Correspondence between functional magnetic resonance imaging somatotopy and individual brain anatomy of the central region: comparison with intraoperative stimulation in patients with brain tumors

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Object. The goal of this study was to determine the somatotopical structure–function relationships of the primary motor cortex in individual patients by using functional magnetic resonance (fMR) imaging. This was done to assess whether there is a displacement of functional areas compared with anatomical landmarks in patients harboring brain tumors close to the central region, and to validate these findings with intraoperative cortical stimulation.

Methods. One hundred twenty hemispheres in 60 patients were studied by obtaining blood oxygen level–dependent fMR images in patients while they performed movements of the foot, hand, and face on both sides. There was a good correspondence between anatomical landmarks in the deep portion of the central sulcus on axial slices and the somatotopical organization of primary motor areas. Pixels activated during hand movements were centered on a small characteristic digitation; those activated during movements in the face and foot areas were located in the lower portion of the central sulcus (lateral to the hand area) and around the termination of the central sulcus, respectively. In diseased hemispheres, signal-intensity changes were still observed in the projection of the expected anatomical area. The fMR imaging data mapped intraoperative electrical stimulation in 92% of positive sites.

Conclusions. There was a high correspondence between the somatotopical anatomy and function in the central sulcus, which was similar in normal and diseased hemispheres. The fMR imaging and electrical stimulation data were highly concordant. These findings may enable the neurosurgeon to locate primary motor areas more easily during surgery.

Key Words • functional magnetic resonance imaging • sensorimotor cortex • brain neoplasm • cortical mapping • cortical stimulation

Precise knowledge of the somatotopical structure–function relationships of the primary motor cortex in individual patients has important implications in surgical or intravascular therapy planning and also for several other domains such as the study of anatomico-clinical correlations in patients with central lesions and the reorganization of normal brain activity following brain damage. In brain surgery, locating functional areas surrounding lesions of the central region may assist in the selection of patients for surgery and reduce the risk of postoperative deficit.

The classic homunculus determined by direct electrostimulation of the motor cortex is usually mapped onto the cortical surface, but no obvious correspondence between individual structure and function has been described that would allow us to locate each functional area relative to others during a simple examination of the surface of the cortex. Only few PET or fMR imaging studies have specifically addressed the somatotopical representation of the primary motor cortex. The results of these studies have been reported to be similar to those of cortical stimulation studies; however, an assessment still has not been made concerning whether specific anatomical landmarks within the central sulcus can be related to different functional areas in individual patients. Recently, a characteristic aspect of the precentral gyrus, described as a “typical hook,” a “bayonet-shaped” entity, a “sigmoidal shape structure,” an “omega-shaped structure,” or a “knob,” has been reported to correspond to the hand area, thereby localizing the central sulcus more accurately than classic land-
marks. Thus, the morphological characteristics of the depth of the central sulcus appear more informative than its surface. However, this landmark has only been validated in a small number of healthy volunteers by using PET or fMR imaging studies, and the correspondence between structure and function of other segmental body parts has not been studied.

In the present study, we report on the relationships between individual brain anatomy and the somatotopical primary motor areas by using fMR imaging in 120 hemispheres in 60 patients harboring lesion of the central region. The aims of the present study were as follows: 1) to determine whether specific individual relationships exist between function and anatomy for segmental body parts including the foot, hand, and face in the 60 normal hemispheres of the patients; 2) to assess whether there is a modification of these relationships due to the presence of the tumor in the 60 diseased hemispheres; and 3) to validate these findings with intraoperative cortical stimulation.

### TABLE 1

Comparison between normal and diseased hemispheres in patients with brain tumor*

<table>
<thead>
<tr>
<th>Factor</th>
<th>Hemispheres—No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>location of activation</td>
<td>Normal</td>
</tr>
<tr>
<td>hand (60 patients)</td>
<td>7</td>
</tr>
<tr>
<td>not determined</td>
<td></td>
</tr>
<tr>
<td>mediolateral</td>
<td></td>
</tr>
<tr>
<td>knob only</td>
<td>32</td>
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<tr>
<td>lateral extension</td>
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</tr>
<tr>
<td>medial extension</td>
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<td>anteroposterior</td>
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</tr>
<tr>
<td>anterior/posterior</td>
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</tr>
<tr>
<td>anterior</td>
<td>1</td>
</tr>
<tr>
<td>posterior</td>
<td>1</td>
</tr>
<tr>
<td>foot (51 patients)</td>
<td>14</td>
</tr>
<tr>
<td>anterior/posterior</td>
<td>21</td>
</tr>
<tr>
<td>anterior</td>
<td>15</td>
</tr>
<tr>
<td>posterior</td>
<td>1</td>
</tr>
<tr>
<td>face (29 patients)</td>
<td>4</td>
</tr>
<tr>
<td>not determined</td>
<td>4</td>
</tr>
<tr>
<td>anterior/posterior</td>
<td>21</td>
</tr>
<tr>
<td>anterior</td>
<td>4</td>
</tr>
<tr>
<td>posterior</td>
<td>0</td>
</tr>
<tr>
<td>overlap between territories</td>
<td></td>
</tr>
<tr>
<td>hand/face</td>
<td>6</td>
</tr>
<tr>
<td>present</td>
<td>6</td>
</tr>
<tr>
<td>absent</td>
<td>19</td>
</tr>
<tr>
<td>hand/foot</td>
<td>1</td>
</tr>
<tr>
<td>present</td>
<td>1</td>
</tr>
<tr>
<td>absot</td>
<td>36</td>
</tr>
</tbody>
</table>

* Location of activation: in the mediolateral direction, hand activation was either restricted to the knob area or spread toward the adjacent medial or lateral parts of the central sulcus. In the anteroposterior direction, activated pixels were superimposed on the anterior or posterior bank of the central sulcus only or on both anterior and posterior banks. The degree of overlap between the adjacent functional somatotopical territories was assessed in the hand, foot, and face areas. "Not determined" includes discarded data (head movements or artifact), examinations not performed, and examinations in which no activation occurred in the sensorimotor cortex. No statistical difference was found in any of the measures between the normal and diseased hemispheres.*17 and crosscorrelation with a reference waveform of the MR imaging signal time course. Activated clusters were defined as follows: a minimum of three contiguous pixels, a correlation coefficient.

### Clinical Material and Methods

#### Patient Population

Sixty patients harboring tumors close to the central region were retrospectively studied. Patients ranged in age from 20 to 74 years (mean 42 years). Lesions included oligodendroglioma in 17 patients; low-grade astrocytoma in 14; anaplastic oligodendroglioma in six; metastasis and oligoastrocytoma in three patients each; high-grade glioma in two patients; and ganglioglioma, anaplastic astrocytoma, ganglioneuroblastoma, xanthoastrocytoma, and lymphoma in one patient each. In 10 patients, a neuropathological diagnosis was unavailable. Tumors were located in the frontal lobe (left side in 28 patients and right side in 20), parietal lobe (left side in two patients and right side in six), or in both lobes (left side in two patients and right side in two). Motor deficit was either mild (nine patients) or absent (51 patients). Hemihypesthesia (four patients) and discrete language deficit (three patients) were also observed.

#### Neuroimaging Study

The MR imaging protocol was conducted using BOLD fMR imaging performed with the aid of a 1.5-tesla unit. The protocol included two types of images: 1) 12 axial gradient-echo–echoplanar images covering the whole frontal lobes (TR 5000 msec, TE 60 msec; flip angle 90°; 5-mm slice thickness with no gap; inplane resolution 3.75 × 3.75 mm); and 2) axial inversion-recovery 3D fast spoiled-gradient recalled images for anatomical localization. Images were acquired in less than 60 minutes.

#### Motor Tasks

Four different tasks were performed by the patients during the imaging session. The tasks consisted of self-paced flexion/extension of the fingers (60 patients) and toes (51 patients) of the right and left sides successively and contraction of the lips (39 patients). Specific instructions concerning the movements to be made were given to the patients immediately before the experiment. Movements were shown to the patients by an examiner at a rate of approximately 1 Hz, without any explicit instruction given concerning the movement frequency. Before the image was obtained, the patients performed each movement for approximately 15 seconds. During image acquisition, the patients lay in darkness. In the rest condition, they were told to remain in a resting awake state. Task-switching instructions were given to the patients through a microphone. The paradigm consisted of seven periods of 30 seconds each, alternating between rest and activation (42 volumes were acquired over 3.5 minutes, the first four volumes were discarded to reach signal equilibrium).
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greater than 0.45, an autocorrelation coefficient greater than 0.3, and a probability value less than 0.001. Activated pixels were overlaid on axial anatomical images using a color scale representing the correlation coefficient. Pixels were then localized according to the individual anatomy of each patient using multiplanar analysis and 3D surface rendering of the cortex. Overall, in 57 (95%) of 60 patients, activation of the sensorimotor cortex was obtained during at least one task. Data were discarded in only five patients for hand, three patients for foot, and one patient for face movements (Table 1). In these patients, failure was due to large head movements (> 0.6 mm, corresponding to approximately 20% of pixel size in the axial plane; seven patients) resulting from difficulty in performing the tasks because of motor (six of seven patients) or cognitive (frontal dysfunction in one patient) deficits, susceptibility artifacts due to ferromagnetic material implanted in the skull during surgery (one patient), and schizophrenia (one patient).

Magnetic Resonance Anatomical Analysis of the Central Sulcus

Identification of the central sulcus and the precentral gyrus was first made by one examiner (S.L.), who was blinded to the functional data, by using anatomical landmarks observed on axial slices only. These landmarks included the hand knob on the posterior border of the precentral gyrus and the junction between the superior frontal and precentral gyri. In difficult-to-analyze cases, examination of the surface rendering of the cortex, which was reconstructed using commercially available software, and of oblique sections located parallel to the surface of the frontal cortex was also performed. Findings were then confirmed by comparison with fMR imaging and intraoperative cortical stimulation data.

Comparison Between Normal and Diseased Hemispheres

To evaluate the possibility of a mediolateral or anteroposterior displacement of activated areas in diseased hemispheres compared with individual anatomical landmarks found in normal hemispheres, several parameters were studied: 1) the mediolateral localization of hand activation according to the hand knob (that is, whether activation was restricted to the knob area or spread toward the adjacent medial or lateral portions of the central sulcus); 2) the anteroposterior localization of activated pixels on the central sulcus (anterior or posterior bank of the central sulcus alone or both); and 3) the degree of overlap between adjacent functional somatotopical territories (that is, the hand and foot and the hand and face).

Intraoperative Stimulation

Forty-five patients underwent surgery, five underwent only stereotactically guided biopsy, and 10 did not undergo any surgical procedure. Direct cortical and subcortical stimulations were performed in 26 patients by using a bipolar probe equipped with tips spaced 5 mm apart. A train of constant-current biphasic square-wave pulses was used at a frequency of 60 Hz and a single-pulse phase duration of 1 msec. The current amplitude was 4 to 16 mA. A comparison with the results of MR imaging was obtained using intraoperative photographs of the stimulated sites labeled on the cortical surface (11 patients) and snapshots of the position of the cortical electrodes on the MR images obtained in the patient (15 patients) using a neuronavigation system. A total of 44 stimulations (three for foot, 36 for hand, and five for face) elicited motor responses.

For intraoperative photographs, a comparison between areas studied using cortical stimulation and fMR imaging were obtained as follows: 1) activated areas were displayed on the MR surface rendering of the cortex of the patients; 2) the scale of the intraoperative photographs and that of the MR surface rendering were adjusted using commercially available graphic software; and 3) the location of each positive site of stimulation, such as inside or outside the margin of the activated area, was recorded. The distance between the margins of the activated area and each positive site of stimulation located outside the activated area was also measured. For the neuronavigation system, the comparison between the two techniques was performed comparing the location of positive electrode sites on axial slices relative to corresponding fMR imaging sections.

Sources of Supplies and Equipment

The ACTIV software was developed at the Commissariat à l’Energie Atomique (Orsay, France) by Drs. D. Le Bihan, E. Lobel, and A. L. Paradis. The Interactive Data Language Program was obtained from Research Systems International France (Paris, France) and 3D surface rendering of the cortex was performed using Voxeltool software produced by General Electric Medical Systems (Milwaukee, WI). Intraoperative stimulation was performed using the Ojemann cortical stimulator, manufactured by Radionics, Inc. (Burlington, MA). Elekta (Grenoble, France) manufactured the neuronavigation system. Magnetic resonance surface rendering was adjusted by using Adobe Photoshop, produced by Adobe Systems, Inc. (San Jose, CA).

Results

Morphological Identification of the Central Sulcus

Normal Hemispheres. Identification of the junction between the superior frontal and precentral gyri was easy in 49 hemispheres (82%) and uncertain in 11 (18%) hemispheres because of anatomical variations (a connection between the precentral and central sulci and a lack of connection between the superior frontal and precentral sulci). The hand knob could be identified in all normal hemispheres. This knob corresponded to a small digitation appearing posteriorly convex, situated in the middle portion of the central sulcus and lying in continuity with the superior frontal sulcus (Fig. 1). The digitation was present in the depth of the central sulcus and was less visible at the surface of the sulcus. The knob had a typical omega shape in 44 hemispheres (73%; Figs. 1 and 2). In 14 hemispheres (23%), the knob was bilobular (Figs. 1 and 2), epsilon shaped, and composed of two adjacent digitations; in two hemispheres, three digitations were observed (Fig. 1E).

Pathological Hemispheres. Identification of the junction between the superior frontal and precentral gyri was easy
in 40 hemispheres (67%), impossible in 12 hemispheres (20%) because of tumor extension (Fig. 1A and B), and uncertain in eight hemispheres (13%) because of anatomical variations. The hand knob could be identified in 52 diseased hemispheres (87%). In these hemispheres, the knob was omega shaped in 45 (75%; Figs. 1 and 2), bilobular and epsilon shaped in six (10%; Figs. 1 and 2), and composed of three digitations in one (Fig. 1). Identification of the hand knob was difficult in eight diseased hemispheres because of tumor mass effect and/or invasion (Fig. 2C and D). The termination of the central sulcus (foot area) was easily recognizable in all but two diseased hemispheres (Fig. 2C and D). Anatomical identification of the central sulcus was confirmed in all 120 hemispheres by fMR imaging and cortical stimulation data.

**Correspondence Between Anatomy of the Central Sulcus and Activation in Normal Hemispheres**

**Hand Area.** Pixels with the highest correlation coefficients were always superimposed on the knob area (Figs. 1 and 2). In 32 hemispheres, the activated area was restricted to the knob itself (Fig. 2C–F), centered on the central sulcus. In 50 hemispheres, activation extended in both the pre- and the postcentral gyri (Table 1). In hemispheres with bilobular knobs (14 hemispheres), signal-intensity changes most frequently involved both digitations (10 hemispheres), with a tendency to predominate around the external or internal ones (six and one hemispheres, respectively; Figs. 1 and 2). In the coronal plane, activation was found at the same axial level as the superior frontal sulcus and the upper portion of the medial frontal gyrus (three–six axial slices).

**Face.** Pixels activated during lip contraction were located lateral to the knob area, in the lower portion of the central sulcus (Fig. 3). Signal-intensity changes usually started at the lower portion of the knob or on the immediately lower slice, extending three to seven slices inferiorly. In only six hemispheres did activation obtained for face movements overlap the external portion of the hand knob. Activation either spanned the whole mediolateral extent of the lower portion of the central sulcus (11 hemispheres) or was more restricted to a smaller medial (five hemispheres), central (three hemispheres), or, more frequently, lateral portion of its surface (six hemispheres). The remaining four hemispheres exhibited no activation on the normal side. On coronal projections, they were located at the same level as the lower part of the middle frontal gyrus, the inferior frontal sulcus, and the upper part of the inferior frontal gyrus.
Activation associated with toe movement was observed around the termination of the central sulcus in all patients (Fig. 3). Activation was located in the uppermost portion of the central area, extending to the upper portion of the paracentral lobule (two–five slices). The termination of the central sulcus was a reliable anatomical landmark for the foot area that was easily recognizable in all normal hemispheres. Most patients had signal-intensity changes located in both the pre- and the postcentral gyri (21 hemispheres), and overlap between the hand and foot areas was uncommon (Table 1). The border between the primary motor (caudal) and supplementary motor (rostral) areas was frequently not clear cut (13 patients).

**Nonprimary Sensorimotor Areas.** Signal-intensity changes were also observed in the supplementary motor area (Figs. 1–3; in 46 patients for hand movements). Activation in the supplementary motor area was located in the posterior portion of the medial frontal gyrus, caudal to the vertical line passing through the anterior commissure, perpendicular to the anterior commissure–posterior commissure plane, and anterior to the upper termination of the precentral sulcus. Premotor activation (37 patients for hand movements) was usually observed on the anterior bank of the precentral gyrus, close to the site of connection with the superior frontal sulcus (Fig. 2). Parietal activation was observed in the antero-inferior parietal cortex and the lateral fissure, forming a distinct cluster that was separated from the postcentral primary sensory area. Activated pixels were less frequently observed around the intraparietal sulcus and the basal ganglia.

**Functional Neuroanatomy of the Central Sulcus in Diseased Hemispheres**

Compared with normal hemispheres, no difference in the relationship between anatomy and activation in either somatotopical territory was demonstrated in diseased hemispheres by using the parameters studied (location of activation relative to anatomical landmarks and overlap between territories). These data are summarized in Table

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**Foot.** Activation associated with toe movement was observed around the termination of the central sulcus in all patients (Fig. 3). Activation was located in the uppermost portion of the central area, extending to the upper portion of the paracentral lobule (two–five slices). The termination of the central sulcus was a reliable anatomical landmark for the foot area that was easily recognizable in all normal hemispheres. Most patients had signal-intensity changes located in both the pre- and the postcentral gyri (21 hemispheres), and overlap between the hand and foot areas was uncommon (Table 1). The border between the primary motor (caudal) and supplementary motor (rostral) areas was frequently not clear cut (13 patients).

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1. Activation during hand movements was restricted to the hand knob in most hemispheres (Figs. 1 and 2). Spread of the activated area outside the knob boundaries was not significantly different between normal and diseased sides. Similar to normal brain, in a few patients were pixels activated in the pre- or the postcentral gyrus only during each of the three motor tasks (Table 1). Overlap between the hand/face and foot/hand activated areas was similar in the normal and diseased hemispheres. Activation obtained for face movements extended in the external portion of the hand knob in six pathological hemispheres, as in normal hemispheres. A separate analysis of patients in whom tumor extended into the precentral gyrus (26 patients; Fig. 2C–F) or in whom there was preservation of the precentral gyrus (34 patients; Figs. 1 and 2A and B) confirmed that the correspondence between the anatomy of the central sulcus and activation was preserved in both groups. However, anatomical landmarks were displaced because of mass effect or edema in some patients. In these patients, signal-intensity changes were still observed in the expected anatomical area, either displaced at the margins of the tumor (Fig. 2C and D) or, in fewer patients, within apparent tumor boundaries (Fig. 2E and F). When present, displacement was highly predictable, given the location of the tumor and the expected anatomical area (Fig. 2C). Thus, the correlation between function and anatomy was very close in both normal and diseased hemispheres.

Correlation of fMR Imaging and Cortical Stimulation

There was good agreement between intra- and preoperative mappings in all patients (Figs. 4 and 5). Thirty-three (92%) of 36 positive sites of stimulation for the hand were located within the margins of the activated area. The remaining sites were within 15 mm of the margins of activated areas. All sites of positive stimulation for the foot and face were within the margin of the activated area. The size of the primary sensorimotor areas activated using fMR imaging was frequently larger than that observed using cortical stimulation. Two patients who presented pixels activated inside tumor boundaries underwent surgery. Cortical stimulation confirmed the presence of motor responses inside tumor boundaries.

Discussion

The main findings of the present study may be summarized as follows. The central sulcus could be identified in all hemispheres by using anatomical landmarks (hand knob) only. There was a high correspondence between anatomical landmarks in the deep portion of the central sulcus on axial slices and the somatotopical organization of primary motor areas. This correspondence was preserved in the diseased hemispheres. Functional MR imag-
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Fig. 4. Correspondence between fMR images and cortical stimulation using intraoperative photographs. A: Surface rendering of the cortex obtained in a patient with a left premotor low-grade glioma who was performing hand movement. The activated area is projected on the surface of the cortex in red around the central sulcus (arrow, both panels). B: Intraoperative view of the same patient obtained in the same orientation as that shown in A. Letters outline the tumor margins. Numerals correspond to the sites of stimulation that elicited hand movements. The positive sites are labeled in A by asterisks. Ant = anterior; Lat = lateral; Med = medial; Post = posterior; T = tumor.

Fig. 5. Correspondence between fMR imaging and cortical stimulation demonstrated using the neuronavigation system. A: Activation obtained for movement of the right hand in a patient presenting with a large low-grade glioma of the left frontal lobe. The central sulcus is indicated by arrowheads in both panels. Pixels with the highest correlation coefficients are superimposed on the knob area. A few pixels are also found in the adjacent premotor and parietal areas, the supplementary motor area, and the contralateral parietal cortex. B: Intraoperative image demonstrating the location of a site that elicited hand movement in the same patient as in A at a corresponding axial level. The positive site of stimulation is circled in red. The corresponding location in A is indicated by the asterisk.
variations in the location of signal changes and the spatial extension of the activated surface. In the majority of patients, signal-intensity changes were located in both pre- and postcentral gyri. Activation in the postcentral gyrus may reflect the sensory components of the movements. Another explanation may be that the motor cortex may also be found in the postcentral gyrus. This hypothesis is supported by electrophysiological studies, although others found the border between areas 4 and 3 consistently within 1 cm of the fundus of the central sulcus. In three patients in the present study, there was activation only in the postcentral gyrus, a finding already reported. This pattern was due to a mismatch (one or two pixels) between anatomical and functional images, and no positive stimulation site was found in the postcentral gyrus. Such a mismatch may be due to echoplanar image artifacts (B0 field variations, geometric distortions, and so forth) and can be simply demonstrated by superimposing the activated pixels on native echoplanar images.

Variations in the spatial extent of the activated area, which are frequently observed in normal as well as in diseased hemispheres, may reflect interindividual variations in the cortical representation of the functional areas, as evidenced in monkeys. For hand movements, the activated area was larger than the knob in some hemispheres, in line with cortical stimulation data, which sometimes elicits motor responses outside the knob area, although in its immediate vicinity. Thus, the knob may not be exactly co-extensive with the motor representation of the hand. Brain plasticity due to the presence of the tumors may also account for variations in the activated surface. The influence of tumors on the number of activated pixels, which was not the topic of the present study, must be specifically addressed. Last, overlap was uncommon between hand/foot and hand/face areas.

Correspondence Between fMR Imaging and Intraoperative Data

There was a good agreement between fMR images and intraoperative mappings. Stimulation confirmed anatomical or fMR imaging data in all 26 patients who underwent stimulation. Ninety percent of positive motor stimulations were found within activated areas, in line with previous results, and the remaining sites were located nearby (within 15 mm of the corresponding area). The size of the activated sensorimotor cortex, however, was frequently larger than that observed using cortical stimulation. Several reasons may account for this fact. First, intraoperative motor responses (short motor event elicited by direct
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cortical stimulation of the surface of the brain only in a patient in a state of general anesthesia and fMR imaging tasks (simple self-paced movement) are different. Second, signal changes associated with task activation may not be confined to small capillaries, but may spread to larger veins. The working model of BOLD contrast imaging postulates that an increase in neuronal activity causes blood flow to increase such that the amount of paramagnetic deoxyhemoglobin in the microvasculature is reduced, leading to an increase in $T_2^*$ and, thus, in signal intensity.11,12 The exact origin of signal-intensity changes (tissue, capillaries, or larger veins) is still a matter of debate, but the contribution of small veins rather than capillaries is favored by the use of a standard 1.5-tesla MR imaging unit, compared with a higher field-strength magnet, and gradient-echo sequences, compared with spin-echo sequences.9 Clinical investigations performed at 1.5 tesla are inherently limited by these technical reasons. In our series, activation followed the structure of the cortical folding and not that of the sulcal vein,13 an outcome arguing against an important contribution of large veins to the signal changes observed. Third, thresholds used to define statistical coefficients influence the size of activated clusters. A higher threshold increases specificity at the expense of sensitivity, however. Despite these inherent methodological problems, the correspondence between findings on fMR imaging and those achieved using cortical stimulation was high.

Conclusions

Present data show that there was a good correspondence between individual brain anatomy and function in the precentral gyrus, confirming previous results for the hand area and showing that the same applies for the foot and face areas. This correspondence was preserved in diseased hemispheres. Neuronavigation techniques giving access to the deep portion of the sulcus during surgery will enable the neurosurgeon to locate primary motor areas more easily by using these anatomical landmarks. Last, these findings may facilitate studies of the reorganization of normal brain activity in individual patients after brain damage.

References


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