NeuroImage **11,** 473–481 (2000)
doi:10.1006/nimg.2000.0556, available online at http://www.idealibrary.com on IDEAL®

fMRI Evaluation of Somatotopic Representation in Human Primary Motor Cortex

M. Lotze,*,† M. Erb,* H. Flor,‡ E. Huelsmann,* B. Godde,† and W. Grodd*

**Section for Experimental Magnetic Resonance of the Central Nervous System, Department of Neuroradiology, and †Institute for Medical Psychology and Behavioral Biology, University of Tübingen, D-72074 Tübingen, Germany; and ‡Department of Psychology, Humboldt-University, Berlin, Germany*

Received July 26, 1999

We used fMRI to map foot, elbow, fist, thumb, index finger, and lip movements in 30 healthy subjects. For each movement type confidence intervals of representational sites in the primary motor cortex (M1) were evaluated. In order to improve the precision of their anatomical localization and to optimize the mapping of cortical activation sites, we used both the assessment of locations in the conventional 3D system and a 2D projection method. In addition to the computation of activation maxima of activation clusters within the precentral gyrus, centers of gravity were determined. Both methods showed a high overlap of their representational confidence intervals. The 2D-projection method revealed statistically significant distinct intralimb locations, e.g., elbow versus index finger movements and index finger versus thumb movements. Increased degree of complexity of finger movements resulted in a spread of the somatotopic location toward the arm representation. The 2D-projection method-based fMRI evaluation of limb movements showed high precision and was able to reveal differences in intralimb movement comparisons. fMRI activation revealed a clear somatotopic order of movement representation in M1 and also reflected different degrees of complexity of movement.

INTRODUCTION

Somatotopy in the Primary Motor Cortex

Jackson (1873/1958) postulated distinct cortical activation centers for different types of movements after having observed isolated movements of different body parts during epileptic convulsions. He further hypothesized that the size of the cortical area which represents movements is not proportional to the size and strength of the muscle group involved in the movement but to the degree of differentiation and specialization of the type of movement. These ideas of Jackson were directly tested by electrical stimulation of the cortex in the second part of the 19th century. Fritsch and Hitzig (1870) used galvanic stimulation of a dog's brain to show that specific movements (forelimb extension) could be elicited by stimulation of a particular cortical location. Ferrier (1875) extended these results to monkeys and discovered a precise somatotopic map of movement representations. The differentiation of pre- and postcentral gyri, the former as motor—the latter as sensory—cortex, was first observed by Gruenbaum and Sherrington (in Leyton and Sherrington, 1917). Foerster (1936) as well as Penfield and Boldrey (1937) described a somatotopic order of movements in the human precentral gyrus comparable to the somatotopic representation of somatosensory stimuli in the postcentral gyrus. A review of somatotopic representations based on cortical microstimulation is given in Phillips and Porter (1977).

More precise electrical stimulation techniques in monkeys (e.g., Kwan *et al.*, 1978; Nudo *et al.*, 1992) suggest that the concept of a somatotopic organization of the primary motor cortex (M1) is probably adequate only in a gross approximation. The representation areas of finger and hand movements in M1 show strong overlap, indicating that movements of different representational sites share at least some neural substrates. This overlap may be due to a lack of isolation of different movements. For instance, Schieber and Hibbard (1993) reported that monkeys trained to execute finger movements show comovements of nonparticipating fingers. Furthermore, the functional overlap may also be due to stabilization of distal movements by the more proximally located muscle groups. Representational areas of different limbs and body parts which do not share functional coactivation, as for instance during proximal stabilization, rarely overlap (Huntley and Jones, 1991). Schieber and Hibbard (1993) argued that patches of neuronal groups may enable different movements of one limb embedded in a functional integrity. Each finger movement appears to be specified by a neuronal population distributed throughout the M1 hand area. Lesion studies also suggest that neuronal groups in M1 are represented in functional integrities

1053-8119/00 $35.00

rather than being somatotopic: patients with tiny lesions in the M1 hand area never present with isolated paresis of one finger (Schieber, 1999). Kakei *et al.* (1999) showed that more M1 neurons display changes in activity related to the direction of wrist movement in space than related to patterns of muscle activity utilized to generate the movement. Taken together, these results suggest that movement representations in primary motor cortex are not related to distinct representational sites.

Imaging Somatotopy

Functional imaging studies also showed a high overlap of representational sites of the fingers in M1 (Sanes *et al.*, 1995; Rao *et al.*, 1995). However, Kleinschmidt *et al.* (1997) showed that the subtraction of maps of individual finger movements from those of the other fingers yielded a somatotopic representation of the individual fingers. They concluded that somatotopy within the hand area of M1 is represented as "quantitative predominance of certain movement or digit representation embedded in an overall joint hand area." Using positron emission tomography, Grafton *et al.* (1993) reported distinct activation maxima in M1 for shoulder, elbow, wrist, and finger movements if an individual analysis was performed. This distinction was lost after group analysis. Earlier (Grafton *et al.*, 1991), this group reported confidence intervals in M1 for different pointing movements directed toward a visual target. These movements were evaluated with a projection method that enabled a mapping of distances between representational sites and anatomical references on the cortical surface. A normalization of the evaluated distances to the total length of the precentral gyrus (measured from the central fissure to lateral fissure of each site) was performed. Confidence intervals proved to be quite precisely different between movements of the arm, finger, tongue, and toe.

The purpose of the present study was to evaluate the somatotopy of M1 using functional magnetic resonance imaging. We were especially interested in determining to what extent not only movements between different extremities but also intralimb movements could be differentiated by fMRI.

In addition to the conventional 3D-evaluation method, a 2D-projection tool similar to the method used by Grafton *et al.* (1991) was used. Compared to Grafton *et al.*, the projection was largely automated in order to avoid evaluator-specific variations. In addition, activation maps were described not only by the activation maxima (AM), which may be quite variable if the same subject is investigated twice, although the activation map may be constant, but also by their centers of gravity (COGs). COGs seem to provide higher spatial resolution as shown in transcranial magnetic stimulation studies (Boroojerdi *et al.*, 1999). To obtain a data set for standard locations in healthy controls for later comparison with patient data, movements that are easy to perform for patients with paresis were selected. Movements involving the same finger muscles were performed in three degrees of complexity in order to investigate the influence of complexity on the size and intensity of the activation maps and the location in M1 as well as in secondary cortical motor areas.

METHODS

Subjects

fMRI measurements were performed in 30 right-handed subjects (16 male, 14 female, average age 28.12 years, SD 6.29, range 19–40 years) with no neurological pathology. Handedness was evaluated by the Edinburgh Inventory of Handedness (Oldfield, 1971). The local ethics committee approved the study.

Task

The subjects lay supine in the scanner with their eyes closed. Their heads and the proximal limbs were secured in order to minimize involuntary movements. Subjects performed the following movements: right foot (elevation of the foot at the ankle), right elbow (flexion and extension), right hand (making a fist), right digits (abduction of the thumb, tapping of the thumb, tapping of the index finger), right finger opposition with various degrees of complexity (all fingers against the thumb, sequential finger opposition against the thumb in a simple sequence (fingers 2, 3, 4, 5), complex sequence (fingers 2, 4, 3, 5)), left hand (making a fist), and lips (lip pursing). The number of subjects per condition varied from 5 to 10. All movements were externally paced by an acoustic metronome with a frequency of 1 Hz.

Data Acquisition

fMRI was performed with a 1.5-T scanner (Siemens Vision) using echo-planar imaging (EPI; matrix 96 × 128, FOV 250 mm, TE 59 ms, scan time 8 s, repetition time 10 s) of the whole brain with 45 axially oriented slices of 3 mm slice thickness without a gap. Forty-eight measurements (units of 6 measurements, each during movement and rest, alternating four times) were performed per condition. Additionally, a T1-weighted anatomical 3D data set containing 192 sagittal slices (FLASH, effective thickness 1.5 mm; matrix 224 × 256; field of view 250 mm; TR 9.7 ms) was acquired for each subject prior to the functional data acquisition.

Statistical Evaluation

The fMRI data were evaluated with the Statistical Parametric Mapping program (SPM96, Wellcome De-

partment of Cognitive Neurology). The scans of each individual were realigned with each other to correct for interscan movement artifacts. The functional images of each subject were coregistered on the anatomical data sets after manually defining the anterior commissure as reference point. For individual comparisons, the EPI data were smoothed with a Gaussian filter of 4 mm. Statistically significant differences between movement and rest were assessed by Z tests ($P < 0.01$ for individual and $P < 0.001$ for group data) and an additional extent threshold ($P < 0.05$) using the delayed boxcar model. Individual image files of the statistical parametric maps and the anatomy were used for further data evaluation in the projection method. For the conventional evaluation of group data, the functional data were linearly normalized using the SPM96 template and the normalized data were evaluated in a statistical group design.

Measurement of Location of Activation

3D distances were evaluated with SPM96 according to the following procedure: the distance from CZ (coordinate of the intersection of the interhemispheric fissure and the central gyrus) to the coordinate of the activation maxima in the contralateral precentral gyrus (determined by overlay of the coregistered T1-weighted anatomy) of the nonnormalized individual data was calculated using the Pythagorean formula. The same procedure was carried out for group data after normalization (coordinates for normalized CZ: $x = 0$; $y = -44$; $z = 80$).

For the evaluation of distances with the 2D-projection method, called ISOVIEW, the activation maps were superimposed on 3D-MRI data sets. From an individually selected center between the bottom and the roof of the fourth ventricle, an ellipsoid shell of 20 mm thickness located at the surface of the cortex was fitted to the individual brain. The averaged gray values of the 3D data set and the activation map of the functional data were superimposed as illustrated in Fig. 1 (for further details of this method see Erb *et al.*, 1999). The representational sites were evaluated on the cortical surface using corrections for the ellipsoid surface of the shell. The intensity of activation (expressed by the Z values between rest and activation) and the size of activation clusters around the central gyrus (number of activated voxels) were evaluated using SPM96.

The total length of the precentral gyrus from CZ was measured on the cortical surface of each subject. The average length of the left precentral gyrus in all subjects was 106.1 mm; SD 6.8 mm. Location of the AM or COG was expressed by individually measuring the distance from CZ to AM/COG. A scaling factor was calculated by dividing the average length of the precentral gyrus of all subjects by the actual length. Thus, a normalization to the average gyrus length and an evaluation of distances in millimeters was possible. After SPM96 group normalization, the AMs in the precentral gyrus were evaluated in SPM96 coordinates by combining SPM group normalization and the ISOVIEW projection method. A statistical parametric image of group statistics and a T1-weighted reference 3D-data set of the brain (quite similar to the normalization reference of the averaged 305 Montreal-brains (see SPM96)) were projected and evaluated with the ISOVIEW method.

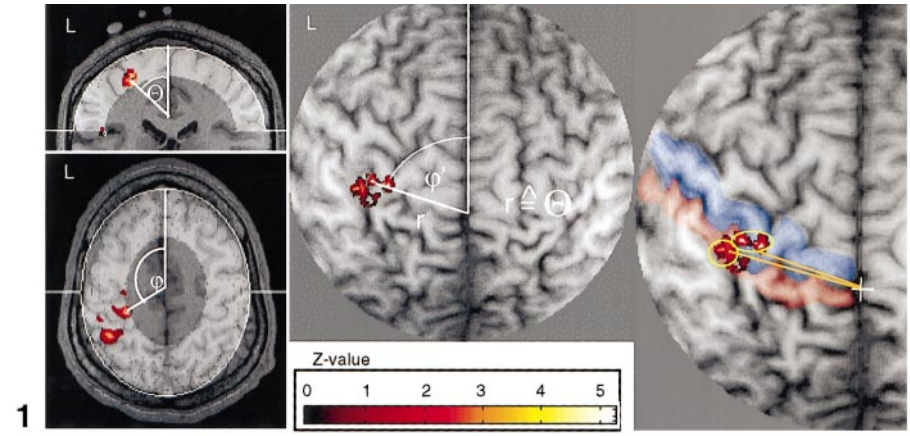
Reference intervals for intersubject variations were computed by calculating the 95% confidence interval for each movement (see Table 2 and Figs. 2A and 2B). Distinct locations for interindividually assessed representational sites were statistically tested by t tests after confirmation of a normal distribution of the data by the Kolmogorov–Smirnov test. These statistics were performed with the Statistical Package for the Social Sciences, Version 8.0.

RESULTS

SPM96 3D evaluation of interindividual movement representation differences between the AM localizations in the left hemisphere (see Fig. 2A and Table 1) revealed significant differences between foot and fist ($t(3) = 4.46$; $P < 0.05$), fist and lip ($t(7) = 3.50$; $P < 0.01$), all fingers and the foot ($t(4) > 10$; $P < 0.01$), and index finger and lip ($t(7) = 6.06$; $P < 0.005$) but not for the intralimb representations (elbow, hand, finger tapping). In the right hemisphere, fist and lip showed distinct representational sites ($t(6) = 5.53$; $P < 0.005$).

The interindividual ISOVIEW evaluation of the AMs and the COGs also showed distinct cortical representations of foot, fist, index finger, and lip movements (Fig. 2B). In the left hemisphere, the fist representation was significantly different from that of the foot ($t(4) = 4.46$; $P < 0.05$) and the lip ($t(9) = 8.61$; $P < 0.001$). Furthermore, significant differences in intralimb somatotopy were observed. The location of the index finger was significantly different from that of the elbow ($t(4) = 4.57$; $P < 0.01$) and, for the AM-evaluation, also from that of the thumb ($t(4) = 5.30$; $P < 0.01$). In the right hemisphere fist and lip were discretely located ($t(9) = 8.94$; $P < 0.001$). Location sites were not significantly different for the fingers and the hand (fist versus opposition tasks: $t < 1.50$) and the two different thumb movements did not differ from each other. Activation maxima of fist and elbow movements showed a trend toward a significant difference in their representational sites ($t(4) = 2.62$; $P = 0.059$).

Distances measured between representational sites showed no significant differences between the two methods. For the 3D method, the distances between



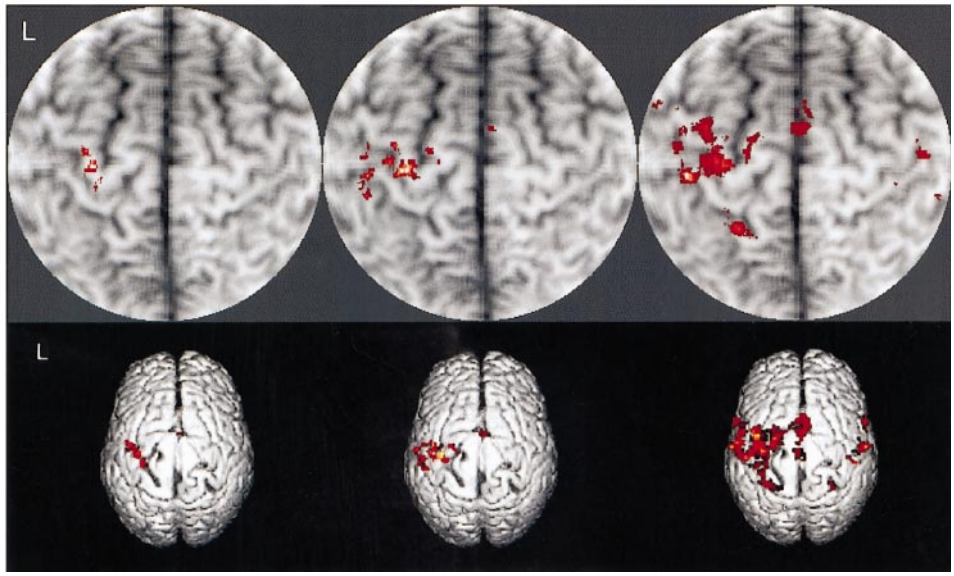


FIG. 1. Thumb movement. Demonstration of ISOVIEW projection method. Left: After the functional and anatomical data sets were overlaid, an ellipsoid shell of 2 cm thickness (light gray-shaded area) was fitted to the cortical surface. For each point of the ellipsoid a vector, starting at the center of the brain and extending to the surface of the ellipsoid, was calculated. The angles θ and φ define the location of each point on the surface of the shell. The color coding for the *Z* value of the activation maps is given on the bottom. The two-dimensional plane, which was derived from the ellipsoid shell, is shown on the left. The point of interest is defined by the two variables r and φ' with $r = \theta$ denoting the distance from the center and $\varphi' = \varphi$ (polar angle referenced to the center). r and φ' thus define each point of activation. The center of gravity was computed from all activated voxels in the pre- or postcentral gyrus that exceeded a statistical threshold of $P < 0.01$ and an extent threshold of $P < 0.05$. The distance from the intersection of the interhemispheric fissure and the central sulcus to the center of gravity or the activation maximum of the activation cluster was measured (yellow line).

FIG. 3. Evaluation of group statistics during a finger-opposition task with increasing complexity. Upper row: ISOVIEW projection of SPM96 group data. Lower row: SPM96 group data demonstrated in the 3D-rendered brain. Left: Right thumb opposition against all other fingers. Middle: Right thumb opposition against fingers 2, 3, 4, 5, sequentially. Right: Highly complex opposition of the right thumb against fingers 2, 4, 3, 5, sequentially.

activation maxima of the index finger to the elbow amounted to 17.18 mm (SD 12.82 mm). The distance of the index finger and the thumb movement was 9.61 mm (SD 5.08 mm). The 2D method showed an average distance of 18.4 mm (SD 8.90 mm) from the index finger to the elbow and of 11.2 mm (SD 11.52 mm) from the index finger to the thumb measured by the COG on the cortical surface.

Group statistics of 3D-SPM96 normalized data showed a somatotopic order for feet, fist, and lip movements with the right fist representation 40.50 mm distant from the right foot (see Table 1 and Fig. 2C). This somatotopic representational pattern was also seen for the 2D evaluation of SPM normalized group data with fist movement 37.10 mm distant from the foot movement (see Fig. 2D).

Most movements showed activation in both the pre- and the postcentral gyrus; these could be differentiated with the 2D but not with the 3D evaluation (clustered activation maps). The contralateral representation ar-

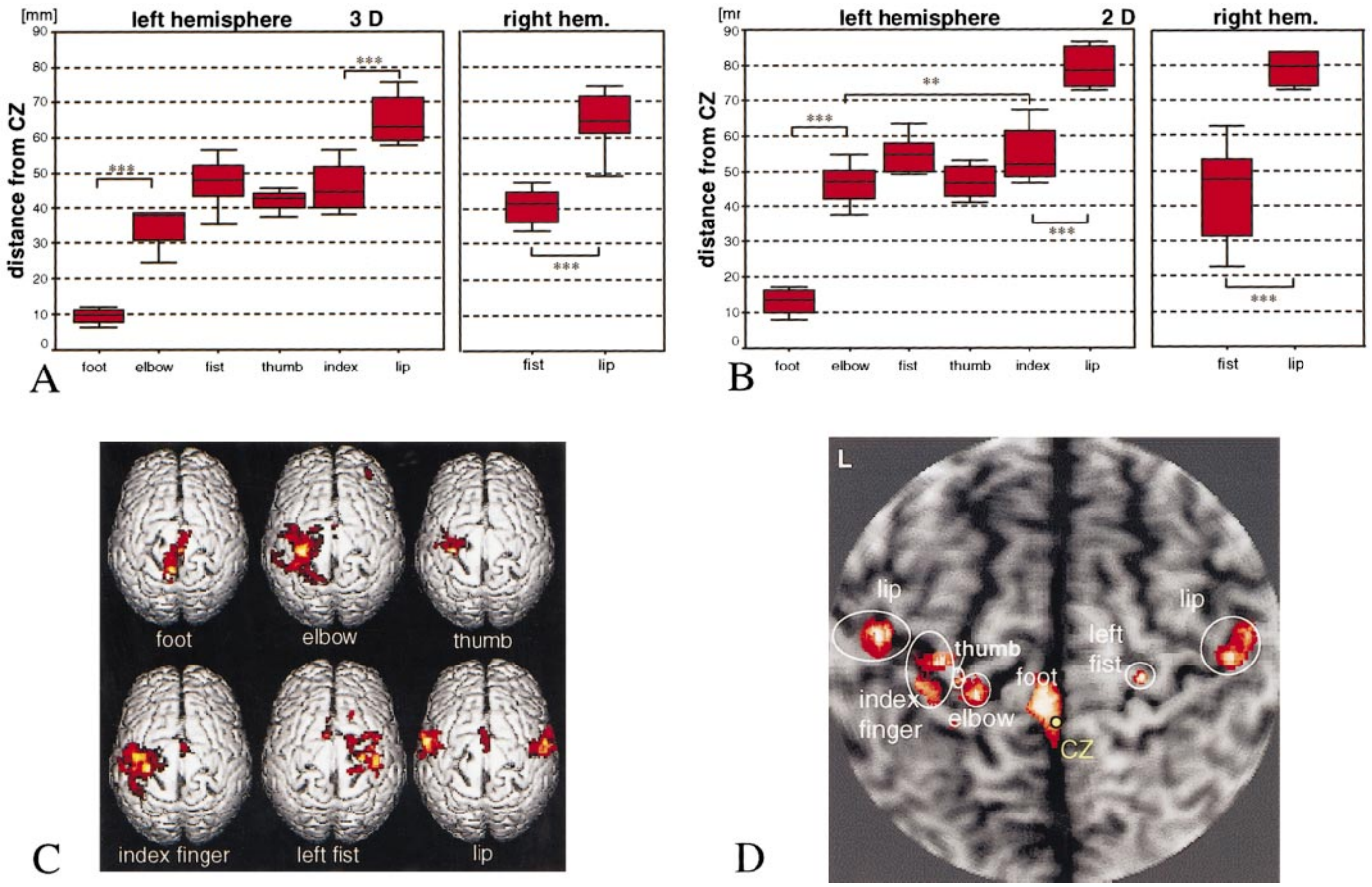


FIG. 2. (A and B) Comparison of all evaluation methods. Boxes describe the distance between the first and third quartile (75th percentile), lines describe the confidence intervals (95%) grouped around the averages, the horizontal thick line describes the median. Brackets and stars mark significant differences of dependent variables evaluated by *t* tests (***$P < 0.001$; **$P < 0.01$). Individual analysis (movement and number of subjects per task): foot ($n = 5$), elbow ($n = 5$), fist ($n = 10$), thumb ($n = 5$), index finger ($n = 5$), lip ($n = 10$). (A) Distances from CZ to AM of individually evaluated data without SPM normalization in three-dimensional system. (B) Distances from CZ to COG of individual evaluation with ISOVIEW projection in 2D. (C and D) Group analysis.(C) Calculation of activation maxima for SPM96 group analysis in the 3D space. (D) Combination of group analyses with SPM96 and ISOVIEW 2D evaluation of distances from CZ to AM.

eas in M1 and S1 (primary sensory cortex) during right and left hand movements were grouped (Gaussian filter with 4 mm extent) in one activation cluster in 70% of the subjects (60% right hand, 80% left hand).

Lip representation was highly symmetrical between both hemispheres, independent of the evaluation method (i.e., for the individually performed ISOVIEW-AM method, we observed an average difference between the left and the right hemisphere of 2.7 mm, for the ISOVIEW-COG method no difference at all). Numbers of activated voxels and *Z* values did not differ between the hemispheres. The activation intensities (*Z* values of activation maxima) were significantly different for lip versus fist activation (lower *Z* value for the lip: left hemisphere $t(7) = 2.83$, $P < 0.05$; right hemisphere $t(7) = 3.01$, $P < 0.02$). The same was observed for the number of activated voxels (left hemisphere $t(7) = 4.10$, $P < 0.01$; right hemisphere $t(7) = 5.23$, $P < 0.005$). Thumb tapping showed lower *Z* values than index finger tapping ($t(4) = 3.47$, $P < 0.05$).

The confidence intervals for the 95% probability of AM locations in M1 are given in Table 2 for individual data of the 3D- and 2D-evaluation strategies. Average interval deviations from mean were 8.16 mm (SD 6.09) for 3D- and 7.31 mm (SD 1.87) for the 2D-evaluation method. Both methods showed that the left fist is represented nearer to CZ than the right fist (3D 6.83 mm, 2D 10.45 mm). Left and right lip representational sites showed similar variations (variation differences for 3D 1.19 mm, 2D 1.27 mm).

Finger opposition (using the same target muscles with movements differing in complexity; Table 3 and Fig. 3) showed the same location of activation maxima in the group evaluation (normalization with SPM96). An increasing amount of complexity led to more activated voxels (ISOVIEW method). The higher the complexity of the task, the higher was the disseminated pattern of activation clusters in contralateral M1 and S1. During increased complexity, higher activation was furthermore observed in SMA (supplementary motor

TABLE 1

Representational Sites in Contralateral M1 in Millimeters and in Talairach-like SPM96 Coordinates from CZ with Different Methods in 2D and 3D Space

	Movement (number of subjects) (main muscle involved)						
	Right foot (n = 5) (tibialis anterior)	Right elbow (n = 5) (biceps/triceps brachii)	Right fist (n = 10) (flexor/extensor carpi rad./uln.)	Left fist (n = 10) (flexor/extensor carpi rad./uln.)	Right thumb tap (n = 5) (flex./extensor policis brevis)	Right index finger tap (n = 9) (flex./ext. indices proprius)	Bilateral lip pursing (n = 10) (orbicularis oris)
No normalization: SPM96							
AM each, mean (SD)	9.4 (2.4)	34.8 (6.3)	47.6 (6.0)	40.7 (5.1)	42.0 (3.3)	45.5 (6.7)	le: 64.8 (8.1)
3D distance (in mm)							ri: 64.8 (8.0)
Normalization: SPM96							
AM group, ordinates	−8/−38/76	−28/−24/64	−26/−34/64	24/−20/60	−32/−24/58	−40/−16/56	le: −58/−14/40
3D distance (in mm)	10.8	38.0	51.3	39.4	43.7	54.4	76.6
							ri: 52/−8/36
							77.1
No normalization: ISOVIEW							
AM; COG each, mean (SD)	13.7 (5.6);	47.2 (3.4);	46.7 (7.5);	41.9 (12.5);	47.2 (6.1);	56.5 (6.8);	le: 76.6 (8.1);
2D distance (in mm)	13.1 (3.5)	46.4 (5.9)	54.9 (6.5)	44.5 (10.5)	47.0 (4.5)	54.8 (7.1)	79.2 (5.8)
							ri: 74.0 (8.9);
							79.1 (4.7)
SPM96 normalized: ISOVIEW							
AM group, mean	10.3	31.2	47.4	36.7	40.4	51.5	le: 76.7
2D distance (in mm)							ri: 76.9
Z value each, mean (SD)	4.66 (1.72)	4.85 (1.09)	4.99 (0.86)	4.40 (0.50)	4.01 (0.85)	5.21 (0.89)	le: 3.74 (0.67)
Voxels each, mean (SD)	1536 (1271)	1012 (577)	2195 (1004)	1704 (706)	373 (83)	1099 (822)	324 (196)
							ri: 3.54 (0.74)
							327 (263)

TABLE 2

Areas Representing a 95% Confidence Interval of Representational Sites in Contralateral M1 with Two Different Evaluation Methods

Movement (number of subjects)	3D: SPM96 (in mm) without normalization	2D: ISOVIEW (COG) (in mm)
Foot elevation ri. (5)	5.64(–9.43)–13.21	6.59(–13.05)–19.51
Elbow flexion ri. (5)	23.93(–34.75)–45.56	38.23(–46.37)–54.51
Fist making ri. (10)	43.01(–47.56)–52.10	49.26(–54.94)–60.63
Fist making le. (10)	37.06(–40.73)–44.39	35.39(–44.49)–53.58
Thumb abduction ri. (5)	20.97(–43.85)–66.73	32.28(–43.03)–53.78
Thumb tapping ri. (5)	31.91(–41.99)–52.06	38.70(–46.98)–55.26
Index finger tapp. ri. (10)	40.30(–45.47)–50.62	48.42(–54.73)–61.03
Lip pursing left hem. (10)	59.13(–64.79)–70.46	73.00(–79.17)–85.36
Lip pursing right hem. (10)	57.92(–64.79)–71.65	74.17(–79.08)–84.00

area), premotor cortex, and, for the highly complex task, also in ipsilateral M1 and the superior parietal cortex. For individual data evaluation, AM was 11.2 mm more medially located (COG 11.7 mm) during the highly complex than during the simple opposition task.

DISCUSSION

All methods—whether 3D- or 2D-evaluation strategies—succeeded in demonstrating distinct representational sites of movements between feet, lip, and hand. Since intralimb movements overlap extensively, a distinct localization of movements of the same limb can be demonstrated only if a method which is able to localize the activation maps within the primary motor cortex is used. This was demonstrated for the 2D-projection method: activation maxima of index finger and elbow movements were distinct for the mapping of both AMs and COGs. A distinct localization for thumb and index finger movements could be shown only for the AMs. Although the distinct representation for thumb and index finger movement could not be demonstrated for COGs, this method may be superior to the AM evaluation because of its relative independence from evaluator-specific interpretations. Since fist movement includes activation of all fingers, it was not distinct from finger tapping. A comparison of movements of the same joint, but with different muscles involved (tapping (extensor and flexor pollicis brevis) and abduction of the thumb (abductor pollicis brevis)), revealed a high overlap of representational sites.

The better elucidation of distinct activation sites of intralimb movements with the 2D projection may be related to several factors: Euclidean distances, as evaluated in the 3D method, are of limited use as they only provide the shortest connection between cortical activation patterns and reference points under the surface of the brain. A direct measurement of activation areas projected on the cortical surface, as previously also demonstrated by Grafton *et al.* (1991), gives the opportunity of measuring distances directly on the cortical surface, which approximates more closely the distances measured intraoperatively on the cortical relief. An orientation on the cortical relief is preferable because representational sites in the pre- and postcentral gyri can be differentiated. The projection method furthermore provides an overview over the anatomical and functional data, which are lost if AMs are superimposed on the anatomical data in SPM96. Orientation in the projected anatomical structure is easily achieved

TABLE 3

Representational Sites in Contralateral M1 Measured with ISOVIEW after SPM96 Evaluation

Finger opposition right (n = 5)	ISOVIEW AM/COG each (in mm) mean (SD)	ISOVIEW AM group (in mm) mean	SPM96 group coordinates	ISOVIEW activated voxels			
				M1c	S1c	SMA	M1i
Simple	53.5 (2.4) 53.5 (1.8)	48.1	−42/−10/58	129	12	—	—
Complex	53.4 (1.9) 52.8 (2.3)	48.1	−34/−18/−52	196	162	27	—
Highly complex	42.3 (8.0) 41.8 (9.2)	48.7	−34/−16/50	474	396	268	66

Note. Coordinates from SPM96 group data are given. The activated voxels were evaluated within the cortical shell (M1c, contralateral M1; M1i, ipsilateral M1).

by referring to the superior frontal sulcus leading to the anterior border of the precentral gyrus and to the hand knob in the precentral gyrus (Yousry *et al.*, 1995).

The confidence intervals of each movement, however, were much larger in our study than those described by Grafton *et al.* (1991). This may be due to a higher interpersonal variation during movement execution in our experiment (a simple repetitive task chosen to also be suitable for patients with impaired motor performance) and to the fact that Grafton *et al.* calculated differences between movements and the control situation in which subjects followed the target visually. The higher variances are not due to differences in the evaluation of activation sites, since both techniques were quite similar. Nevertheless, the present evaluation method is highly automated and therefore less dependent on interpretations of activation sites by the evaluator.

To determine whether the large confidence intervals were related to the measurement of distances between an anatomical reference to the activation site, differences between intralimb activation sites were also evaluated. These showed nevertheless high variances and did not differ significantly between the two evaluation methods.

Activation intensity was significantly decreased for the thumb compared to index finger movement (see Table 1), an observation also made by Grafton *et al.* (1993).

Group statistics after normalization showed a somatotopic pattern, but after this transformation there is no further information on intra- and interpersonal variances of representational sites. Grafton *et al.* (1993) showed that representational sites of the shoulder, elbow, and wrist were almost at the same location after normalization, whereas individual analysis could demonstrate somatotopic representation. This is due to a distortion process which may make an exact assignment of representational sites to an anatomical location almost impossible. For example, when using the normalization according to Talairach, using a reference point located near the basal ganglia, the distortion at the level of the central sulcus amounts up to 2 cm (Talairach and Tournoux, 1988). A differentiation of activation sites between the pre- and the postcentral gyrus according to Talairach normalization is impossible (see Lotze *et al.*, 1999).

Furthermore, the Talairach-like coordinates which are given for AM in SPM96 after normalization are of limited use since a definite conclusion as to the anatomical structure in which they occur is not possible and a transfer from Talairach coordinates into Brodmann's areas is obsolete (Roland and Zilles, 1998). Zilles suggests a differentiation based on multiple criteria such as the cyto-, myelo-, and receptoarchitecture. For the precentral sulcus, the cyto- and receptoarchitecture exhibit a differentiation in an anterior and a posterior Brodmann's area 4 (Geyer *et al.*, 1996). With some interindividual variations, area 4 is oriented along the precentral gyrus, precisely limited by the central sulcus from the somatosensory areas. Therefore, an orientation to the anatomical macrostructure of the individual cortical gyri is superior to an orientation in the Talairach system.

The execution of a movement with different degrees of complexity—involving the same muscle groups—revealed no significant differences in representational sites over all subjects, although an intraindividual evaluation of the data showed a trend for a location of the activation site in the direction of the arm representation with increasing complexity. Two reasons for this phenomenon have to be considered: a spillover of muscle activity from the moving members or muscle activity necessary for more proximal stabilization during increasing complexity of the task. Our data confirm the results of Gordon *et al.* (1998) and Kim *et al.* (1995): the more complex the finger opposition task, the more activated voxels in contralateral M1 and S1, bilateral SMA, and ipsilateral M1 (see also Table 3). Furthermore, we also observed left-sided activation in the superior parietal cortex. This is consistent with studies of patients with parietal lesions who showed deficits in unimanual complex action production (Halsband, 1998).

In conclusion, with the additional usage of an evaluation method which determines activation sites precisely within anatomical structures, as performed here with a 2D-projection method, significant differences for representational sites of intralimb movements can also be demonstrated.

ACKNOWLEDGMENTS

The study was funded by the "Bundesministerium für Bildung und Forschung," the "Volkswagen-Stiftung," and the "Deutsche Forschungsgemeinschaft."

REFERENCES

Boroojerdi, B., Foltys, H., Krings, T., Spetzger,U., Thron, A., and Töpper, R. 1999. Localization of the motor hand area using transcranial magnetic stimulation and functional magnetic resonance imaging. *Clin. Neurophysiol.* **110:** 699–704.

Erb, M., Lotze, M., and Grodd, W. 1999. ISOVIEW: Two-dimensional display of cortical fMRI-activation. *NeuroImage (Suppl.)* **9:** S32.

Ferrier, D. 1875. Experiments on the brain of monkeys. *Proc. R. Soc. London* **23:** 409–430.

Foerster, O. 1936. The motor cortex in man in the light of Hughlings Jackson's doctrines. *Brain* **59:** 135–159.

Fritsch, G., and Hitzig, E. 1870. Über die elektrische Erregbarkeit des Grosshirns. *Arch. Anat. Physiol. Wiss. Med.* **37:** 300–332.

Gordon, A. M., Lee, J. H., Flament, D., Ugurbil, K., and Ebner, T. J. 1998. Functional magnetic resonance imaging of motor, sensory, and posterior parietal cortical areas during performance of sequential typing movements. *Exp. Brain Res.* **121:** 153–166.

Grafton, S. T., Woods, R. P., Mazziotta, J. C., and Phelps, M. E. 1991. Somatotopic mapping of the primary motor cortex in humans: Activation studies with cerebral blood flow and positron emission spectroscopy. *J. Neurophysiol.* **66:** 735–743.

Grafton, S. T., Woods, R. P., and Mazziotta, J. C. 1993. Within-arm somatotopy in human motor areas determined by positron emission tomography imaging of cerebral blood flow. *Exp. Brain Res.* **95:** 172–176.

Geyer, S., Ledberg, A., Schleicher, A., Kinomura, S., Schormann, T., Burgel, U., Klingberg, T., Larsson, J., Zilles, K., and Roland, P. E. 1996. Two different areas within the primary motor cortex of man. *Nature* **382:** 805–807.

Halsband, U. 1998. Brain mechanisms of apraxia. In *Comparative Neuropsychology* (A. D. Milner, Ed.), pp. 184–212. Oxford Univ. Press, London.

Huntley, G. W., and Jones, E. G. 1991. Relationship of intrinsic connections to forelimb movement representations in monkey motor cortex: A correlative anatomic and physiological study. *J. Neurophysiol.* **66:** 390–413.

Jackson, J. H. 1873/1958. On the anatomical and physiological location of movement in the brain. In *Selected Writings of John Hughlings Jackson* (J. Taylor, Ed.). Basic Books, New York.

Kakei, S., Hoffman, D. S., and Strick, P. L. 1999. Muscle and movement representations in the primary motor cortex. *Science* **285:** 2136–2139.

Kim, S. G., Ashe, J., and Hendrich, K. 1993. Functional magnetic resonance imaging of motor cortex: Hemispheric asymmetry and handedness. *Science* **261:** 615–617.

Kwan, H. C., MacKay, W. A., Murphy, J. T., and Wong, Y. C. 1978. Spatial organization of precentral cortex in awake primates. II. Motor outputs. *J. Neurophysiol.* **41:** 1120–1131.

Kleinschmidt, A., Nitschke, M. F., and Frahm, J. 1997. Somatotopy in the human motor cortex hand area. A high-resolution functional MRI study. *Eur. J. Neurosci.* **9:** 2178–2186.

Leyton, A. S. F., and Sherrington, C. S. 1917. Observations on the excitable cortex of a chimpanzee, orang-utan and gorilla. *Q. J. Exp. Physiol.* **11:** 135–222.

Lotze, M., Montoya, P., Klose, U., Hülsmann, E., Flor, H., Birbaumer, N., and Grodd, W. 1999. Activation of cortical and cerebellar motor areas during executed and imagined hand movements: An fMRI study. *J. Cognit. Neurosci.* **11:** 491–501.

Nudo, R. J., Jenkins, W. M., Merzenich, M. M., Prejean, T., and Grenda, R. 1992. Neurophysiologic correlation of hand preference in primary motor cortex of adult squirrel monkeys. *J. Neurosci.* **12:** 2918–2947.

Oldfield, R. C. 1971. The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia* **9:** 97–113.

Penfield, W., and Boldrey, E. 1937. Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation. *Brain* **60:** 389–443.

Phillips, C. G., and Porter R. 1977. Corticospinal neurons. Their role in movement. *Monogr. Physiol. Soc.* **34:** 1–450.

Rao, S. M., Binder, J. R., Hammeke, T. A., Bandettini, P. A., Bobholz, J. A., Frost, J. A., Myklebust, B. M., Jacobsen, R. D., and Hyde, J. S. 1995. Somatotopic mapping of the human primary motor cortex with functional magnetic resonance imaging. *Neurology* **45:** 919–924.

Roland, P. E., and Zilles, K. 1998. Structural divisions and functional fields in the human cerebral cortex. *Brain Res. Brain Res. Rev.* **26:** 87–105.

Sanes, N. J., Donoghue, J. P., Thangaraj, V., Edelman, R. R., and Warach, S. 1995. Shared neural substrates controlling hand movements in human motor cortex. *Science* **268:** 1775–1777.

Schieber, M. H. 1999. Somatotopic gradients in the distributed organization of the human primary motor cortex hand area: Evidence from small infarcts. *Exp. Brain Res.* **128:** 139–148.

Schieber, M. H., and Hibbard, S. 1993. How somatotopic is the hand area? *Science* **261:** 489–492.

Talairach, J., and Tournoux, P. 1988. *Co-planar Stereotactic Atlas of the Human Brain. 3-D Proportional System: An Approach to Cerebral Imaging.* Thieme, Stuttgart/New York.

Yoursy, T. A., Schmid, U. D., Jassoy, A. G., Schmidt, D., Eisner, W. E., Reulen, H.-J., Reiser, M. F., and Lissner, J. 1995. Topography of the cortical motor hand area: Prospective study with fMRI and direct motor mapping at surgery. *Radiology* **195:** 23–29.