Presurgical identification of the primary sensorimotor cortex by functional magnetic resonance imaging

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The ability of functional magnetic resonance (MR) imaging to detect a selective sensorimotor cortex activation in healthy subjects and the feasibility of motor activation in patients with lesions around the central sulcus has been investigated. Twenty-five healthy volunteers performed 100 motor activation trials, using a variety of motor tasks, which were monitored by several image analysis methods. The functional images were obtained using a 1.5-tesla standard MR imaging system magnet with blood oxygenation level–dependent contrast. Four patients were assessed using functional MR imaging and invasive cortical mapping. Rolandic cortex activation was observed in 98% of the trials performed on healthy subjects in which no head motion occurred. Nevertheless, the cortical response was not selective in a task-rest analysis due to concurrent activation of neighboring regions. Across-task comparison analyses were useful in canceling nonrelevant activity in most cases (86%). In the patient group, the region identified as the sensorimotor cortex by invasive means corresponded accurately to the area that was activated in functional MR imaging. Present data support the feasibility of detecting selective activation of the rolandic cortex, even in the clinical setting, leading the authors to suggest the usefulness of this widely available technique in surgical planning.

Key Words • sensorimotor cortex • functional magnetic resonance imaging • cortical mapping

Functional magnetic resonance (MR) imaging based on blood oxygen level–dependent contrast has proved to be sensitive in the detection of functional activity in the primary sensorimotor cortex. This imaging method has been proposed as a noninvasive tool to identify essential cortex prior to surgery, thus improving surgical planning and minimizing postoperative neurological deficits. The potential clinical usefulness of this new MR imaging application has been emphasized in two pioneer studies in which a good correlation between motor mapping with functional MR imaging and invasive cortical stimulation was observed.

Although preliminary results have been encouraging, validating studies are necessary before this functional method can be widely accepted. It has not yet been established which activation task and image analysis methods are suitable for producing strong but selective activation of the primary motor cortex. Rao, et al., elegantly demonstrated that a hand movement that activates the motor cortex may produce no activation if it is externally paced with a metronome and that imagined motor tasks (without real hand movements) activate cortical areas outside the primary motor cortex. Thus, hand movements that display a similar external appearance may activate primary motor cortex, produce no activation, or activate other nearby regions. Conversely, the activation capability of lesions that alter normal motor functioning and distort normal sulcal anatomy is not known.

In this article, we discuss the ability of functional MR imaging to detect a selective activation of the primary sensorimotor cortex using clinically applicable methods in healthy subjects, and the feasibility of using this method to test motor activation in patients with lesions around the central sulcus. Under investigation in our study were both the activation effect of different motor tasks and the imaging procedures that provided identification of the rolandic cortex.

Clinical Material and Methods

This study was approved by the research committees of Santa Creu i Sant Pau and Bellvitge Hospitals.

Healthy Subjects

Twenty-five right-handed volunteers (five men and 20 women), ranging in age from 23 to 35 years, participated
Functional activity around the central sulcus was the most relevant motor cortex using the simple thumb-to-finger opposition task. Sensation tasks (tactile, thermal, and proprioceptive), and one of the remaining tasks. Each of the four subjects performed the simple motor task (the reference task), and one of the remaining tasks. Each of the subjects were instructed to focus on both speed and accuracy of the commands. Four thumb-to-finger opposition tasks, similar in external appearance but different in intentional and attentional requirements, were used. To perform the first motor task (automated motor task), the subjects were instructed to make repetitive thumb-to-finger opposition movements, in unison, at an approximate rate of one per second, and as automatically as possible. For the second motor task (simple motor task), the same movements at the same rate were required, but the subjects were instructed to exert moderate pressure at each finger contact. For the third motor task (alternating motor task), the subjects were required to perform the movements in the second task, but were specifically instructed to force both the flexion and extension phases of the cyclic movement. For the fourth task (complex motor task), the repetitive thumb-to-finger movement was individual and sequential, beginning with the little finger, followed by the middle finger, the ring finger, and finally the index finger. Subjects were instructed to focus on both speed and accuracy of movements. The rate of movements in the demonstration session was 0.5 sequences per second, that is, two opposition movements per second.

Each subject performed two motor activation attempts with both hands (four consecutive motor trials). Twenty-four subjects performed the simple motor task (the reference task), and one of the remaining tasks. Each of the nonreference tasks was performed 16 times (48 activation attempts). One subject performed the simple motor task twice with both hands and, thus, 100 motor activation attempts were completed.

Motor performance was monitored during imaging by two observers, who computed the movement rate achieved. Although the same rate (one movement per second) was required for Tasks 1, 2, and 3, performance was dissimilar during tasks. The number of thumb-to-finger oppositions (mean ± standard deviation) per second that were performed was 1.23 ± 0.6 for Task 1; 0.55 ± 0.3 for Task 2; 0.46 ± 0.1 for Task 3; and 1.54 ± 0.6 for Task 4.

**Motor Task Procedures.** All subjects were trained before assessment in a preparatory session. They were specifically instructed to perform motor tasks without head motion. The procedure and timing were always the same during the tasks. Each subject was positioned supine in the MR imaging system and motion was minimized by using a head holder. In each trial, the first 55 seconds corresponded to the rest condition (eight baseline images) during which the subject was instructed to do nothing. Then a specified motor task was performed successively by each hand for 62 seconds (two sets of nine activation images). The order of tasks was balanced so that half of the subjects started with the right hand and the other half with the left hand.

**Imaging Procedures.** A 1.5-tesla Signa system (General Electric Medical Systems, Milwaukee, WI) with a standard quadrature head coil was used. Functional images were oblique–axial slices selected from a T1-weighted midsagittal view and located halfway between the superior border of the brain and the cingulate sulcus (15 ± 2 mm from the cerebral vertex). The slice was inclined caudally to encompass at least the postcentral sulcus, as illustrated in Fig. 1.

The functional sequence was a spoiled gradient recalled acquisition in a steady state (GRASS) (repetition time 100 msec; echo time 60 msec; pulse angle 28°) with a 256 × 64–pixel matrix within a field of view of 22 cm, and with a section thickness of 5 mm. First order flow compensation gradients were used. Each trial consisted of 26 consecutive images at a single section location, each lasting 6.9 seconds (0.5 seconds for preparatory pulses and 6.4 seconds for real-image imaging). Field homogeneity was adjusted in each subject and in each location by manual shimming of the three axes.

Images were reconstructed in a 256 × 256–pixel matrix. We excluded the first image of each trial because of its precarious steady-state condition and also the images corresponding to the time when the subject was given commands (ninth and 18th images). A t-test image processing method was adopted. The activation images resulted from the pixel-by-pixel calculation of t statistics, comparing signal intensity obtained from different conditions. We displayed only those pixels with a t value of greater than 2.1 (p < 0.05) contained in clusters greater than 13 pixels and pixels with a t value of greater than 4.1 (p < 0.001) contained in clusters greater than three pixels. This threshold selects functional changes above the random level and takes into account both the extent and the consistency of the activations. Each activation attempt was analyzed twice, performing a task-rest comparison.

**Fig. 1.** Blood oxygen level–dependent functional magnetic resonance images showing the selective activation of the sensorimotor cortex using the simple thumb-to-finger opposition task. Functional activity around the central sulcus was the most relevant finding in the picture. The red area is proportional to the activation consistency (t value) of the pixels. The oblique line in the sagittal view represents the anatomical level at which functional activity was assessed in healthy subjects.
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and an “across-hand” comparison (Fig. 2). This latter analysis consisted of the comparison of the right-versus-left hand activation and vice versa (t-test images between the two sets of nine activation images). This analysis may be able to cancel shared (nonlocalized) activity (that is, bilateral changes occurring in premotor areas) and, therefore, to increase selectivity of the activation results. To guide analysis and display results, each activation (t-test) image was fused to a corresponding anatomical (T1-weighted and flow-sensitized) image. The composite images allowed us to identify and exclude nonlocalized changes in the major vascular structures (see Figs. 1–5). We also excluded activity that occurred outside the brain contour delimited in the anatomical image. This procedure enabled us to minimize misinterpretation from nonfocal changes in nonvisualized low-velocity cortical veins and to exclude cerebrospinal fluid artifacts. The presence of motion was finely detected using a cine display. Sequences showing head displacements were rejected.

**Activation Criteria.** The central sulcus was identified using well-established anatomical criteria. Under normal conditions, at the superior axial levels of the brain the precentral sulcus can be easily identified as the sulcus forming a right angle with the superior frontal sulcus. The next posterior sulcus is the central sulcus. When functional changes above the random level were found around this sulcus, the sensorimotor cortex was considered “activated.”

The sensorimotor cortex was considered functionally “identified” in cases in which activity surrounding the central sulcus was the most striking feature in the activation image. Operatively, the number of activated pixels necessary to fulfill the identification criterion was fixed to be at least twice the number of pixels found activated in any other single region.

A nonparametric chi-square test was applied to examine task effects.

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**Fig. 2.** Blood oxygen level–dependent functional magnetic resonance images depicting the widespread activation of the cortical motor system during the complex motor task. Changes occurred in the contralateral sensorimotor cortex and, bilaterally, in premotor regions and supplementary motor area. Identification of the central sulcus was not possible using functional criteria alone in this task-rest analysis (A and B). The “across-hand” comparison analysis (C and D) produced an important cancellation of nonprimary cortex findings and allowed satisfactory functional identification of the central sulcus.

**Fig. 3.** Blood oxygen level–dependent functional magnetic resonance images depicting the cortical activity detected during the simple motor task in the patients in Case 1 (A and B) and Case 2 (C and D), at two slightly different levels. The anatomical relationship between the tumor and the activated cortex could be established even in cases in which the central sulcus was notably displaced (C and D). The sensorimotor cortex could be successfully identified despite the supplementary motor area activation in some trials. The asterisks indicate the central sulcus according to the invasive mapping.
Patient Population

Four patients were assessed using both functional MR imaging and invasive cortical mapping. These patients were surgical candidates, selected on the basis of tumor presence around the central sulcus detected in a standard MR study. The clinical characteristics of this group are described in Table 1.

Each patient was required to perform the simple thumb-to-finger opposition task six times with each hand. Thus, 24 of the 48 trials performed by patients corresponded to the hand contralateral to the lesion. The imaging procedures used and the activation criteria applied were the same as those specified in the tests of healthy subjects, but functional assessment was performed at several anatomical levels of the distorted region.

Direct intraoperative cortical stimulation was used to identify the rolandic cortex in each patient. This mapping technique is fully described by Berger and Ojemann. Direct stimulation was initiated with a low current (2 mA), which was increased 0.5 to 1 mA each time until the desired responses were observed. When a motor response was elicited or the patient reported a specific feeling, the cortical site was marked with a small numbered ticket. The tumor served as a reference landmark to compare the results obtained with functional MR imaging and intraoperative electrical stimulation. The identification of the central sulcus with MR imaging was considered validated when the position of the activated cortex in relation to the tumor (in anteroposterior, superioinferior, and mediolateral slices) coincided in both functional methods. The amount of normal tissue extending between the tumor and the activated cortex was also estimated.

Sagittal, axial, and coronal routine projections were used to locate the activated area. High-resolution three-dimensional spoiled GRASS sequences (repetition time 44 msec; echo time 4 msec; flip angle 45°; section thickness 1.2 mm; field of view 22 cm; and matrix size 256 × 160 pixels) were also obtained to investigate which display method provided the most useful anatomical approach. These three-dimensional sequences were reconstructed on a workstation (SPARCstation 20; Sun Microsystems, Mountain View, CA), using commercially available software (GE Advantage Windows software, Version 1.2; General Electric Medical Systems, Milwaukee, WI).

Results

Motor Activation in Healthy Subjects

Twelve of the 100 motor trials performed by healthy subjects were excluded from the analysis due to head motion. Task activation of the primary sensorimotor cortex occurred in 98% of the 88 trials that were analyzed. Consequently, in only two cases were functional changes not found around the central sulcus.
Although activation of the primary cortex was customary, the task-rest analysis alone was not sufficient to accomplish successful identification of the motor strip in most cases, because other regions also appeared activated in the functional image. Indeed, rolandic functional activity stood out from that of other regions in only 44% of cases. Nevertheless, when the task-rest and across-hand analyses were combined, activity in the primary cortex was the most relevant finding in 86% of the trials. Thus, because of the cancellation effect of activity in nonprimary cortex, the across-hand analysis increased the selectivity of the findings substantially. Changes found around the central sulcus, however, had similar localization using the two types of analyses. Table 2 shows the activation results. The signal difference between motor task and rest was 7.0% ± 1.3% on average (in the pixels surrounding the central sulcus with t = 4.1 and p < 0.001).

**Task Effect.** Table 2 details the findings from each different task. The activation produced during the simpler tasks had a tendency to be more selective but weaker, whereas that produced during the more complex tasks was stronger but more diffuse.

The only two cases of failure to activate the sensorimotor cortex occurred during the automated motor task. However, selective activation of the primary sensorimotor cortex occurred more frequently during the simpler tasks (Tasks 1 and 2) than in the more complex tasks (Tasks 3 and 4). Indeed, after the task-rest analysis, the primary cortex could be identified in 51.7% of the automated and simple motor trials (on average), and in 30% of alternating and complex trials (chi-square = 3.78, p = 0.049). The difference disappeared when task-rest and across-hand analyses were combined.

Activation of regions other than the primary sensorimotor cortex was common (Table 2). The supplementary motor area was the region found to be activated in most motor activation attempts (66%). The more complex tasks activated a greater number of secondary regions. To make the analysis simpler, we assessed Tasks 1 and 2 again as a single group and Tasks 1 and 2 as another group. The simpler tasks activated 32.8% of these three secondary regions, whereas the more complex hand movements activated 61.1%. Differences were highly significant (chi-square = 19.2, p = 0.00007).

**Motor Activation in Patients**

Of 24 attempts to activate the sensorimotor cortex on the lesion side, 10 (42%) could not be analyzed because of excessive head motion. This occurrence was significantly higher (chi-square = 11.6, p = 0.001) than the corresponding proportion in healthy subjects (12%). Functional activity was absent in the rolandic cortex in three of the 14 analyzed sequences (21%). This proportion was also higher in the patient group (chi-square = 9.5, p = 0.002).

### TABLE 1

**Clinical characteristics of patients**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Presenting Symptoms</th>
<th>Preop Motor Deficit</th>
<th>Preop Sensory Deficit</th>
<th>Preop Medication</th>
<th>Pathological Diagnosis</th>
<th>Neurological Examination*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>34, M</td>
<td>complex partial seizures</td>
<td>none</td>
<td>none</td>
<td>dexamethasone</td>
<td>low-grade astrocitoma</td>
<td>unchanged</td>
</tr>
<tr>
<td>2</td>
<td>31, M</td>
<td>generalized seizures</td>
<td>mild</td>
<td>mild</td>
<td>benzodiazepine</td>
<td>single metastasis</td>
<td>unchanged</td>
</tr>
<tr>
<td>3</td>
<td>25, M</td>
<td>generalized seizures</td>
<td>mild</td>
<td>moderate</td>
<td>dexamethasone</td>
<td>adenocarcinoma</td>
<td>unchanged</td>
</tr>
<tr>
<td>4</td>
<td>54, M</td>
<td>focal motor seizures</td>
<td>moderate</td>
<td>severe</td>
<td>carbamazepine</td>
<td>oligodendroglioma</td>
<td>unchanged</td>
</tr>
</tbody>
</table>

* Assessed 2 months after surgery.

### TABLE 2

**Activation results in analyzed trials of 25 healthy subjects**

<table>
<thead>
<tr>
<th>Type of Motor Task</th>
<th>Automated (14 trials)</th>
<th>Simple (44 trials)</th>
<th>Alternating (16 trials)</th>
<th>Complex (14 trials)</th>
<th>Total Tasks (88 trials)</th>
</tr>
</thead>
<tbody>
<tr>
<td>rolandic activation</td>
<td>12 (86%)</td>
<td>44 (100%)</td>
<td>16 (100%)</td>
<td>14 (100%)</td>
<td>86 (98%)</td>
</tr>
<tr>
<td>rolandic identification</td>
<td>12 (86%)</td>
<td>44 (100%)</td>
<td>16 (100%)</td>
<td>14 (100%)</td>
<td>86 (98%)</td>
</tr>
<tr>
<td>task-rest analysis</td>
<td>7 (50%)</td>
<td>23 (52%)</td>
<td>5 (31%)</td>
<td>4 (29%)</td>
<td>39 (44%)</td>
</tr>
<tr>
<td>overall analysis</td>
<td>12 (86%)</td>
<td>40 (91%)</td>
<td>12 (75%)</td>
<td>12 (86%)</td>
<td>76 (86%)</td>
</tr>
<tr>
<td>coactivated areas</td>
<td>7 (50%)</td>
<td>26 (59%)</td>
<td>14 (87%)</td>
<td>11 (79%)</td>
<td>58 (66%)</td>
</tr>
<tr>
<td>supplemental motor area</td>
<td>1 (7%)</td>
<td>4 (9%)</td>
<td>6 (37%)</td>
<td>8 (57%)</td>
<td>19 (22%)</td>
</tr>
<tr>
<td>precentral</td>
<td>6 (43%)</td>
<td>13 (29%)</td>
<td>9 (56%)</td>
<td>7 (50%)</td>
<td>35 (40%)</td>
</tr>
<tr>
<td>postcentral</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
Three patients showed selective and consistent activation of a specific region, which was assumed to be the sensorimotor cortex. Figures 3 and 4 depict the nature of these findings. Functional activity at the putative location of the supplementary motor area was observed in two patients, although these changes were less consistent (Fig. 3). The results obtained from the patient in Case 4 were poor. Five of the six sequences that were performed could not be analyzed because of excessive motion. In the remaining trial, functional changes were not very focal, although they surrounded a discrete gyrus (Fig. 5). The most striking changes, however, were found within the tumor; these changes corresponded to enlarged venous vessels, which could be verified during surgery.

Intraoperative cortical stimulation confirmed the findings obtained with functional MR imaging. The correspondence between the MR findings and electrical stimulation was complete in Cases 1, 2, and 3 (with regard to establishing the relative positions of the central sulcus and tumor and assessing the amount of normal tissue existing between both structures). In Figs. 3A, 3D, 4A, and 5, we placed an asterisk between the sensory and motor cortices to indicate the point at which direct cortical stimulation produced the consistent responses. Note the good correlation between both methods concerning the identification of the central sulcus; note also the tendency of functional MR imaging to detect activity that is deep (because the veins draining the sensorimotor cortex are also deep).

Discussion

The analysis of a large series of motor activation attempts allowed us to establish the ability of clinically applicable functional MR imaging to detect a selective task activation of the primary sensorimotor cortex. Reference standards from healthy subjects are necessary to determine the effect of motor dysfunction and anatomical distortion on the sensitivity of functional MR imaging in patients.

The activation of the sensorimotor cortex was observed in 98% of the analyzed trials. Thus, self-paced repetitive motor tasks seem appropriate to produce a noticeable cortical response. The movement rate was not a decisive factor to activate primary areas, but directing the subject's attention to task performance could be beneficial in minimizing the risk of activation failure. As in previous reports of shorter series, the sensitivity of the technique applied was sufficient to detect functional changes occurring during fine finger movements.

The finding of functional activity in the primary cortex must be selective to distinguish the eloquent region from the others. Functional changes in premotor (including the supplementary motor area) and postcentral regions were common and depended, to some extent, on the complexity of the task; however, they did occur during even the simplest tasks (as noted previously by Boecker and associates1). A strategic image analysis is useful to highlight meaningful changes. Indeed, the identification of the sensorimotor cortex became common when the task-rest and across-hand image analyses were combined. Despite this, the activation of neighboring regions, together with the presence of head motion, accounted for an important amount of identification failure. Although activation attempts can be repeated many times in a single subject and in a single session, further effort must be made to minimize these sources of unsuccessful attempts.

Interesting conclusions may be drawn from the initial experience in patients. By applying the functional MR imaging procedures used to obtain the motor activation pattern in healthy subjects, selective activation of the sensorimotor cortex was obtained in three patients. In the other patient, changes were somewhat widespread. Intraoperative mapping accurately verified imaging findings, and, thus, we can conclude that lesions that distort the cortical topography of sulci do not necessarily impede presurgical functional identification of the central sulcus.

The functional MR imaging technique used in this study detects changes proceeding from venous vessels, both large and small. Localized changes are only those that can be ascribed to a small region of the cortex. The most striking changes we observed in functional MR images could be anatomically related to the central sulcus (see Figs. 1–5). Nevertheless, these changes most probably corresponded to the central sulcus's major draining vessels and, thus, may not indicate an exact level in the homunculus or in the bank of the gyrus that was specifically activated during the motor task. From a practical point of view, however, a major contribution to surgical planning would be to establish the relative position of the central sulcus and the lesion and to estimate the amount of normal tissue between both structures. Our findings and those of Jack and colleagues11 and Yousry, et al., suggest that these data can be provided by current functional MR imaging.

Because signal changes may occur throughout the entire draining system in blood oxygenation level–dependent contrast functional MR imaging, venous structures far from the cortex of interest can be mistaken for active cortex unless previously identified. The anatomical and flow-sensitized reference image, acquired at the same location as the functional experiments, allowed us to localize major vascular structures and to exclude accurately nonlocalized changes outside the brain contour. Magnetic resonance angiography, which emphasizes the low-velocity (venous) flow, may also be useful in minimizing this source of misinterpretation.

The tumor was the reference landmark used to compare functional MR imaging and intraoperative mapping. An accurate illustration of the functional findings may play a relevant role in planning the neurosurgical approach. A volume rendering of the brain surface may be useful; however, in our opinion, depiction of the activations on an oblique slice, capable of reproducing the surgeon’s view after craniotomy, is better because it shows increased anatomical resolution (Fig. 4).

Although their attitude was fully collaborative, our patients represented a less selective study group in terms of their proficiency in understanding the exact instructions of the task and in avoiding head motion. This can explain in part the increase in failed activation attempts recorded in patients. In addition, the specific clinical status of each patient may potentially include factors capable of interfering with cortical reactivity.

It remains to be established whether severe motor dysfunction will reduce the probability of finding focal activation in the motor cortex. Findings from the patient in...
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Case 4 agree with this possibility and are in accordance with previous functional studies in which widespread cortical activity has been described in patients with severe pyramidal system damage.21 Similarly, it is unknown whether the alteration in brain activity associated with seizures (or the interictal state) may change cortical responses. In a preliminary report, however, signal changes in epileptic patients approximated those observed in volunteers.14 Furthermore, the effect of many different parameters—such as age, medical treatments (dexamethasone, antiepileptic drugs, or benzodiazepines), paramagnetic iron deposits due to past hemorrhage, and anomalous venous vessels near the tumor—on the capability of this functional technique to detect selective functional activity is unknown.

Although further research will be necessary to establish which specific patients can benefit from this noninvasive functional method, our initial experience showed that functional MR imaging is feasible in the clinical setting and leads us to suggest the usefulness of this widely available method in surgical planning.

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