Somatotopic mapping of the human primary motor cortex with functional magnetic resonance imaging

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Article abstract-We applied functional magnetic resonance imaging (FMRI) to map the somatotopic organization of the primary motor cortex using voluntary movements of the hand, arm, and foot. Eight right-handed healthy subjects performed self-paced, repetitive, flexion/extension movements of the limbs while undergoing echo-planar imaging. Four subjects performed movements of the right fingers and toes, while the remaining subjects performed movements of the right fingers and elbow joint. There was statistically significant functional activity in the left primary motor cortex in all subjects. The pattern of functional activity followed a topographic representation: finger movements resulted in signal intensity changes over the convexity of the left motor cortex, whereas toe movements produced changes either at the interhemispheric fissure or on the dorsolateral surface adjacent to the interhemispheric fissure. Elbow movements overlapped the more medial signal intensity changes observed with finger movements. Functionally active regions were confined to the cortical ribbon and followed the gyral anatomy closely. These findings indicate that FMRI is capable of generating somatotopic maps of the primary motor cortex in individual subjects. *NEUROLOGY 1995;45* 919-924

Since the discovery by Fritsch and Hitzig [1] that electrical stimulation of the exposed cerebral cortex of the dog could evoke movements of contralateral body parts, investigators have been interested in mapping the brain centers that control voluntary movements. In a classic series of experiments, Ferrier [2] observed that stimulation of the primate precentral motor cortex (Brodmann area 4) near the interhemispheric fissure resulted in movements of the leg, whereas stimulation near the lateral fissure produced movements of the tongue and mouth. Upper extremity movements were evoked with stimulation sites located between the lateral and interhemispheric fissures. Leyton and Sherrington [3] expanded upon these findings by mapping the precentral motor cortex of several primate species and showed an orderly representation of the movements elicited in differing parts of the body by cortical stimulation. This work was further refined by Woolsey et al, [4] who obtained some of the most accurate and detailed maps of the primate motor cortex. Penfield and Boldrey [5] extended mapping of the motor cortex to the human species by using direct cortical stimulation of awake patients prior to surgical resection for the treatment of epilepsy. The Penfield studies produced a somatotopic map for motor output that has become known as the motor "homunculus". More recently, others [6-8] have demonstrated somatotopy noninvasively in humans by electrical and magnetic stimulation of the motor cortex through the scalp. The motor responses evoked by stimulation approaches, however, are qualitatively different from those evoked by focal synaptic inputs under conditions of natural activation,

thus limiting the generalizability of the resultant maps [9].

An alternative approach is to localize regions of brain activity while subjects perform voluntary movements. During the past decade, functional imaging studies have demonstrated movement- induced increases in regional cerebral blood flow (rCBF) in the primary motor cortex, [10-12] although somatotopy has been the subject of only three studies [11,13,14]. Grafton et al [13] found that arm and finger movements produced indistinguishable areas of increased rCBF approximately two-thirds of the distance from the lateral fissure to the interhemispheric fissure. In contrast, toe movements resulted in rCBF changes extending from the interhemispheric fissure to the dorsolateral surface, and tongue movements resulted in bilateral changes close to the lateral fissure. This study [13] demonstrated that PET can resolve the gross details of the motor map. In a follow-up study, Grafton et al [14] examined within-arm somatotopy, comparing shoulder, elbow, wrist, finger, and thumb movements of the right hand. They demonstrated an overlapping somatotopic distribution in the motor cortex, with thumb responses most ventrolateral and shoulder responses most dorsomedial. Colebatch et al [11] compared rCBF changes in several upper extremity movements, including abduction of the index finger, making a fist, sequential finger-to-thumb opposition, and shoulder flexion. Shoulder movements produced rCBF changes higher on the primary motor cortex than the movements of more distal limb segments, which overlapped in area. Other techniques for examining somatotopy during voluntary movements include magnetoencephalography [15] and scalp-recorded EEG potentials [16].

Functional magnetic resonance imaging (FMRI) is a new, noninvasive imaging tool based on fast acquisition techniques, such as echo-planar imaging [17]. The observed signal enhancement may be due to a decrease in deoxyhemoglobin concentration in the microvasculature [18] resulting from local increases in blood oxygenation during cerebral tissue activation, [19] producing an increase in magnetic homogeneity. The resulting MR signal change has been called the BOLD (blood oxygen level dependent) contrast effect. Recent FMRI studies [20-23] have demonstrated changes in signal intensity within the contralateral primary motor cortex during self-paced, repetitive finger movements. In a recent study, [24] we used FMRI to examine the effects of motor task complexity on patterns of activation within the primary and secondary motor cortices. We did the current study to determine if the FMRI technique is capable of generating somatotopic maps of the primary motor cortex in response to voluntary movements of the hand, arm, and foot in individual subjects.

Methods. Subjects. Eight healthy volunteers (table), ranging in age from 22 to 40, served as subjects. All subjects completed the Edinburgh Handedness Inventory [25] and were strongly right-handed. Potential subjects were excluded if they had a history of neurologic disorders (including seizures and serious head injuries), psychiatric illness, or substance abuse. Also excluded were potential subjects taking psychoactive medications. Subjects were paid for their participation and gave informed consent according to institutional guidelines.

Imaging procedures. FMRI was conducted on a commercial 1.5-T scanner (Signa, General Electric Medical Systems, Milwaukee, WI) equipped with a prototype 30.5-cm internal diameter three-axis local gradient head coil and an elliptical endcapped quadrature radiofrequency coil (designed by E.C. Wong [26,27]). The gradient and radiofrequency coils enable whole-brain echo-planar imaging in axial, sagittal, or coronal planes. Foam padding was used to limit head motion within the coil. The subject's neck was flexed 25 degrees forward in the scanner (relative to standard MRI orientation) to enable the entire primary motor cortex to be observed in the same coronal plane.

Scanning began with the acquisition of sagittal images obtained with standard GRASS (gradient-recalled

at steady-state) pulse sequences using the following imaging variables: 24-cm field of view, 600-msec TR, 10-msec TE, 90 degrees flip angle, 5-mm section thickness, and a 256 x 128 matrix. These standard images were used to locate positions for the three coronal images used for functional imaging. The centers of the coronal sections were located 5, 15, and 25 mm anterior to the postcentral sulcus, as visualized from the sagittal localizers. The coronal GRASS images (5-mm thickness) served as the high-resolution anatomic images upon which functional activity was subsequently superimposed (see "Image analysis" section below).

Functional imaging was conducted using a single-shot, blipped, gradient-echo echo-planar pulse sequence [21]. Data acquisition time was 40 msec to acquire a 64 x 64 image (voxel dimensions = 3.75 x 3.75 x 10.0 mm) with a field of view of 24 cm. A series of 104 sequential images was collected simultaneously from the three 10-mm contiguous axial sections. The interscan interval (TR) was 2 seconds (total scanning duration = 208 seconds).

Motor activation techniques. Each 104-image echo-planar series consisted of multiple periods of "baseline" alternating with periods of muscle "activation". Each series began with four baseline images (8-second interval) allowing MR signal equilibrium to be reached, followed by 100 images during which activation alternated with baseline every 10 seconds (10 images/cycle, 20 seconds/cycle, 10 cycles for a total data collection time of 200 seconds). The beginning and end of each motor activation period was signaled by digitized human speech ("go" or "stop") presented over a pneumatic audio system; precise timing was controlled with a microcomputer. Subjects were instructed to keep their eyes open throughout the scanning series. Subjects were provided instructions and allowed to practice the motor activation tasks prior to scanning.

The activation tasks consisted of self-paced, unconstrained, repetitive movements of the fingers, elbow, and toes on the subjects' right, dominant side. The finger movements consisted of simultaneous flexion and extension of the metacarpophalangeal (MCP) joints (except the thumb) as quickly as possible. Subjects tapped their fingers on a flat surface. The toe movements consisted of repetitive, simultaneous flexion and extension of the MCP joints. The arm movements consisted of flexion and extension of approximately 25 degrees at the elbow in midposition at the forearm; the shoulder was at approximately 20 degrees flex, internal rotation, and neutral position with respect to abduction-adduction. Four subjects performed movements of the fingers and toes; the remaining four subjects performed movements of the fingers and elbow Table 1.

Subject	Sex	Age	LQ	Condition
1	M	26	85	F, T
2	F	22	78	F, T
3	M	40	100	F, T
4	M	22	85	F, T
5	F	24	100	F, E
6	F	24	100	F, E
7	M	28	60	F, E
8	F	30	100	F, E

LQ Laterality quotient.
F Fingers.
T Toes.
E Elbow.

Table 1. Subject information

Image analysis. The method employed at our medical center to generate functional images from FMRI data has been described in detail elsewhere [24,28]. Briefly, functional images were generated off-line

on a workstation using software image analysis programs custom-written at our institution. The generation of functional images consisted of a three-stage process, as described previously [24]. The first stage involved a thresholding procedure, which identified only those voxels displaying signal changes corresponding to the temporal pattern of the activation task. This was accomplished by correlating the normalized imaging data from each voxel with a reference waveform. For the present study, we have assumed that the functional activity resembled a sinusoidal waveform. All voxels with a correlation less than $r = 0.50$ were excluded from further analysis. This cutoff value was selected to correspond with the Bonferroni-adjusted alpha level ($p = 2.4 \times 10^{-} 5$) required when performing multiple statistical comparisons, ie, based on an estimated maximum of 2,100 voxels in a coronal brain section.

Because the correlation contains no information concerning response magnitude, the second stage reintroduced magnitude information for voxels surviving the threshold analysis; for each voxel the correlation coefficient was multiplied by the standard deviation. This value was then multiplied by a constant to adjust the brightness of the pixels in the functional image (the same constant was used for all images).

The final stage was the superimposition of the functional image on the high-resolution anatomic images. This was accomplished by interpolating both the functional and anatomic images to 256 x 256 pixels. The functional images were colorized in the following manner: positive values (ie, pixels in phase with the reference waveform) were displayed on a red (minimum) to yellow (maximum) scale, negative values (ie, pixels 180 degrees out of phase with the reference waveform) were displayed on a blue (minimum) to cyan (maximum) scale, and pixels not making the cutoff (stage 1) were made transparent. These colorized functional images were then superimposed on the anatomic images.

Results. For all eight subjects, maximal functional activity was observed in the second (middle) section, which most closely corresponds to the posterior area of the precentral gyrus according to sagittal and axial localizers. Functional activity from the anterior and posterior images was either redundant with the second section or nonexistent. Consequently, functional activity is presented from the middle brain section only.

Statistically significant MR signal changes were observed within the left motor cortex in all subjects and movement conditions. Functional images comparing finger and toe movements and finger and elbow movements are presented in the Figure 1. Finger movements resulted in the most robust signal changes, which were located over the convexity of the left motor cortex. The areas of activation followed the gyral anatomy closely, with almost all signal changes occurring within the gray matter either at the cortical surface or within the folds of the cortical gyri.

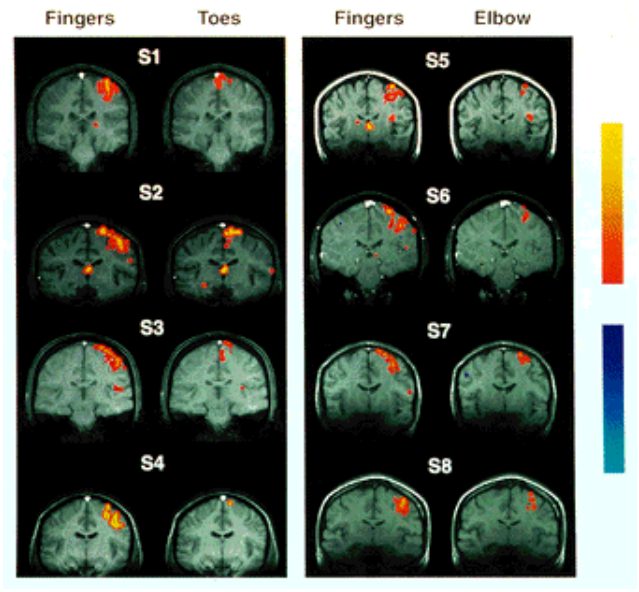

Figure 1. Functional images for finger and toe movements for subjects 1 through 4 and finger and elbow movements for subjects 5 through 8. Positively correlated pixels (ie, in phase with the reference waveform) are indicated on a red (minimum) to yellow (maximum) color scale, while negatively correlated pixels (ie, 180 degrees out of phase with the reference waveform) are displayed on a blue (minimum) to cyan (maximum) scale. The subject's right is on the reader's left

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Movements involving the toes produced signal intensity changes in the left hemisphere that were more medial than those produced by finger movements. Signal changes were located within the interhemispheric fissure, on the dorsolateral surface adjacent to the interhemispheric fissure, or both. Little or no spatial overlap was observed between motor cortex activation sites for toe and finger movements.

Signal intensity changes for elbow movements overlapped those observed with finger movements. The region of activation, however, was smaller and more medially positioned on the motor cortex according to visual inspection of the figure.

Some degree of intersubject variability was present, possibly due to variations in normal gyral anatomy as well as some variability in the orientation of the brain section relative to the primary motor cortex. No functional activity was observed in the ipsilateral, right hemisphere. Less consistent areas of activation were observed adjacent to the third ventricle and around the insular region of the left hemisphere.

Discussion. These preliminary findings suggest that FMRI can noninvasively produce somatotopic maps of the primary motor cortex in individual human subjects. The resultant maps are generally consistent with those obtained from electrophysiologic and PET techniques, establishing the convergent validity of the FMRI method. Regional areas of activation were present in all subjects in each of the paired motor conditions. The strongest sites of activation were always confined to the cortical gray matter of the left motor cortex, contralateral to the side of movement. Toe movements resulted in a medial area of activation that did not overlap with finger or elbow movements. In contrast to the intraoperative maps generated by Penfield, but consistent with recent PET studies, [11,14] finger and elbow movements overlapped, with the elbow site being smaller and located within the more dorsomedial region of the finger movements.

In comparing our FMRI maps with those generated by cortical stimulation methods, voluntary movements seemed to result in larger regions of activation along the motor cortex than those evoked by electrical stimuli. Even simple movements of a single joint can require the coordinated activity of

several muscle groups depending on the extent of limb stabilization provided. Flexions of the fingers are often accompanied by contractions of muscles of the wrist and even the elbow [29]; likewise, movements of the toes may involve ankle muscles. That we observed functional activity in regions of the motor cortex thought to subserve wrist and elbow movements during finger movements is, therefore, not surprising. Activity in the presumptive "ankle" region (on the lateral surface of the interhemispheric fissure) was also present in three of four subjects (S1, S2, and S3) during toe movements. Thus, the maps generated during voluntary movements are useful in gaining a more comprehensive understanding of the functional brain systems involved in the programming of even simple, repetitive movements.

The spatial resolution used in the present study was relatively coarse (3.75 x 3.75 x 10 mm or 0.14 ml). Higher spatial resolutions are needed, however, to examine the fine details of the somatotopic map, a subject that has generated considerable debate in the animal literature. Using intracortical microstimulation methods, for example, Strick and Preston [30,31] mapped the motor representation of digits and wrist in the motor cortex of the lissencephalic squirrel monkey and found two spatially separate representations of the digits and wrist. Somatosensory afferent input from the cutaneous receptors (hair, skin) projected to the caudal zone and the deep receptors to the rostral zone. In the macaque, Murphy et al [32] demonstrated that the forelimb is represented by concentric and overlapping rings, with the wrist, elbow, and shoulder around a central core of finger representation. Waters et al [33] noted that the baboon motor cortex is topographically organized in a mosaic fashion with multiple representations of the same muscle. In a recent single-unit recording study, Schieber and Hibbard [34] found considerable spatial overlap of cortical territories for movements of different fingers. They conjectured that rather than being specified by a somatotopic map, each finger movement appears to be specified by a neuronal population distributed throughout the motor cortex hand area. These conflicting findings from nonhuman primates have not been examined in detail with high-resolution functional imaging techniques in humans. Menon et al [35] observed activation-induced FMRI signal changes in voxel sizes as small as 1.2 microliters, and Engel et al [36] demonstrated reliable differences in activity between cortical locations separated by less than 1.4 mm. Thus, FMRI may play a future role in resolving some of the controversies regarding the fine details of somatotopy within the human primary motor cortex.

Three methodologic limitations should be noted regarding this study. First, we observed that echo-planar pulse sequences produce unreliable functional maps from facial and tongue movements. Such images are distorted by changes in homogeneity within the local magnetic field, occurring most often with movements within and around the oral cavity. Second, we allowed subjects to perform the tasks in an unrestrained, self-paced manner; in future studies, researchers may wish to control and manipulate the subjects' rate, force, amplitude, and duration of movement. Finally, movements may not have been confined to a single joint because proximal joints were not constrained. Future studies may require the use of splinting and stabilization devices coupled with the use of EMG recordings to establish that movements were confined to the muscle groups of interest.

We conducted the present study on a commercial MR imager. With FMRI capability a possibility in most major medical centers in the near future, we can envisage functional mapping studies of patients being performed at the same time structural MR studies are performed [37]. In the surgical control of epilepsy, for example, FMRI functional maps may augment and potentially replace invasive, intraoperative techniques that require the patient to be awake during the surgical procedure.

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