An Integrated Functional Magnetic Resonance Imaging Procedure for Preoperative Mapping of Cortical Areas Associated with Tactile, Motor, Language, and Visual Functions

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OBJECTIVE: **To evaluate an integrated battery of preoperative functional magnetic resonance imaging (fMRI) tasks developed to identify cortical areas associated with tactile, motor, language, and visual functions.**

METHODS: **Sensitivity of each task was determined by the probability that a targeted region was activated for both healthy volunteers (n = 63) and surgical patients with lesions in these critical areas (n = 125). Accuracy of each task was determined by the correspondence between the fMRI maps and intraoperative electrophysiological measurements, including somatosensory evoked potentials (n = 16), direct cortical stimulation (n = 9), and language mapping (n = 5), and by preoperative Wada tests (n = 13) and visual field examinations (n = 6).**

RESULTS: **For healthy volunteers, the overall sensitivity was 100% for identification of the central sulcus, visual cortex, and putative Wernicke's area, and 93% for the putative Broca's area (dominant hemisphere). For patients with tumors affecting these regions of interest, task sensitivity was 97% for identification of the central sulcus, 100% for the visual cortex, 91% for the putative Wernicke's area, and 77% for the putative Broca's area. These sensitivities were enhanced by the use of multiple tasks to target related functions. Concordance of the fMRI maps and intraoperative electrophysiological measurements was observed whenever both techniques yielded maps and Wada and visual field examinations were consistent with fMRI results.**

CONCLUSION: **This integrated fMRI task battery offers standardized and noninvasive preoperative maps of multiple critical functions to facilitate assessment of surgical risk, planning of surgical routes, and direction of conventional, intraoperative electrophysiological procedures. Thus, a greater range of structural and functional relationships is brought to bear in the service of optimal outcomes for neurosurgery.** (Neurosurgery 47:711–722, 2000)

Key words: Brain mapping, Cerebral neoplasms, Functional magnetic resonance imaging, Functional mapping, Intraoperative brain mapping

Preservation of function during brain tumor resection is an essential goal of neurosurgery, and various intra- and preoperative brain mapping techniques are currently used for this purpose (3). Functional magnetic resonance imaging (fMRI) has recently emerged as a preoperative technique to observe task-specific cortical activity, and fMRI maps of sensory and motor functions, either alone or in combination with other neuronavigation techniques (10, 21, 30), have been shown to be effective in directing brain tumor resections away from cortical regions that have residual function in these critical areas (1, 10, 18–20, 26, 29, 35).

Tasks used for functional mapping of sensory and motor-sensitive regions have generally been developed by separate research groups in the service of neurosurgical planning. As a consequence, many task variants have been used. For example, motor tasks are sometimes accomplished by single finger-thumb tapping (20) and in other cases by multiple finger-thumb tapping (6, 9, 18). Other approaches include self-paced clenching and spreading of the hand (5, 8, 27, 35) or sponge squeezing (19, 26). Tactile stimulation has included palm brushing (19), administration of compressed air puffs to the hand (26), and scratching of the ventral surface of the hand (20). The length of the activity cycle and the number of epochs in a run are also nonstandard and introduce variations arising from statistical stringency and related data processing procedures.

Similarly, functional mapping of language areas has been accomplished by a range of tasks and procedures, including naming objects and generating verbs (11), naming animals starting with a given letter (18), generating words in alphabetical order (12), or designating a category in response to an auditory presentation of nouns (2). It is not known, however, how these various tasks compare with respect to sensitivity or targeted regions of interest. Assessment of cortical activity associated with visual stimulation has been accomplished with intermittent binocular photic stimulation (9, 17, 18) as well as with various projected pattern stimuli (32). Although all of these tasks for sensory, motor, language, and visual functions may be individually effective, rigorous efforts to evaluate and integrate multiple functional maps have not been a primary focus of previous studies.

The potential benefits of a cohesive set of tasks include the opportunity to exploit the reliability advantages of multiple tasks to target related functions. In this study, we aimed to evaluate an interrelated battery of fMRI tasks that targeted cortical regions associated with tactile, motor, language, and visual-sensitive cortical areas when performed during one fMRI session. In addition to the advantage of mapping multiple functions during a single procedure, the task battery offers the following features: the imaging time is no more than 30 minutes, the procedures are standardized and performed by trained MRI technicians, the targeted functions are selective for regions frequently considered most critical for surgical decisions, the task battery is applicable to patients with a wide range of symptoms and abilities to comply with task directions, because all functions are repeated using both “active” (volitional) and “passive” (receptive) modes, and the multiple tasks that target common critical areas can boost overall sensitivity. Any subset of these tasks may be selected for specific clinical objectives while retaining the advantages of the standardized procedures with validation based on responses of both healthy volunteers and patients.

PATIENTS AND METHODS

Functional imaging

A 1.5-T MRI unit and a standard head coil (General Electric, Milwaukee, WI) were used to obtain T2*-weighted images with a gradient echo pulse sequence (TR, 4000; TE, 60; flip angle, 60 degrees), which was sensitive to magnetic resonance signal changes caused by alterations in the proportion of deoxyhemoglobin in the local vasculature accompanying neuronal activation (22). The cubic size of each volume element, or voxel, was 10 mm^3, in which the in-plane resolution was approximately 1.5×1.5 mm and the slice thickness was 4.5 mm. Twenty-one contiguous slices of brain were obtained parallel to a standard reference line that intersected the superior edge of the anterior commissure and the inferior edge of the posterior commissure. This orientation allowed direct comparison of the acquired images with the Talairach and Tournoux human brain atlas (31) for identification of targeted brain structures. Conventional high-resolution (T1-weighted) images were also acquired along sagittal planes and at the same axial plane locations as the T2*-weighted images during each imaging session and served as a reference for subsequent anatomic labeling. However, the images acquired for intraoperative navigation (BrainLab GmbH, Heimstetten, Germany) were obtained on straight axial orientations.

Thirty-six images of the whole brain were acquired during each run, which lasted 2 minutes 24 seconds. The initial three images of each run were not retained to ensure that all acquisitions were acquired at a common level of magnetic susceptibility. A standard block design was used, in which 10 images (40 s) were acquired during an initial baseline epoch, followed by a stimulation or task epoch of 10 images (40 s), and a recovery baseline epoch of 10 images (40 s). In all cases, a fixation crosshair was viewed during the initial and final 40-second baseline epochs as an aid to minimize head movements. Two runs were acquired for each task; thus, the total imaging time per task was 4 minutes 48 seconds. This “double pass” method served to minimize the duration of each run and tended to benefit patient compliance with a reminder of the directions before each activity epoch while at the same time offering the statistical benefits of a larger number of acquisitions.

Data analysis

All acquired images were exported from the console to the image processing facility located in the fMRI laboratory at Memorial Sloan-Kettering Cancer Center, where they were reconstructed and aligned to correct for movement artifacts and to allow direct comparisons among all conditions using a common coordinate system (34). A two-dimensional gaussian filter (approximately two to three voxels at half-height) was applied to enhance signal-to-noise characteristics, and voxel-by-voxel intensities were statistically compared during baseline, stimulation, and recovery epochs, as illustrated in *Figure 1*.

Significant signal changes were identified by a multistage statistical analysis that compared average signals acquired during baseline and stimulation epochs. An active voxel was, therefore, defined as any voxel in which the magnetic resonance signal during the period of stimulation was significantly different from both the initial and recovery baseline levels on two separate occasions (13). This coincidence requirement (all statistical criteria met on both runs) is based on the assumption that a signal caused by an actual cortical response associated with a task performance is often distinguishable from an apparent signal (noise) by its reliable recurrence at the same location with repeated stimulation. The requirement that all statistical criteria be met on two separate runs therefore serves to increase the probability that observed activity is due to a reliable event. The criterion for significance, P, of two replicated events was set at false-positive rates of $P \leq 0.0001$, $P \leq 0.00025$, and $P \leq 0.0005$ (depicted as *yellow*, *orange*, and *red*, respectively, on brain images in *Fig. 1*), and was empirically determined from analyses of images acquired in individuals during resting conditions (13, 16). This technique offered advantages of short imaging runs with a high level of confidence appropriate for surgical patients. These statistical methods are readily achieved on most commercially available fMRI data analysis packages.

Multifunction task battery

The specific tasks selected for the task battery were intended to be universally applicable and to use common stimuli and procedures (14); they consisted of four separate procedures (*Fig. 2A*), as follows:

1. Passive tactile stimulation of a hand (either the dominant hand or the hand relevant to the hemisphere of surgical interest), achieved by gently rubbing the patient's palm and fingers with a mildly abrasive plastic surface. Simultaneously, the patient viewed a reversing checkerboard pattern that was backprojected onto a screen visible through a slanted mirror mounted on the head coil. This visual stimulation also aided the patient with head stabilization.
2. Active hand movement (finger-thumb tapping), performed with the same hand that was used in the passive tactile stimulation task while repeating the simultaneous visual stimulation (reversing checkerboard).
3. Picture naming by internal (silent) speech, performed in response to visually displayed black-and-white line drawings (selected from the middle range of the Boston Naming Test) (15), presented at 4-second intervals.
4. Listening to recordings of spoken words (names of objects), presented through headphones designed to reduce scanner noise (Resonance Technologies, Northridge, CA). A visual crosshair remained present throughout the run to help prevent head movement.

The aims of these four conditions included localization of sensory and motor cortices, and by inference, prediction of the location of the central sulcus; localization of language-related activity, and by inference, prediction of the locations of Broca's and Wernicke's areas and the dominant hemisphere for speech; and localization of primary and secondary visual areas.

The targeted functions and structures associated with each task in a healthy volunteer are illustrated in *Figure 2B*. The sensory and motor tasks targeted the post- and precentral gyri, respectively, and are shown in the *left panels*. These figures also illustrate the expected overlap along the pre- and postcentral gyri between activity associated with sensory and motor stimulation. The language tasks target the putative Broca's and Wernicke's areas, which are found within the inferior frontal gyrus and the superior temporal gyrus, respectively, on the dominant hemisphere for language (*Fig. 2B, middle panels*). Both areas are redundantly targeted by expres-

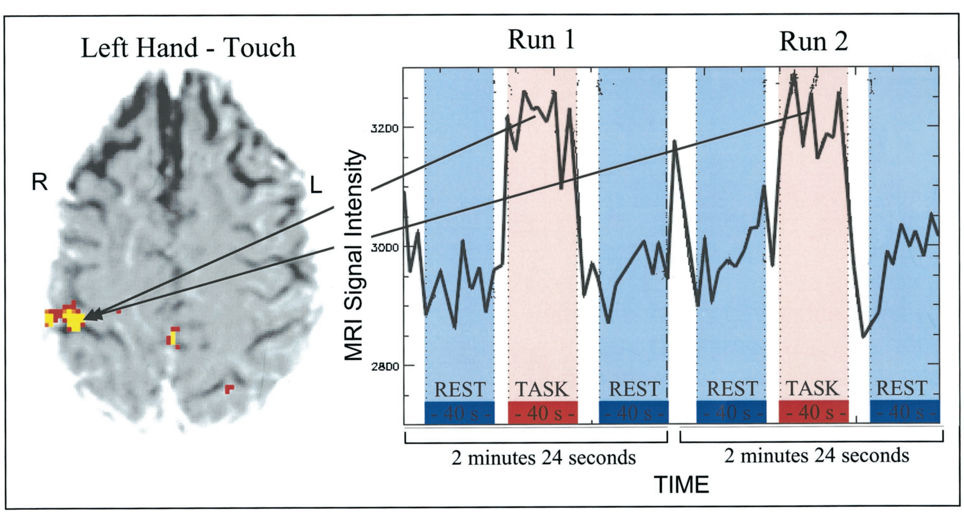

FIGURE 1. Signals illustrate the MRI changes in susceptibility observed in response to passive tactile stimulation of the left hand of a healthy volunteer and originate from a single voxel (1.5 × 1.5 × 4.5 mm) on two separate runs. Each run lasted 2 minutes 24 seconds, during which 36 images were acquired, including 10 images for each of three epochs: initial resting baseline (*blue bar*), task (left-hand touch) (*pink bar*), and final resting baseline (*blue bar*). All voxels in the brain for which the statistical criteria were met (such that the average amplitude of the signal during the activity epoch was different from that of the baseline signal) are indicated by either a *yellow*, *orange*, or *red* color superimposed on the T2*-weighted image at the voxel address, and they signify decreasing levels of statistical confidence (see Patients and Methods). *Arrows* point to the source voxel, which is centered within a cluster of similar (*yellow*) voxels and located in the right (*R*) hemisphere of the brain along the postcentral gyrus.

A

fMRI Task Battery for Cortical Mapping of Sensory, Motor, Language and Vision-Related Areas

1. SENSORY Touch/hand	+	VISION Reversing Checkerboard
2. MOTOR Finger/Thumb tapping	+	VISION Reversing Checkerboard
3. LANGUAGE/active Picture Naming	+	VISION Pictures
4. LANGUAGE/passive Listening to Words	+	AUDITION Spoken words

B

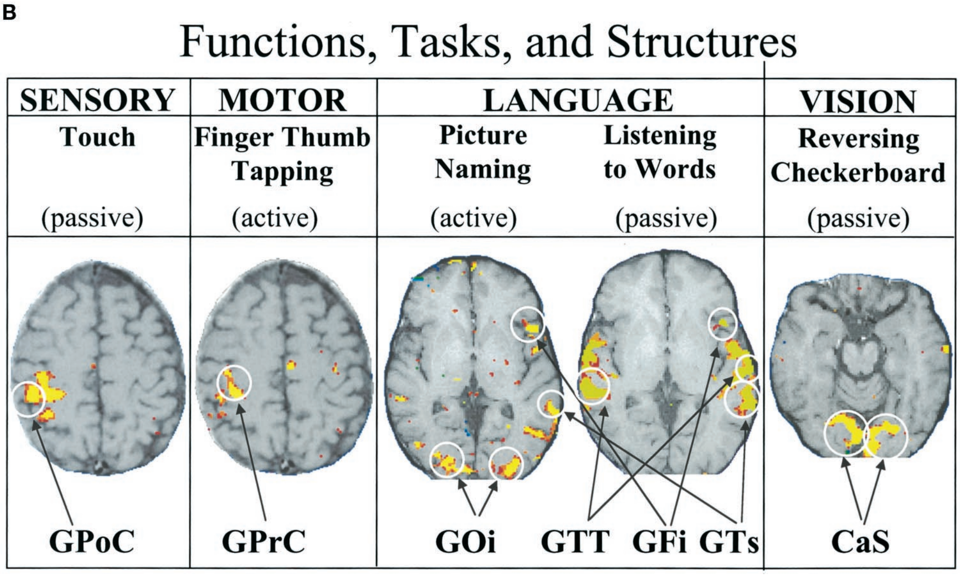

FIGURE 2. *A*, summary of each of the functions mapped by the four conditions in the task battery; *B*, selected MRI slices for a healthy brain, illustrating targeted (*circled*) structures labeled according to the Talairach and Tournoux human brain atlas (31) for each of the functions and tasks: from *left* to *right*, sensory, or passive touch of the hand using a rough plastic surface, targets the postcentral gyrus (*GPoC*); motor, or active finger-thumb tapping, targets the precentral gyrus (*GPrC*); language, picture naming (expressive), and listening to spoken words (receptive) target the inferior frontal gyrus (*GFi*; Broca's area) and the superior temporal gyrus (*GTs*; Wernicke's area) on the dominant hemisphere; and vision, or viewing of the reversing checkerboard, and picture naming target the calcarine sulcus (*CaS*) and the inferior occipital gyrus (*GOi*). Primary auditory activity expected to be associated with the listening task is also observed bilaterally in the transverse temporal gyrus (*GTT*).

sive (active) and receptive (passive) language tasks, and by visual and auditory techniques. Visual and auditory systems are also revealed by the activity in the inferior occipital gyrus and the transverse temporal gyrus, respectively (*Fig. 2B, left* and *right language panels*). Vision-related activity via the reversing black-and-white checkerboard stimulations also target the primary visual cortex, found along the calcarine sulcus (*Fig. 2B, far-right panel*). Given the levels of statistical confidence, we assumed that activity not circled also represented true physiological activations that were task-related and distributed outside the targeted region of interest.

Healthy volunteers and patients

A total of 63 healthy volunteers (24 women and 39 men) participated in the development of the specific set of tasks targeted to identify brain regions most likely to be surgical regions of interest as indicated by the distribution of cases considered appropriate for mapping by the neurosurgery service at Memorial Sloan-Kettering Cancer Center (*Table 1*). Consent of the subjects was obtained according to guidelines approved by the institutional review board. Eligibility criteria for healthy volunteers consisted of the absence of any preexisting or present neurological condition. Eligibility criteria for the surgical patients required that the patient be a potential neurosurgical candidate and scheduled for a conventional therapeutic MRI study related to a primary brain tumor, brain metastasis, seizure disorder, or cerebrovascular malformation. All 125 patients presented with surgical regions of interest that included sensorimotor (n = 63), language (n = 56), or visual (n = 6) functions. All consecutive patients referred for fMRI mapping during this protocol were included to ensure a representative database.

RESULTS

Sensitivity of task battery: healthy volunteers

The purpose of this stage of the study was to determine the sensitivity of the battery of tasks for healthy volunteers. Each task was associated with the targeted region of interest, and the percentage of patients showing activity in those regions (sensitivity) was determined (*Table 2*). This task battery provided two opportunities to observe the targeted region. For example, whereas the superior temporal gyrus was activated in only 73% of healthy volunteers during picture naming, it

TABLE 1. Epidemiological Information

	Age (yr)		Sex (No. of Patients)	Handedness[a] (No. of Patients)	Disorder (No. of Patients)
	Range	Average			
Healthy subjects	18–70	29	M (39) F (24)	Right (59) Left (3) Not determined (1)	None
Surgical patients	11–79	42	M (65) F (60)	Right (87) Left (14) Not determined (24)	Primary brain tumor (84) Metastases (19) Seizure disorder (8) Vascular malformations (6) Unknown (8)

[a] Based on Oldfield RC: The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia* 9:97–113, 1971 (24).

TABLE 2. Evaluation of Task Sensitivity[a]

Task and Structure	Healthy Subjects: Targeted Regions of Interest (%)				Surgical Patients: Surgical Regions of Interest (%)			
	Central Sulcus (n = 30)	Broca's Area (n = 45)	Wernicke's Area (n = 45)	Visual Cortex (n = 15)	Central Sulcus (n = 63)	Broca's Area (n = 22)	Wernicke's Area (n = 34)	Visual Cortex (n = 6)
Touch								
GPoC	100				94			
Finger-thumb tapping								
GPrC	100				89			
Picture naming								
GFi		90				72		
GTs			73				65	
Listening to spoken words								
GFi		93				54		
GTs			100				88	
Checkerboard pictures								
CaS				100				100
GOi				100				100
Composite sensitivity (%) ("Logical OR")	100	93	100	100	97	77	91	100

[a] GPoC, postcentral gyrus; GPrC, precentral gyrus; GFi, inferior frontal gyrus; GTs, superior temporal gyrus; CaS, calcarine sulcus; GOi, inferior occipital gyrus.

was 100% effective in listening to spoken words. Overall, the sensitivity of the entire battery for identifying the language-related cortex in the superior temporal gyrus was 100% for the population of healthy volunteers (*Table* 2, composite sensitivity). Specifically, the composite sensitivity is the result of a "Logical OR" decision rule based on two tasks that target a specific region. The central sulcus and the visual cortex were identified in 100% of cases, and Broca's area in 93%.

Sensitivity of task battery: surgical population

After task sensitivity was determined for healthy volunteers, similar determinations were made for surgical candidates with disorders in the specified cortical regions of interest. This enabled assessment of the fMRI task within the affected cohort of patients. These subgroups served as the basis for evaluation of the respective tasks. All patients, regardless of the region of surgical interest, completed all tasks in the battery; however, *Table* 2 shows only the task sensitivity within each surgical group, thus indicating sensitivity in the presence of disease. The tactile stimulation task revealed activity in the postcentral gyrus in 94% of patients with lesions in or close to the motor strip, whereas the finger-thumb tapping task predominantly demonstrated function in the area of the precentral gyrus in 89% of patients. Of the two patients for whom the central sulcus was not identified, one was characterized by excessive (not correctable) head movement and marginal compliance. Neurological deficits were the most likely contributing factor in the second case. Overall, the location of the central sulcus, indicated by either its posterior or anterior margins, was identified in 97% of the patients with disease in this region, and is indicated as the composite sensitivity (*Table* 2). This boost in sensitivity was achieved by exploiting the two approaches toward locating the central sulcus and by using a "Logical OR" combinatorial decision rule between the two tasks.

By combining the picture naming and passive listening task performances, we observed fMRI signal in Wernicke's area in 31 (91%) of the 34 patients with disease in the superior temporal gyrus, and in Broca's area in 17 (77%) of the 22 patients with disease in the inferior frontal gyrus (*Table 2*). Reasons for the three unsuccessful observations in the former patients included movement artifact (n = 1) and probable lack of compliance (n = 2). In the latter patients, unsuccessful observations were due to neurological deficits (n = 3), probable marginal compliance (n = 1), and a head movement artifact that was not correctable (n = 1), although a false-negative finding cannot be ruled out. The fMRI signal was observed in the visual cortex (calcarine sulcus and inferior occipital gyrus) in each of the six patients with lesions in these cortical areas.

Comparison of task sensitivity between patients and healthy volunteers

Although the sensory and motor probes of the postcentral and precentral gyri were each 100% effective in the healthy volunteers, they were 94% and 89% effective, respectively, in patients with tumors in those regions. These observations include patients with such severe symptoms as hemiparesis and loss of sensory function. However, by combining the two tasks with the "either/or" decision rule, the central sulcus was identified in 97% of cases. By combining the "hit rates" for the picture naming and listening to spoken words tasks for the healthy volunteers, the targeted Broca's area (inferior frontal gyrus) and Wernicke's area (superior temporal gyrus) were activated in 93% and 100% of cases, respectively. Correspondingly, for the surgical patients, these areas were activated in 77% and 91% of the cases, respectively. The reduction in patient sensitivity for the language areas presumably reflects tumor-related receptive and expressive aphasias as well as related cognitive losses. The visual functions within the calcarine sulcus and inferior occipital gyrus were 100% effective in both healthy subjects and surgical patients, in whom the unaffected hemisphere provided the comparison.

Accuracy of task battery: comparison with intraoperative electrophysiological measurements

Accuracy of the fMRI observations was assessed for all surgical patients, for whom both procedures were included in the treatment plan by comparing the fMRI maps with conventional intraoperative mapping methods. Both fMRI preoperative mapping and intraoperative electrophysiological monitoring were performed in 16 patients (*Table 3*). Intraoperative recording of somatosensory evoked potentials (SSEPs) was performed to localize the central sulcus (7), and successful recordings were obtained in 15 cases. Direct cortical stimulation was performed in 11 of these cases, with successful stimulations in 9 cases. The areas of electrophysiological response were referenced to axial images with the use of an intraoperative frameless stereotactic navigation device (ISG Systems, Toronto, Ontario, Canada; BrainLab) and compared with the preoperative fMRI images. Owing to the differences in the orientations of the acquired slices, however, precise measurements of the two outcomes were not possible. In each case, the surgeon judged the correspondence as consistent, and this judgment was corroborated by the photographs (see illustrative case, below).

The fMRI maps revealed activity in the precentral gyrus in 16 (100%) of 16 cases and in the postcentral gyrus in 13 (81%) of 16 cases. However, the combined maps revealed the location of the central sulcus in all cases. When both methods (fMRI and electrophysiological monitoring) revealed the central sulcus, the locations concurred in 100% of cases for SSEP results (15 of 15 cases) and in 100% of cases for direct cortical stimulation (9 of 9 cases), as determined within the spatial accuracy of both methods, and are in accordance with findings reported previously (4, 25, 26).

Comparison of fMRI, Wada, and intraoperative language mapping

Hemispheric language dominance was predicted by the fMRI language-related maps and compared with preoperative Wada procedures (33) in 13 cases. Identification of the dominant hemisphere for language as determined by Wada testing was consistent with fMRI results in all 13 cases by a double-blind study, and is consistent with findings of previous investigations (2). In a subsequent cohort of five patients, this integrated battery of tasks was applied before intraoperative language mapping with consistent findings between the two methods (28).

Comparison of fMRI and visual fields

Homonymous visual field defects were compared with fMRI response patterns in the primary visual cortex in six cases. Visual fields determined by formal static perimetry (Octopus 123; Interzeag AG, Schlieren, Switzerland) indicated hemianopic or quadrantanoptic field deficits consistent with known disruptions of visual projection pathways and were consistent with the fMRI cortical maps as compared with activity within the unaffected hemisphere. That is, gross absences of hemispheric symmetry along the calcarine sulcus in regions expected to correspond to the visual field were taken as demonstrations of field and fMRI consistency.

Illustrative case

A 43-year-old right-handed man presented with mild headaches and brief episodes of receptive language disturbance as well as occa-

TABLE 3. Comparison: Functional Magnetic Resonance Imaging/Intraoperative Electrophysiological Recording[a]

fMRI Identification of:		Intraoperative Electrophysiological Recording	
GPrC	GPoC	Somatosensory Evoked Potentials	Direct Cortical Stimulation: Motor Responses
16/16 (100%)	13/16 (81%)	15/16 (94%)	9/11 (82%)
Concordance with fMRI		15/15 (100%)	9/9 (100%)

[a] **fMRI, functional magnetic resonance imaging; GPrC, precentral gyrus; GPoC, postcentral gyrus.**

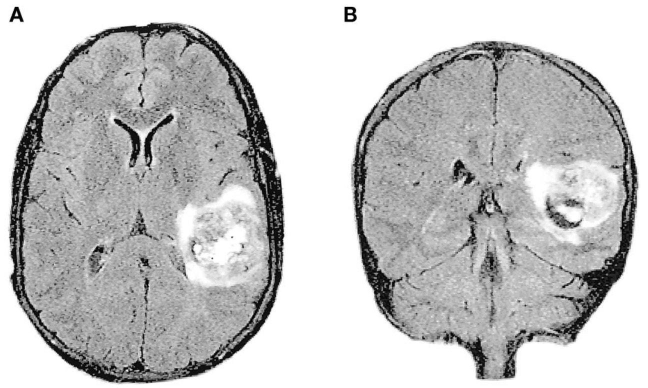

FIGURE 3. Conventional T1-weighted presurgical magnetic resonance images revealing a rounded, 4.5-cm-diameter, partially hemorrhagic lesion located in the left posterior temporal lobe, as shown on the axial (*A*) and coronal (*B*) images. Postsurgical disease was consistent with ependymoma. Primary regions of surgical interest based on tumor location included Wernicke's and Broca's areas and the central sulcus.

sional word-finding difficulties. Preoperative neuropsychological evaluation revealed no language deficits. MRI revealed a rounded, partially hemorrhagic lesion, 4.5 cm in diameter, located in the left posterior temporal lobe (*Fig. 3*). To optimize a therapeutic plan, functional maps were obtained using the multifunction task battery (results are summarized in *Fig. 4*). The central sulcus was clearly identified by the sensory and motor tasks. The language tasks revealed language-related activity in the left hemisphere adjacent to both the posterior and anterior margins of the mass (superior temporal gyrus and inferior frontal gyrus). The visual stimulation was reliably associated with signals within and along the primary visual areas (calcarine sulcus). Owing to the proximity of the tumor to language-related activity, an awake craniotomy with electrophysiological mapping of motor and language functions was performed.

Mapping of sensory and motor functions

Recording of SSEPs indicated the location of the central sulcus (*Fig. 5*), which was confirmed by direct cortical stimulation of the precentral gyrus. Comparison with the location of the central sulcus by fMRI indicated good agreement with both techniques.

Mapping of language functions

Direct cortical stimulation of the left inferior frontal gyrus with the Ojemann bipolar stimulator (Radionics, Burlington, MA) disrupted the patient's ability to count, and similar stimulation of the superior temporal gyrus produced language disturbances, including literal paraphasic errors and word-finding difficulties, respectively (*Fig. 6*). Sites of observable responses were tagged with numbers, photographically documented, and cross-referenced to the fMRI maps.

Postsurgical status

Total resection was achieved with sparing of these functional regions. The pathological abnormalities were consistent with ependymoma. Immediately after surgery, no impairment of language function was detected; however, postoperative recovery was complicated by temporary mixed aphasia and seizures. Subsequently, within 10 days, the patient's condition was substantially improved, and no further adjuvant treatment was planned. A 6-month postsurgical fMRI study was consistent with previous findings, and neuropsycho-

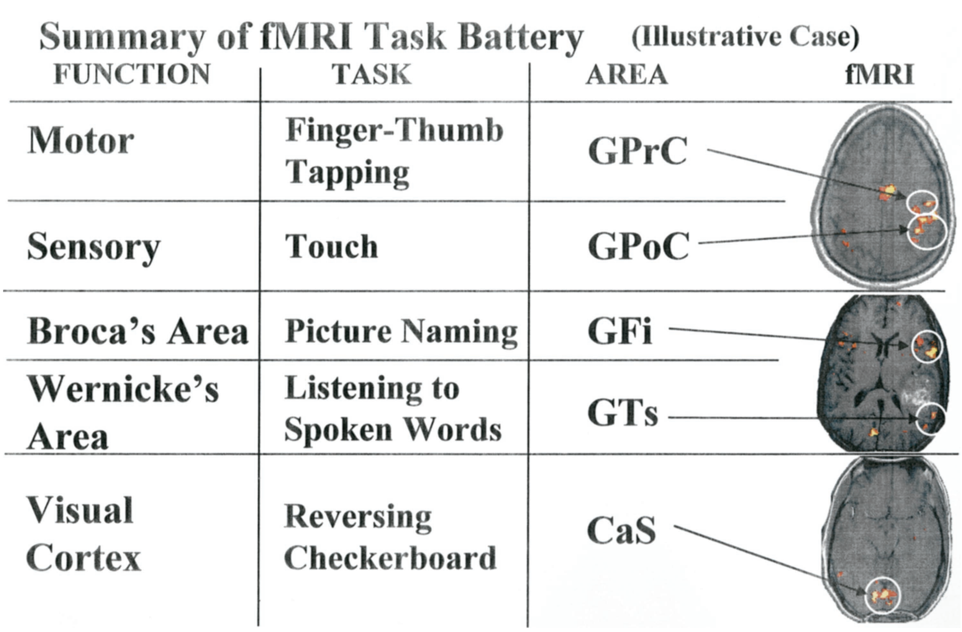

FIGURE 4. Selected MRI slices (*right*) illustrate cortical responses associated with each of the tasks and the targeted regions of interest. Sensory and motor tasks elicited activity within the precentral gyrus (*GPrC*) and postcentral gyrus (*GPoC*) and predicted the location of the central sulcus on multiple contiguous slices. The slice illustrated shows a relatively inferior representation. The two language tasks, picture naming and listening to spoken words, elicited activity in the left hemisphere within the inferior frontal gyrus (*GFi*) and the superior temporal gyrus (*GTs*) (*arrows*). In this case, the specific locations of the activity within the GFi and GTs were replicated on both tasks, and the overlapping regions were taken as the best predictor of Broca's and Wernicke's areas, respectively. Finally, the reversing checkerboard indicated the primary visual cortex, as illustrated by the activity labeled *CaS* (calcarine sulcus). Similar to the language-related regions, these regions were replicated across the multiple visual tasks and served to increase confidence in these results.

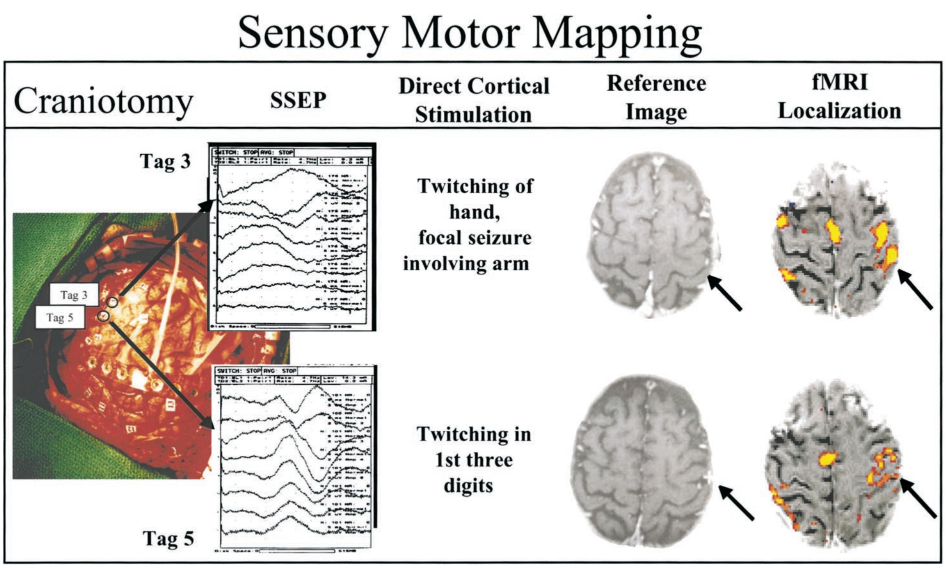

FIGURE 5. **Needle-recording electrodes were placed at Erb's point, and stimulating electrodes were placed over the left or right median nerve at the wrist. After a craniotomy and exposure of the cortex, subdural strip electrodes were placed in the operative field. The median nerve was stimulated to elicit epicortical responses, measured with the electrodes. A consistent phase reversal between electrode sites (*Tags 3* and *5*) was taken as the physiological identification of the sensorimotor cortex and therefore the central sulcus (indicated by *arrows* on the reference images). These recordings of SSEPs were made with an 8-Channel Viking IV7 and standard filter settings (30 Hz to 3 kHz). Direct cortical stimulation of the exposed cortex directed by the SSEP results was performed using the Ojemann bipolar stimulator (1-s trains of 1-ms pulses at 60 Hz) varied from 2 to 18 mA, peak to peak, resulting in hand twitching and a focal seizure of the right arm (*top row*) and twitching of the first three digits of the hand (*bottom row*). Using a frameless intraoperative navigation system (BrainLab), the tagged locations were referenced to anatomic axial magnetic resonance images localized by using a viewing wand, and subsequently compared with areas of activation on corresponding fMRI images as illustrated by comparison of the images in Columns 4 and 5 (*arrows*). The T2*-weighted images (*right column*) and the conventional T1-weighted images (reference image) were not acquired at exactly corresponding plane orientations, which accounts for the variation in the two structural images and limits the precision with which the electrophysiological and fMRI locations can be compared.**

logical evaluation revealed residual, mild word-finding difficulties and occasional literal paraphasic errors.

DISCUSSION

The protection of functions potentially at risk during brain surgery may be facilitated by functional mapping of critical areas. Implementation of a variety of techniques to identify cortical areas involved in sensory, motor, and language functions has become standard practice. These include intraoperative electrophysiological recording with motor and language mapping, preoperative Wada testing, and visual field examinations. However, the added risk, time, and expense of multiple mapping procedures could be reduced if a single, noninvasive, preoperative procedure proves effective for mapping these functions. fMRI, based on the representation of local blood flow changes that correlate with neural activity, has emerged as a technique for preoperative functional mapping. In this study, we introduced an interrelated battery of multiple fMRI tasks designed to target specific areas of the brain specialized for multiple functions, including somatosensory, motor, language, and vision.

These functions were selected on the basis of their general importance to quality of life for neurosurgical patients, the risks inherent in resecting the cortical areas mediating these functions, and the observed distribution of cases within our neurosurgical service. The sensitivity of these tasks was evaluated by targeting specific cortical regions expected to be specialized for these functions; that is, somatosensory and motor functions (pre- and postcentral gyri), language functions (inferior frontal and superior temporal gyri), and vision functions (calcarine sulcus and inferior occipital gyrus). The probability that each task would activate the targeted region was determined for healthy volunteers and surgical patients with tumors near or within these critical areas.

Accuracy of the fMRI maps was confirmed by concordance of the spatial locations with conventional mapping, including SSEPs, direct cortical stimulation, language mapping, Wada testing, and visual field examinations in those patients for whom these procedures were included as part of the conventional therapeutic plan. A novel feature of this battery of integrated fMRI tasks is the redundancy in the measurements. For example, language-sensitive regions are mapped by both active (expressive) and passive (receptive) tasks, as are the regions sensitive to motor (active tapping) and sensory (passive touching) tasks. Visual areas are also assessed by passive viewing of the reversing checkerboard stimulus (no response required) and active viewing of pictures during a naming task in which a response was required. Advantages to using more than one task associated with a particular function to isolate eloquent cortical areas include improved confidence when replications are observed and improved sensitivity when the activity is observed during either an active or a passive performance. This feature translates into a greater likelihood of a successful map for patients with neurological deficits. Together, the task sensitivity and accuracy observed for these fMRI maps indicate that this multifunction task battery is likely to yield a reliable estimate of the locations of critical functions potentially at risk during brain surgery and thus to extend the potential of

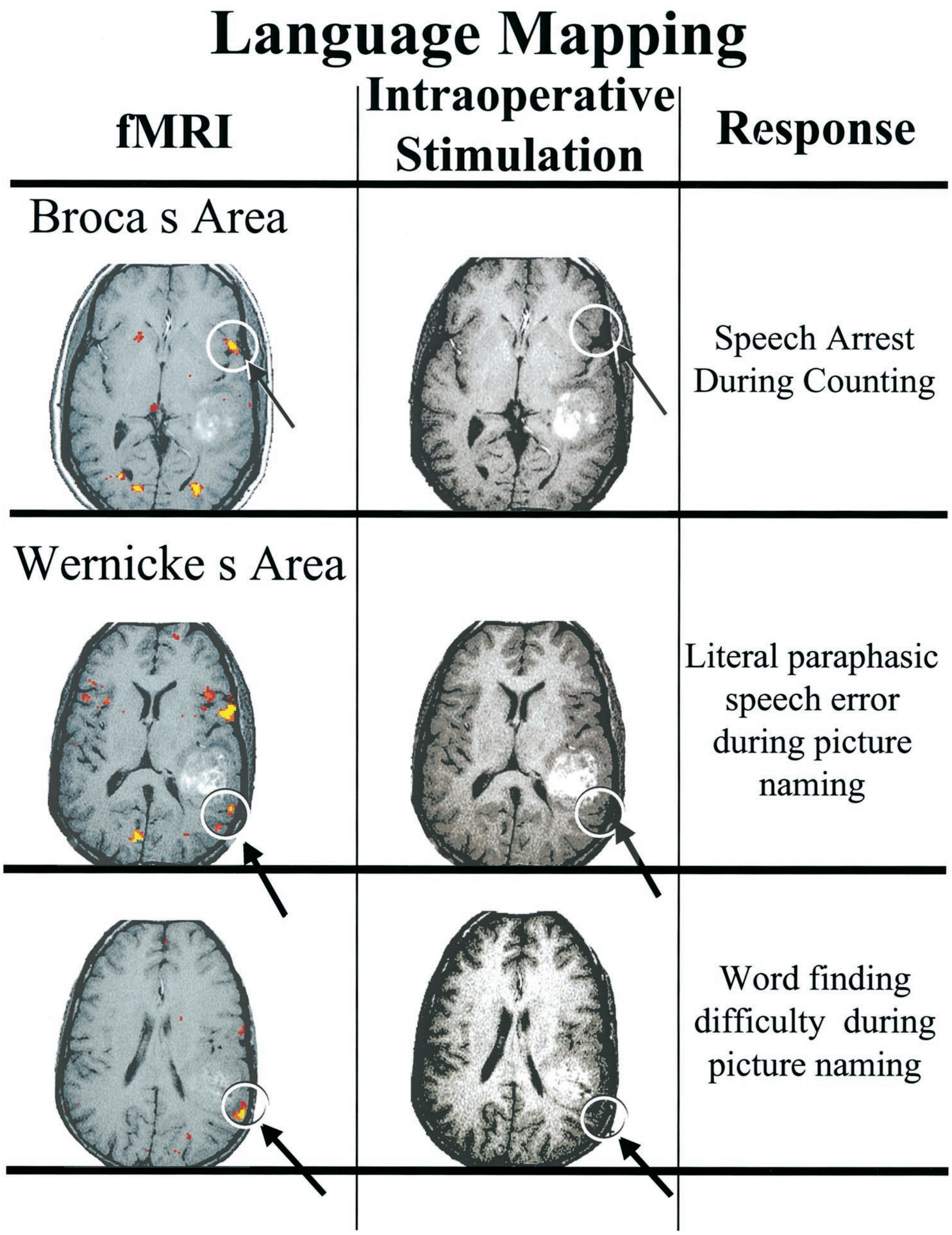

FIGURE 6. **After craniotomy and recording of SSEPs, the patient was awakened and asked to count forward and backward while the cortex in the putative Broca's area was stimulated, as described in *Figure 5*. Subsequently, the picture-naming paradigm used in the fMRI battery of tasks was administered, and stimulation at the site in which the fMRI maps indicated the location of Broca's area resulted in speech disruption (*top row*). Stimulation was systematically repeated and extended to the temporal lobe cortex, and sites of activation revealed by the fMRI maps were specifically targeted, as indicated by the *circles* in the *middle* and *bottom rows*. These stimulations resulted in paraphasic speech errors and word-finding difficulties, as indicated, consistent with disruption of Wernicke's area-related functions, which occurred in two separate locations. The corresponding preoperative fMRI maps (*left column*) confirm the correspondence of cortical areas (*circles* and *arrows*).**

a single preoperative fMRI brain mapping procedure to facilitate optimal outcomes for neurosurgery.

On the basis of our experience with this fMRI task battery, the images serve both pre- and intraoperative objectives. On the preoperative side, the fMRI maps have contributed to our estimates of the risk/benefit ratio and to the decision whether to offer surgery to the patient, although these decisions are based on the entire medical situation taken together and not on any single factor. Communication between the surgeon and the patient is also facilitated by images that summarize the relevant structural and functional issues. On the intraoperative side, as described in the illustrative case presented here, the fMRI results have also served to direct the intraoperative electrophysiological recording and thereby have contributed to the efficiency of the intraoperative procedures. However, we have observed that the information offered by the preoperative fMRI map is often more distributed than that of the intraoperative map, and the question of which active regions are essential to the function is not directly addressed by fMRI (23). A false-positive interpretation is therefore possible on the basis of these associated patterns of activity, whereas a false-negative finding is also possible, owing to the sensitivity, compliance, and imaging artifacts discussed previously. The likelihood of obtaining both types of errors is reduced with repetitions and checks for internal consistency, as suggested by this integrated task battery.

Many future enhancements of this initial task battery are possible using methods that determine task sensitivity and clinical validity, as well as improvement in confidence by reducing the risk of either false-positive or false-negative findings. For example, extension of the battery to include memory functions, high-level cognitive tasks, and perhaps even emotion and affect are viable future directions, as is continued development to improve the tasks to target the sensorimotor and language areas. Techniques used for the advancement of this integrated battery of functions could serve as a basis for developing other similar probes, and thus for extending the potential role of fMRI in neurosurgical planning to more precise and diverse structural and functional relationships.

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COMMENTS

The role of magnetic resonance imaging in the diagnosis and management of patients with brain tumors continues to evolve. Functional magnetic resonance imaging (fMRI) has the capacity to show the differences in brain function that occur when performing a task by showing the associated difference in the proportion of local deoxyhemoglobin. In this study, Hirsch et al. report their findings using a stereotypical battery of tests in a series of healthy volunteers and surgical patients with cerebral lesions. The results may be succinctly summarized: 1) fMRI usually, but not always, agrees with expected function by anatomy; 2) fMRI usually, but not always, agrees with observed location by intraoperative testing; 3) there are a few false-positive findings; and 4) there are a few false-negative findings.

These findings (and those of many other groups) show that fMRI produces interesting and often provocative results. It may help us better understand the function of the brain and has the potential to be widely available. Unfortunately, head movement or noise may produce erroneous results that look "real" and require repetition to extract less ambiguous data. Someone skilled in testing needs to be present to ensure that the task is performed appropriately.

To date, I have not seen compelling evidence that fMRI alone gives sufficient information on which to make critical surgical decisions in the absence of intraoperative testing. Similar to a good knowledge of the functional anatomy of the hemispheres, fMRI will distinguish the surgeon's proximity to a functional area and the need for intraoperative testing. Unlike anatomy, it may give an indication of the nuances of function in a particular patient.

The accurate prediction of speech laterality in this report is encouraging, but the numbers are small (13 double-blind cases). For now, fMRI remains primarily a research tool, but it will probably find its niche as a useful tool in the perioperative management of neurosurgical patients.

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Hirsch et al. have described using fMRI to identify tactile, motor, language, and visual cortical areas. The authors show that using a combination of tasks leads to a highly sensitive identification of these functional areas. They have used intraoperative electrophysiological techniques and preoperative sodium amobarbital testing to corroborate their findings. The unique contribution of this article is that using these multimodal tasks enhances the sensitivity and reliability of functional imaging measures.

It is important for practicing neurosurgeons to realize, however, that changes in cortical blood flow, whether they be increases or decreases, can yield false-positive and false-negative information. There are many reasons for this. The test batteries applied are acute challenges and measure very specific tasks. It is not because there is a change in the functional imaging that surgical encroachment of these areas will necessarily lead to a functional deficit. On the other hand, lack of change also is no guarantee that it is safe to cut through areas that are summoned on functional imaging. fMRI detects changes in blood flow and not necessarily changes in function of individual neurons. One can envisage a scenario in which there are neurons that increase in activity and others that decrease in area with no net change in regional metabolic activity and no change in fMRI signal. Furthermore, fMRI is sensitive to cortical changes and has little sensitivity for subcortical areas and, particularly, for white matter tracts. The interruption of these tracts can lead to major disruptions in neurological function. It is for this reason that functional imaging is a useful guide in preoperative and intraoperative planning but does not replace the need for careful intraoperative mapping in regions of cerebral eloquence. In this respect, electrical stimulation and changes in surface cortical imaging (1) have an important ongoing and future role.

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1. Haglund MM, Ojemann GA, Hochman DW: Optical imaging of epileptiform and functional activity in human cerebral cortex. **Nature** 358:668–671, 1992.

This article presents the concept of an integrated battery of fMRI tasks, enabling imaging of motor, sensory, language, and vision areas. This is supplemented by experience with a large number of control subjects and patients, and a very high success rate is reported in using these data to determine the location of the central sulcus, receptive and expressive speech areas, and visual cortex. It is noteworthy that sensitivities ranging from 77 to 100% were achieved in the setting of pathological involvement of those functional areas, and this is consistent with the recent report of Lehéricy et al. (1).

As functional imaging increasingly becomes a part of surgical decision-making and operative procedure, further understanding of issues raised in this article will necessarily be gained. This study's methodology unfortunately precludes quantified determination of the spatial concordance between fMRI and intraoperative mapping, but validation of fMRI, including three-dimensional accuracy, has been made possible by intraoperative digitizing technology and is in the process of being accomplished by many groups.

The true relationship between structure and function similarly can be better understood than ever before and will refine the fundamental questions for which functional imaging modalities are being used today. Nevertheless, the advantages of efficiency and improved sensitivity and specificity achievable through integrated imaging, although still incompletely understood, certainly must be real.

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Statue of the Praetorian Guard, founded by Augustus. The Guard served as the Emperor's personal bodyguard. Quartered in barracks outside Rome, the Praetorians wore special uniforms, received more pay than typical legionnaires, and served for a shorter period of time. For over 200 years, they were the only Roman troops stationed in Italy.