Functional magnetic resonance imaging of sensory and motor cortex: comparison with electrophysiological localization

AINA PUCE, PH.D., R. TODD CONSTABLE, PH.D., MARIE L. LUBY, M.ENG., GREGORY MCCARTHY, PH.D., ANNA C. NOBRE, PH.D., DENNIS D. SPENCER, M.D., JOHN C. GORE, PH.D., AND TRUETT ALLISON, PH.D.

Neuropsychology Laboratory, Veterans Affairs Medical Center, West Haven, Connecticut; and Section of Neurosurgery, Departments of Neurology and Diagnostic Radiology, Yale University School of Medicine, New Haven, Connecticut

Functional magnetic resonance (MR) imaging was performed using a 1.5-tesla MR system to localize sensorimotor cortex. Six neurologically normal subjects were studied by means of axial gradient-echo images with a motor task and one or more sensory tasks: 1) electrical stimulation of the median nerve; 2) continuous brushing over the thenar region; and 3) pulsed flow of compressed air over the palm and digits. An increased MR signal was observed in or near the central sulcus, consistent with the location of primary sensory and motor cortex.

Four patients were studied using echo planar imaging sequences and motor and sensory tasks. Three patients had focal refractory seizures secondary to a lesion impinging on sensorimotor cortex. Activation seen on functional MR imaging was coextensive with the location of the sensorimotor area determined by evoked potentials and electrical stimulation. Functional MR imaging provides a useful noninvasive method of localization and functional assessment of sensorimotor cortex.

KEY WORDS • functional localization • cortical stimulation • sensorimotor cortex • somatosensory evoked potentials • functional magnetic resonance imaging

Focal magnetic resonance (MR) signal changes related to functional activation of cerebral cortex have been previously reported. The ability to localize cortical function by functional MR imaging could be useful in preoperative neurosurgical planning, potentially sparing patients invasive preoperative investigations. Functional MR imaging makes use of the paramagnetic effect of deoxyhemoglobin, which acts as an endogenous contrast agent; hence, a T$_1$-weighted MR sequence can exploit the signal difference produced by the different magnetic susceptibilities and signal decay rates of activated and nonactivated tissue. The high spatial resolution of functional MR images offers advantages in the study of patients in whom resection may impinge on cortical areas involving language, vision, or sensorimotor function. Functional MR imaging is noninvasive and does not require contrast agents, thus allowing repeated studies in a single patient. Functional MR images of motor cortex have been reported at 4- and 1.5-tesla field strengths.

Functional MR imaging data are presented from activation studies of sensorimotor cortex in normal subjects and in patients undergoing resection for intractable seizures. Imaging was performed with conventional and echoplanar image acquisition on a 1.5-tesla magnet. We demonstrate that activation of the hand area of sensorimotor cortex can be reliably achieved by hand squeezing, brushing the hand, or blowing air over the hand. To validate the functional MR findings, sensorimotor activation was compared to the location of sensorimotor cortex using somatosensory evoked potentials (SSEPs) elicited by median nerve electrical stimulation and the location of motor cortex determined from cortical stimulation.

Clinical Material and Methods

Study Groups

Six neurologically normal control subjects of whom five were right handed (three women and three men) aged 25 to 59 years were studied via functional MR imaging to establish the efficacy of different sensory and motor tasks. Four patients were studied preoperatively: three had a focal seizure disorder secondary to a tumor located within or in proximity to the sensorimotor cortex of the hand.
Functional MR imaging of sensorimotor cortex

and the fourth had intractable posttraumatic seizures, despite previous excision of the putative seizure focus. Localization of the seizure focus included use of long-term electroencephalogram–video monitoring of spontaneous seizures via implanted subdural multicontact grids and strip electrodes. Subdural recordings of SSEPs and electrical stimulation of the brain were performed to localize sensory and motor cortex. All subjects provided informed consent and studies were approved by the Human Investigation Committee of Yale University School of Medicine.

Activation Tasks

In the motor task, all subjects (six controls and four patients) squeezed sponges repetitively (at approximately 2 Hz) for the duration of the imaging. Three sensory tasks were used: 1) electrical stimulation of the median nerve at the wrist (5–30 Hz and 0.5 msec duration, constant-current pulses at 2–8 mA) was performed in three control subjects; 2) an experimenter brushed the subject’s palms and digits continuously with a nonmetallic brush in all controls and used one pulse for two patients; 3) pulsed compressed air, blown through a circular loop of plastic tubing with intermittent holes, was moved continuously over the palm and digits in all controls. In each activation task, the side of stimulation was alternated for each imaging run.

Magnetic Resonance Imaging Studies

A 1.5-tesla MR imager (General Electric Signal, Milwaukee, WI) with a standard quadrature head coil and echo planar capability (Instascan; ANMR Systems Inc., Wilmington, MA) was used. Anatomical sagittal images were obtained ($T_1$-weighted: repetition time (TR), 400 or 500 msec; echo time (TE), 14 msec; number of excitations (NEX), 2; field of view (FOV), 40 cm; slice thickness, 7 mm; and imaging matrix 256 $\times$ 192 or fast spin–echo sequence: TR, 3000 msec; TE, 98 msec; NEX, 2; FOV, 40 cm; slice thickness, 7 mm; echo train length (ETL), 16; imaging matrix 256 $\times$ 192). Contiguous axial slices through the level of sensorimotor cortex (two slices in controls and three in patients) were selected using the midline sagittal image; anatomical MR images were similarly obtained. An axial three-dimensional spoiled-echo gradient-recalled acquisition in the steady-state (SPGR) series was also obtained in all subjects (TR, 25 msec; TE, 5 msec; $\alpha$, 45°; NEX, 2; FOV, 20–24 cm; slice thickness, 2 mm; imaging matrix 256 $\times$ 192). In all patients and some controls, axial MR angiographic images were also acquired (TR, 45 msec; TE, 11 msec; $\alpha$, 45°; NEX, 1; FOV, 18 cm, flow compensation; slice thickness, 1.5 or 2 mm; imaging matrix 256 $\times$ 192).

Functional MR images were acquired using two acquisition protocols: in the first, a conventional gradient-echo series was employed for each task condition in normal subjects (TR, 120 msec; TE, 45 msec; $\alpha$, 40°; NEX, 2; flow compensation; FOV, 40 cm; slice thickness, 7 mm; imaging matrix 256 $\times$ 128). A total scan time of 20 seconds was used for two slices; one image per slice was taken for each subject. Alternated left and right hands, generating 20 images for each task. In the second protocol, a gradient-echo, echo planar image series was used for patients (TR, 1500 msec; TE, 45 msec; $\alpha$, 60°; NEX, 1; FOV, 40 cm; slice thickness, 7 mm; imaging matrix 128 $\times$ 128). Each run, repeated four times for each side, lasted 37 seconds and yielded 20 images for each of the three slices.

Analysis of Functional Magnetic Resonance Imaging Data

Conventional gradient-echo and echo-planar images were screened in a “cine loop” to detect artifacts such as head movement. In addition, the median pixel intensity in the x and y dimensions or “center of mass” of each image was calculated; changes in this measure can identify head movement or other artifacts. Images that had center of mass changes greater than 0.5 pixel were excluded from analyses.

The analysis procedure for functional MR imaging data is demonstrated in Fig. 1. Comparison of left- versus right-sided stimulation was made using a pixel-by-pixel t-test on all pixels in the image (“t-map”). Positive pixels in the t-map indicated areas with increased functional MR signal for left-sided stimulation, whereas negative pixels indicated larger signal for right-sided stimulation (Fig. 1A). Levels of significance or “t-thresholds” (positive or negative) were then set for each tail of the t-distribution to highlight regions of significant activation, so that these could be superimposed on the corresponding anatomical image. The clusters of significant pixels in the thresholded t-map (Fig. 1B) corresponded to the two tails of the t-distribution: positive for left-sided stimulation and negative for right-sided stimulation. To allow direct comparisons of statistical reliability across tasks within subjects, t-thresholds within individual subjects were kept constant across conditions. Thresholded average t-maps were masked to exclude ghost images or flow artifacts outside the brain; the masked activation images were then superimposed on anatomical images (Fig. 1C).

In addition, “split t” comparisons were made. The functional MR data were divided into halves and a t-map was then generated for each half of the data set as described above. The split t-map was generated by retaining only pixels common to both t-maps above a predetermined threshold t-value (Fig. 1D); hence, pixel values in the split t-map were either zero or the average t-value of the two t-maps from each half of the data set. This approach increased the chances of identifying true positives, as pixels in the split t-map were not affected by extreme t-values in only part of the data set. The t-map and the split t-map were usually similar (Fig. 1A and D). This approach was used for both conventional and echo-planar images.

Three-Dimensional Reconstruction of Brain Surfaces

Axial SPGR sequences were used in four patients to generate surface renderings of the brain using the Theraview Program (3D Biomedical Imaging Inc., Shawnee Mission, Kansas). The patient’s tumor, functional MR, and SSEP findings were superimposed on the brain rendering in the following manner: for functional MR imaging data, the motor and sensory activations were superimposed on the anatomical $T_1$-weighted images. The anatomical images were coregistered to their counterparts in the axial SPGR sequence. Activations were then con-
toured in the axial SPGR sequence, reconstructed, and portrayed in the brain surface reconstruction. The axial SPGR images were read into the three-dimensional program and then the surface in each image was contoured by describing a flexible ellipse around the brain. The ellipse contained vertices that could be dragged into the sulci to eliminate structures other than cortex, for example, cerebellum or surface vasculature. The ellipse was then fitted to the brain surface, the tightness of fit being dependent on an operator-adjustable contrast gradient. When all images were contoured, the contour stack was reconstructed to compose the surface rendering. The patient’s tumor, functional MR images, and SSEP findings were superimposed on the brain rendering using the contour method.

Intraoperative photographs of the bare brain were taken using a camera mounted above the surgical field. With the SSEP recording grid in place, photographs were also taken of sites of positive cortical stimulation, indicated by numerical labels. These sites were incorporated into the surface renderings of the brain by using anatomical landmarks on the brain’s surface (gyral and sulcal pattern) and the position of the recording grid relative to these landmarks. In chronic recordings, patients had postimplant anatomical MR images, allowing electrode locations with SSEP and cortical stimulation findings to be incorporated into surface brain renderings.

In Case 1, the patient had a stereotactic biopsy of her lesion. Functional MR activation data and the lesion site were expressed in stereotactic coordinates and the site of the operative field was chosen using these data. Functional MR imaging activation data in this case aided placement of the SSEP grid over the hand sensorimotor cortex.

**Electrophysiological Studies**

Using methods described previously, SSEPs were recorded from grids of stainless steel electrodes placed on the cortical surface. Recordings were referential to a needle electrode placed in a muscle near the craniotomy margin (intraoperative recordings) or on a mastoid bone (chronic recordings). The 32- to 64-channel electroencephalogram was filtered (3.0–1 kHz), digitized at 2 kHz, and averaged. The location of the central sulcus was determined by the polarity reversal of the postcentral N20 and P30 potentials to the precentral P20 and N30 potentials. The N20/P30 or P25/N35 peak-to-peak amplitudes were calculated at postcentral and central electrode sites. Electrode sites with amplitudes greater than 75% of

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**Fig. 1.** Functional magnetic resonance (MR) imaging data analysis procedure depicting generation of masked and thresholded t-maps. A: An unthresholded t-map (data from the motor task) showing significant areas of activation produced at each tail of the t-distribution for right versus left stimulation. Significant areas of activation are seen at extremes of the color scale (right side of figure), where left-sided activation appears as positive t-values and right-sided activation as negative t-values. The values around 0 appear in blue in the remainder of the image. B: Thresholded and masked t-map. Thresholds used: positive tail +3.0 to +10.0; negative tail: −8.0 to −3.0. An individual gradient-echo functional MR image was used to mask the t-map to include only pixels within the brain. C: Overlay of masked and thresholded t-map on anatomical T1-weighted image. A single color has been used for each tail of the t-distribution for optimum visibility (red = positive tail; green = negative tail). D: An unthresholded split t-map. Significant areas of activation produced at each tail of the t-distribution for right versus left motor-task comparison. Note that most t-values now are centered around 0 in the remainder of the image, as shown by the blue background in the image. E: Thresholded and masked split t-map. Thresholds used: positive tail +2.5 to +8.0; negative tail: −6.0 to −2.5. F: Overlay of masked and thresholded split t-map over T1-weighted anatomical image. Activation shown in red denotes the positive tail of the t-test, whereas green shows the negative tail.
maximum amplitude were identified, and their positions were incorporated in the surface reconstructions as described above. Cortical stimulation was performed intraoperatively using 50 Hz, 0.1-msec duration, 10 mA constant-current pulses delivered through a hand-held bipolar probe. In patients with long-term implants, stimulation was delivered through adjacent grid electrodes at intensities of 2 to 10 mA in increments of 2 mA. Stimulation was discontinued if afterdischarges were observed in the electroencephalogram.

Results

Control Population

Controls were studied twice, with the motor task common to both sessions. In all controls the motor task elicited activity confined to a narrow region centered around the contralateral central sulcus. Figure 2 shows the pattern of activation obtained in two control subjects during both replications of the motor task. Figure 2A and B shows activation in both slices for the first session in one control. The activation was reproduced 3 months later in the second session (Fig. 2C and D). A second control (Fig. 2E and F) was also tested 3 months later (Fig. 2G and H) and the activation was again similar as shown in the lower row of Fig. 2.

Brushing of the palm and digits also produced reliable activation in all controls. Figure 3 compares data from the motor (Fig. 3A and B), brushing (Fig. 3C and D), and air (Fig. 3E) tasks. There was considerable overlap of activated regions in the brushing and motor tasks. With this stimulation procedure, however, it is difficult to ensure that no movement occurred in the hand, as some subjects reported resisting the brushing motion. To ensure that only sensory cortex was activated, pulsed compressed air was blown across the palm and digits. A slight reduction of activation was seen in the same subject. In the air task, recorded in another session, slice selection was different (Fig. 3E); hence, comparison should be made with the superior slice in the motor (Fig. 3B) and brushing (Fig. 3D) tasks. No activation was seen in either sensory cortical hand area to alternating left and right median nerve electrical stimulation (not shown), even at liberal t-thresholds.

Electrical stimulation of the median nerve at 5 Hz did not produce reliable activation in the controls. Electrical stimulation was investigated at higher stimulation frequencies in three subjects. Activation-split t-maps for 5, 15, and 30 Hz stimulus frequencies are shown in Fig. 4 for one control. No effect of sensory stimulation was seen at 5 Hz (Fig. 4A). However, at 15 Hz (Fig. 4B) and 30 Hz (Fig. 4C), an area of activation appeared postcentrally, but only in the left sensory cortex. No activation was seen in right sensory cortex to left median nerve stimulation. In the other two controls no activation was seen at higher stimulus frequencies.

Summary of Cases

Case 1

This 26-year-old right-handed woman had a 17-year history of simple partial seizures. Her seizure onset con-
sisted of a “pulling sensation” in the left hand. A $T_2$-weighted MR image showed a lesion with increased signal changes near the right central sulcus. Intraoperative SSEPs were recorded from an $8 \times 8$ grid placed over the right frontoparietal cortex (Fig. 5a and b). Intraoperative cortical stimulation produced movements of the thumb, fingers, or forearm pronation in the region identified as “precentral” by SSEPs (Fig. 5a).

The patient was studied with functional MR imaging using the sensory brushing and motor tasks before resec-
tion of her lesion. Prior to stereotactic biopsy of the lesion, the functional MR results were coregistered, making the locations of sensory and motor activations available in stereotactic coordinates to guide the stereotactic procedure. The area of sensory and motor activation demonstrated in functional MR imaging showed excellent correspondence with both electrical methods (Fig. 5c).

Case 2

This 55-year-old right-handed woman had a 7-year history of simple partial seizures. Her daily seizures began with a sensation in the right arm and sometimes included the right leg. Magnetic resonance imaging studies showed edema and some enhancement in the left posterior medial frontal cortex. A diagnosis of astrocytoma was made at another institution, and the patient was given a course of radiation therapy treatment in 1988. However, her seizures recurred and became increasingly frequent and intractable over the last 2 years.

Subsequent MR imaging confirmed the presence of the lesion seen previously. Functional MR imaging using sensory and motor tasks was performed prior to surgery. Intraoperative SSEPs were recorded from a 4 × 8 electrode grid and showed polarity reversal of the 20- and 30-msec potentials across the central sulcus (Fig. 6a–c). An intraoperative photograph shows the location of the electrode grid and the hand motor area as identified by cortical stimulation (Fig. 6c). Functional MR images showed discrete activation for the motor task anterior to the central sulcus (red area in Fig. 6d) concuring with cortical stimulation; this stimulation was performed under general anesthesia and may explain why this area appears smaller than the corresponding functional MR image activation. The sensory area, as shown by SSEP recording, was posterior and discrete from the motor area. No functional MR activation was observed in the sensory task in any of the three slices. The hand motor cortex in this patient appeared somewhat lateral to that seen in the controls and in other studies1,2 and in Case 1 (Fig. 5d) and may reflect a mass effect of the lesion.

Case 3

This 46-year-old woman had a 2-year seizure history. An MR image showed a mass lesion invading the right frontocentral region; a biopsy of this area suggested a low-grade glioma. She had intraoperative SSEP recordings to median and posterior tibial nerve stimulation as well as cortical stimulation. Functional MR studies showed overlap with the maps of hand sensorimotor cortex produced in electrophysiological studies (Fig. 7A). In this patient, functional MR motor activation (red) was seen in two areas: on the precentral gyrus and in the bank of the central sulcus. This latter area of activation overlapped the functional MR sensory activation (green) and was adjacent to the hand motor region as identified with cortical stimulation (blue). In this case, the area of maximum hand motor response was identified intraoperatively. The full extent of cortex involved was not mapped, including the
more lateral extent of the functional MR image activation for the hand.

Case 4

This 21-year-old right-handed woman had a history of head trauma, excision of multiple meningiomas, and a right frontal polar resection of a putative seizure focus at age 14. Chronic SSEP recordings to median, trigeminal, posterior tibial, and pudendal nerve stimulation were performed, as well as cortical stimulation. Hand motor phenomena were seen to stimulation of precentral electrode pairs (located 1 cm apart); hand movements also occurred in response to stimulation of electrodes spanning the central sulcus (Fig. 7B). Functional MR image activation of motor cortex (Fig. 7B, red) showed overlap with motor hand areas identified by cortical stimulation (blue). The hand area as delineated by SSEP criteria is shown in white. No sensory functional MR studies were performed in this patient.

Discussion

We have demonstrated reliable functional MR image activation of sensory and motor cortex via both conventional and echo-planar imaging sequences; previous studies have only used motor tasks. In this study, activation to the motor task occurred over and anterior to the central sulcus and was consistent with that seen by other researchers. The choice of the optimum imaging plane remains an open question, with some groups preferring to use oblique cuts parallel to the central sulcus.

For the study of the hand area of sensorimotor cortex we chose multiple slices in the axial plane. In this orientation the central sulcus is readily identified by a distinct anatomical signature: an “Ω”-shaped structure that was seen in all control subjects and in the unaffected hemisphere of all patients. The lateral portion of this structure corresponds to the convexity of the central sulcus in the hand area. The identification of the hand sensorimotor cortex from its anatomical signature in axial MR images has been noted by other researchers.

Two of the three sensory tasks produced significant activation of sensory cortex. Electrical stimulation of the median nerve was not an optimum stimulus and produced little activation in the controls. Even when the stimulus frequency was increased to levels that were uncomfortable to the subject, activation was not consistent. The brushing and compressed-air stimulation studies produced clear, discrete areas of activation in or posterior to the central sulcus. It is possible that the brushing and compressed-air stimuli provided a more continuous form of stimulation; hence, the increase in local blood flow and subsequent decrease in local deoxyhemoglobin may have been larger. Because some activation was seen only at the highest frequency of median nerve stimulation, this explanation seems likely. We had predicted that the pulsed compressed-air stimulation would be the optimum method for sensory stimulation, as movements of the subject’s hand would not occur in resisting the stimulus, which might have been the case with the brushing method. In most cases the brushing and air tasks produced comparable results (Fig. 3C and D, and E and F). The brushing task is now used because of its simplicity.

In this and our previous imaging study, the main area of activation was limited to a narrow band in or adjacent to the central sulcus (Fig. 3). In monkeys and humans, the identification of the hand sensorimotor cortex from its anatomical signature in axial MR images has been noted by other researchers.
Functional MR imaging of sensorimotor cortex

the SEP to median nerve stimulation is generated almost entirely in the posterior wall of the central sulcus (area 3b) and in the anterior crown of the postcentral gyrus (area 1). Most of the primary motor cortex (area 4) is similarly contained within the anterior wall of the central sulcus and the posterior portion of the crown of the precentral gyrus. Most of the activation seen in sensory or motor functional MR imaging data may therefore have occurred within or adjacent to the walls of the central sulcus. This may account for the lack of spatial differentiation of sensory and motor activation in some images (Fig. 3).

The delineation of hand sensorimotor cortex using functional MR imaging and two electrophysiological methods revealed good agreement on the location of sensory and motor areas, although the extent of the active regions differed for several reasons: anesthesia can constrict the region mapped by cortical stimulation and by SSEPs, and the extent of the region defined by SSEPs naturally depended on the amplitude criterion chosen (defined here as the region enclosing greater than 75% of the maximum N20/P30 or P25/N35 amplitude). The SSEP findings were also dependent on the interelectrode distances used (0.5 cm intraoperative, 1 cm chronic recordings).

Results of cortical stimulation were also sensitive to this variable (Case 4, Fig. 7B). The active region determined by functional MR imaging varied as a function of the t-threshold used. Nevertheless, the important points were that the three methods yielded comparable results, and that this technique could provide valid noninvasive localization of the hand representation of sensory and motor cortex. This was particularly important in preoperative planning, as in Case 1 in which the siting of the intraoperative grid was based on preoperative functional MR imaging data. The foot and face representations could be localized by SSEPs, and one could infer from preliminary imaging data that these regions might be localized using methods similar to those used in this study. Dipole source analysis of scalp-recorded SSEPs in combination with three-dimensional anatomical MR imaging has been performed to identify the position of the central sulcus preoperatively. Implementation of this technique, however, involved two separate sessions for the anatomical MR images and electrophysiological recordings. The functional and anatomical MR studies described here can be acquired in a single 1-hour session.

An important methodological issue to consider is the effect of vasculature on activations seen in functional MR imaging. The activation seen in this study followed the curvature of the central sulcus, usually being confined to the Ω-shaped anatomical signature that delineated the hand area of the central sulcus, and therefore was unlikely to be due to major vasculature. In all of our patients and some controls, MR angiography was performed to exclude major vasculature as the source of activation. A more subtle but important problem may arise from using gradient-echo imaging sequences, which are thought to be sensitive to susceptibility variations caused by large vessels. Comparison of gradient-echo versus fast spin–echo sequences, which are less sensitive to a large-vessel susceptibility artifact in visual cortex, showed similar activation maps for both types of imaging sequence. The activa-
tion maps for the gradient-echo sequences were larger in area than those seen in fast spin–echo sequence imaging and suggested that gradient-echo activations have some contribution from large vessels. The correspondence of the functional MR imaging and electrophysiological maps, however, argued strongly for the accurate localization of hand sensorimotor cortex by our MR imaging methods. The risk-free relative ease with which functional MR imaging can be noninvasively performed provides a valuable method of functional assessment.

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References