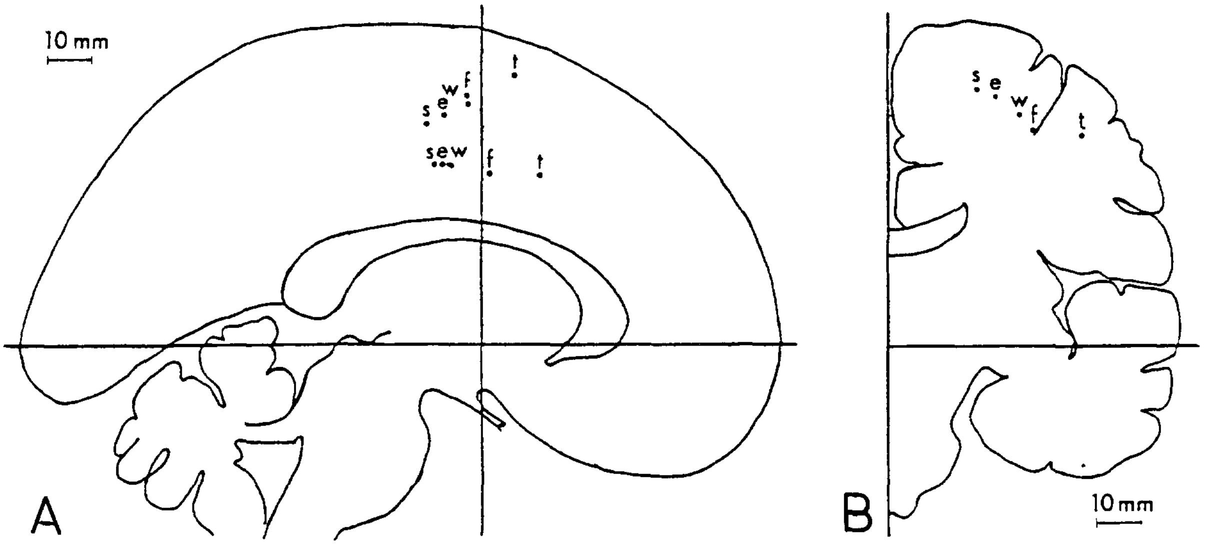

Fig. 1A,B. The location of peak relative cerebral blood flow responses with movement of different segments of the arm during positron emission tomography imaging. The spatial coordinates are the calculated means for each individual, plotted relative to a midline horizontal axis passing through the anterior-posterior commissural line and a midline vertical axis bisecting the anterior commissure (adapted from Talairach and Tournoux 1988). **A** Two discrete homunculi in the mesial frontal cortex. The more dorsal set of responses corresponds to the classic supplementary motor area. The more ventral set of responses is in the cingulate cortex. In both sites distal limb responses are more anterior than proximal responses. **B** A coronal section passing through the primary motor cortex. The section is located 30 mm posterior to the anterior commissure in Talairach coordinates. Characteristic within-limb somatotopy is observed. *s*, shoulder; *e*, elbow; *w*, wrist; *f*, index finger; *t*, thumb

calculated, after accounting for global differences in radioactive counts (Grafton et al. 1991). For each task, the peak relCBF response in the given cortical area was localized relative to the Talairach reference frame (Talairach and Tournoux 1988). In this reference frame, the AC-PC line defines the midline y-axis. A perpendicular line passing through the anterior commissure and midline defines the vertical z-axis. Lateral displacements away from the midline define the x-axis. Significant differences in the location of responses suggesting somatotopy were confirmed statistically using an analysis of variance that compared the coordinates of segmental movements relative to the AC-PC line in the x, y, and z directions.

The reproducibility of the localization method used for each individual subject was also confirmed. A previously reported data set comprised five additional subjects, who performed the visual tracking task with the index finger for three scans and the eye movement control task for three scans (Grafton et al. 1991). This data set was reanalyzed after correcting for any misregistration errors secondary to head movement with the automated registration algorithm. After this correction, the location of a peak relCBF response for each individual varied by less than 3 mm (95% confidence limit) in any direction. The within-subject coefficient of variation for the magnitude of a motor cortex relCBF response was 3%, and across all subjects it was 8%.

Results

After stereotaxic transformation, the grouped statistical maps revealed significant responses in the primary motor cortex, mesial frontal cortex, superior parietal cortex, and ipsilateral anterior cerebellum in association with arm movements ($P < 0.05$ for each site, after Bonferroni correction for multiple comparisons of all brain pixels). The approximate area of the CBF responses for each task overlapped extensively. Despite this overlap, the peaks of the different responses in the motor cortex formed a well-defined homuncular representation, with finger movements most inferolateral and shoulder movements most superior, as summarized in Table 1 and Fig. 1B. Analysis of each individual's peak responses in motor cortex disclosed a similar result. Responses were significantly different in location on the lateral x-axis ($F_{3,14} = 6.27$, $P < 0.01$) and vertical z-axis ($F_{3,14} = 5.70$, $P < 0.01$) relative to the AC-PC line. Movements of the shoulder were associated with a relCBF response covering more cerebral cortex and with a greater relCBF magnitude than the relCBF response associated with more distal movements.

Somatotopy was also present in two sites of the mesial frontal cortex, as shown in Fig. 1A. Responses in the region of the SMA were distributed such that finger responses were dorsal and anterior relative to shoulder responses, located ventrally and posteriorly. Differences in the location of SMA responses along the anterior to posterior y-axis were significant ($F_{3,13} = 3.50$, $P < 0.05$). A separate and distinct set of responses was located inferior to the SMA, in the region of the cingulate sulcus. The ordering of responses was similar to the SMA, with finger movements posterior and shoulder movements anterior. Differences in the location of cingulate responses along the anterior to posterior y-axis were also significant ($F_{3,14} = 6.18$, $P < 0.01$).

The presence of discrete responses in SMA and cingulate areas could not be identified in the grouped analysis. In the grouped analysis, only one large response, an average of these two areas, was observed. The averaging was most likely secondary to spatial smoothing, zooming in the z-axis and the nonlinear stereotaxic transformation used in the grouped method.

Significant relCBF responses were also present in the anterior cerebellum ipsilateral to the moving limb. No somatotopic arrangement could be identified in this area (see Table 1).

Discussion

A rapidly evolving series of electrophysiological experiments in nonhuman primates have led to a reconsideration of how the efferent motor system might be organized both within and outside the primary motor cortex (Asanuma and Rosén 1972; Humphrey 1986; Humphrey et al. 1983; Kwan et al. 1978; Strick 1988; Donoghue et al. 1992). The findings herein are concordant with these experiments and suggest the presence of a within-limb somatotopic distribution of neuronal responses, albeit on a large spatial scale in the human primary motor cortex, SMA, and cingulate cortex. This somatotopy was apparent in all three areas for responses associated with digital movements versus movements across more proximal joints, as well as those associated with thumb versus index finger. There was a large degree of overlap of relCBF responses associated with the different movements, reminiscent of the human corticography maps of Penfield (Penfield and Boldrey 1938). Because of the kinematic limitations inherent with free limb movements, we could not isolate the effect of movement about individual joints from that of individual muscle groups during PET imaging. Thus, our results reflect an approximate somatotopy based on the proximal to distal distribution of both muscle activity and movement across joints. Given the constraints of the PET method for discriminating adjacent relCBF responses, we cannot exclude the possibility of a more complex distribution of efferent neurons that may be present on a spatial scale of less than several millimeters. Such complexity has been shown in several species, including squirrel monkeys, who demonstrate remarkable duplicity of neurons that can be spatially organized locally according to individual muscles, movements, or joints, irrespective of a somatotopic relationship (Strick 1988; Donoghue 1992). Nevertheless, even in these more complex local mappings, there is an overall macroscopic organization that loosely fits into a somatotopic pattern, even within a limb.

Somatotopy was also present in two areas of mesial frontal cortex, within the SMA proper and the more ventrally located cingulate cortex. A recent human corticography study has also identified SMA somatotopy in a distribution that matches our results (Fried et al. 1991). Together, the different methods yield strong evidence for somatotopy in human SMA, similar to other species.

Recent studies in macaque species confirm the presence of at least two motor-specific areas with complete homuncular representations in the cingulate cortex (Dum and Strick 1991; Luppino et al. 1991; Shima et al. 1991). Our results detected only one of these sites, near the ventral bank of the cingulate sulcus. This site is probably the homologue of macaque cingulate area 24d, a motor area that is also located in the ventral bank of the cingulate cortex, with analogous somatotopy, and demonstrating the greatest movement related neuronal activity in cingulate cortex (Luppino et al. 1991). The specific functional attributes of this putative cingulate motor area in humans compared with the SMA is unknown.

In a previous PET report, Colebatch and coworkers observed a somatotopic organization in the motor cortex and SMA during proximal versus distal limb movements, similar to the maps of Woolsey (Colebatch et al. 1991; Woolsey et al. 1952). They used an image analysis method that was similar to our grouped analysis. The present results confirm the previous PET findings and show that, with the grouped image analysis, a single set of responses can be identified in the mesial frontal cortex. By using an individual analysis that included corrections for head movement in the current study, it was possible to examine the location of responses in mesial frontal cortex with greater spatial fidelity and demonstrate the presence of two distinct sets of responses in SMA and cingulate cortex. In the present study, movements were segmented across individual joints more systematically. With this segmentation, a coarse somatotopic representation could be readily identified.

Acknowledgements. The authors thank Karl Friston and Richard Frackowiak of the MRC Cyclotron Unit, London, for generously providing the SPM analysis software used in this study.

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