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Comparative localization of auditory comprehension using functional magnetic resonance imaging and cortical stimulation

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The authors have previously described a functional magnetic resonance (fMR) imaging procedure for the localization of auditory comprehension in which focal activation of posterior temporal and inferior frontal regions of the left hemisphere was reliably demonstrated. Because this past study was conducted in neurologically normal volunteers, it was not possible to determine whether the activated regions were critical to the performance of language tasks; that is, whether the fMR imaging activations provided a rate measure of language processing. A direct comparison of fMR imaging language activation with cortical stimulation must be completed before the tool can be used with confidence in presurgical planning.

Here the authors report a series of 33 consecutive patients who underwent dominant hemisphere resection in which fMR image mapping of auditory comprehension was performed at the Yale neurosurgical program.

In 23 of the 33 patients reliable fMR imaging activation was shown. In 16 of these 23 patients language mapping was performed using either intra- or extraoperative cortical stimulation. Cortical stimulation failed to localize language areas in two of the 16 patients. Electrical stimulation that was performed in close proximity to the fMR image activations interfered with auditory comprehension, object naming, or speech production in 12 of the remaining 14 patients. Five of the 10 cases in which evocation reliable fMR imaging activation failed were attributable to technical problems and/or patient head movement.

Cortical stimulation results and fMR imaging findings were consistent in all but two patients. However, the spatial extent of the activation produced by fMR imaging and the spatial extent of stimulation-induced language disruption that was caused by direct cortical stimulation did not always correspond. Problems in defining the extent of activation by both methods are discussed.

Key Words * functional magnetic resonance imaging * cortical stimulation * brain mapping * comprehension * language

We have previously demonstrated activation of discrete regions in the posterior temporal and inferior frontal cortex of neurologically normal volunteers who listened to sentences spoken in their native English and those spoken in an unfamiliar language.[27] These activations occurred predominantly in the left hemisphere and were clearly differentiated from regions that were activated by pure tone glides and white noise. The sentences were matched in length and volume and were read by the same speaker who attempted to match prosody. Thus, we concluded that the activation was primarily due to the subject's comprehension of the English sentences.

Posterior activation occurred primarily in the posterior superior temporal sulcus extending onto the surface of the middle temporal gyrus. Frontal activation occurred primarily in the inferior frontal gyrus within Brodmann's area.[45] These activation loci suggest, respectively, Wernicke and Broca's areas, which are frequent objectives of presurgical language-mapping studies of the dominant temporal lobe in which cortical stimulation is performed. Wernicke's area is typically identified by stimulation-induced disruption of auditory comprehension and/or object naming, whereas Broca's area is typically identified by stimulation-induced speech arrest.[7,15,16,22,23] Because stimulation mapping requires an awake and cooperative patient and adds time to the surgical procedure when performed intraoperatively, noninvasive alternatives have been sought.[5,9-11,13,14,17,18] Analysis of the results of Schlosser, et al.,[27] and others[1,3-5,6,8,12,19,20,24] suggests that functional magnetic resonance (fMR) imaging may provide a useful alternative or adjunct to cortical stimulation. However, it is first necessary to establish that the areas activated by fMR imaging are critical sites for language processing by demonstrating that language deficits occur when these areas are stimulated and that no areas in which stimulation produces significant deficits are missing from the fMR imaging activation.

We therefore conducted preoperative fMR imaging studies in 33 patients in whom a neurosurgical procedure in the dominant hemisphere was to be performed. The procedure described by Schlosser, et al.,[27] was performed with only minor modifications as noted in a subsequent section. In 14 of these patients, successful language mapping was later performed using intra- or extraoperative cortical stimulation.

CLINICAL MATERIAL AND METHODS

Patient Population

Thirty-three patients from the Neurosurgical service at Yale-New Haven Hospital, including those from the Yale Epilepsy Surgery Program, Yale Neurovascular Surgery Program, and Yale Neuro-oncology Program, were studied using the auditory comprehension task previously described.[27] Patients ranged in age from 11 to 53 years, and all but one were right-handed. All patients were native English speakers who were not familiar with the Turkish language.

Functional Magnetic Resonance Imaging

The auditory-comprehension task has been previously described.[27] Briefly, stimuli consisted of 112 digitized auditory segments, each consisting of one or two sentences that lasted for a total duration of 4.8 to 5.8 seconds. Fifty-six of the segments were spoken in English, whereas the remaining 56 segments consisted of the same sentences spoken in Turkish. The same female speaker produced both language segments, and she attempted to match intonation and prosody closely. Words that sounded similar in each language were avoided. The segments were processed in software to equalize their amplitude range and to ensure a uniform onset.

Patients were presented with four runs, each consisting of an alternating series of English and Turkish auditory segments. Two variants of the task were tested. In the first 10 patients tested, English and Turkish segments were alternated every 6 seconds, and 28 alternations were presented in each run. In the remaining 23 patients, English and Turkish segments were alternated every 12 seconds, and there were 14 alternations in each run. In these latter patients, two English-language digitized segments were presented within each 12-second English alternation, and two Turkish-language digitized segments were presented within each 12-second Turkish alternation. For all patients, two runs started with English (E-T-E-T . . .), and the remaining two runs began with Turkish (T-E-T-E . . .). In the successive English and Turkish segments the same sentences were never used. Stimulation began 12 seconds after the onset of image acquisition. Patients were instructed to listen to all sentences for comprehension. They were informed that half of the sentences would be in Turkish but were unaware that the same sentences were presented in each language over the course of the four runs. A computer was used to control experimental timing and auditory presentation. The sounds were conducted into the MR imaging system by using an intra-MR auditory system (Resonance Technologies, Northridge, CA). All stimuli were binaural.

Imaging Parameters

Images were acquired by using a 1.5 tesla MR imager that was equipped with a standard quadrature head coil and advanced nuclear MR imaging echoplanar subsystem. The patient's head was positioned along the canthomeatal line and immobilized using a vacuum cushion and a forehead strap. Sagittal T_1-weighted MR images were obtained, and a lateral sagittal image was used to identify the sylvian fissure. Eight coronal slices were selected perpendicular to the angle of the sylvian fissure, with the most anterior slice beginning at the anterior tip of the temporal lobe. Axial slices were acquired for the first patient tested, with the most inferior slice occurring at the top of the pons. Functional MR images were obtained using a gradient echo echoplanar imager (repetition time [TR] 1500 msec, echo time [TE] 45 msec, ALPHA 60š, number of excitations [NEX] 1, field of view [FOV] 40 X 20 cm, slice thickness 9 mm, skip 2 mm, imaging matrix 128 X 64, voxel size 3.2 X 3.2 X 9 mm). The images for each of the eight slices were acquired in equally spaced time intervals over the 1.5-second TR in the slice order 1-3-5-7-2-4-6-8. Each of the four imaging runs consisted of 128 images per slice (196-second scan time) preceded by four radiofrequency excitations to achieve steady-state transverse magnetization. The T_1-weighted images were obtained for anatomical coregistration in the same locations and in the same plane (axial or coronal) as the functional images.

Data Analysis

Three consecutive images (per slice) were selected from each of the English-language segments and were compared with an equal number of images selected in the same manner from the Turkish-language segments by conducting an unpaired t test on a voxel-by-voxel basis. Voxels exceeding a t value of ± 1.96 (corresponding to a two-tailed false-positive rate of 0.05, uncorrected for multiple comparisons) were counted for each slice and hemisphere and were depicted as color overlays upon anatomical MR images. Because MR signal intensity during English segments was compared with activation during Turkish segments, voxels with t values that corresponded with the positive tail of the t distribution had greater signal during English than Turkish segments. Voxels with t values corresponding to the negative tail of the distribution had greater signal intensity during Turkish than English segments.

Cortical Stimulation

Of the 23 patients who underwent cortical stimulation, in seven patients stimulation was performed intraoperatively and in 16 patients stimulation was performed extraoperatively. Intraoperative cortical stimulation was performed using 50 Hz, 0.1-msec duration, 8-mA constant-current pulses delivered through a hand-held bipolar probe. Extraoperative stimulation was performed at patients' bedsides by using chronically implanted subdural electrodes. Stimulation was delivered via pairs of adjacent grid electrodes in increasing 2 mA steps beginning at 2 mA and ranging to a maximum intensity of 10 mA. The increasing intensity steps were discontinued if a positive behavioral response was noted or if electroencephalography monitoring indicated after-discharges.

During stimulation, patients were asked to name everyday objects presented on flash cards, to articulate complete simple sentences ("When you have a toothache, you go to the _____"), to carry out simple commands (for example, "Point to your nose"), and to read simple sentences. If errors were noted, the test was repeated and the patient was asked to elaborate on his difficulties (for example, the patient might report that the experimenter's voice sounded garbled or strange or that the patient knew the name of the object depicted upon the flashcard but was unable to speak). The experimenters also noted when stimulation evoked a motor response, such as mouth or hand movement, or a sensory response such as tingling of the fingers.

Three-Dimensional Rendering

Image analysis software (Omniview, 3D Biomedical Imaging, Inc., Shawnee Mission, KS) was used to create a three-dimensional rendering of brain, tumor, electrode location, fMR imaging activation, and electrical stimulation sites. Customized software was used to register the structural and functional MR image series and to locate other points of interest within this volume. In some cases, a frameless stereotactic system (OMI, Columbus, OH) was used intraoperatively to localize the sites in which language deficits were observed. All images were obtained on a Signa 1.5 tesla imager (General Electric, Inc., Schenectady, NY). One of two source series was used to create the reformatted series: 1) a coronal spoiled grass series (1.5-mm contiguous slices, FOV 220-240 mm, TR/TE 25/5, NEX 2, matrix 256 X 192) or 2) an axial spoiled grass series (1.5-3.0 mm contiguous slices, FOV 220-240 mm, TR/TE 25/5, NEX 2, matrix 256 X 192).

RESULTS

Table 1 provides a summary of results for each of the 33 patients studied. In 10 patients, reliable fMR imaging activation in response to the English-language sentences was not obtained. Three of the failures were caused by computer error during image acquisition. Two studies included an unacceptable amount of head movement that resulted in uninterpretable data. In the remaining five patients, failure to obtain fMR imaging activation is unexplained.

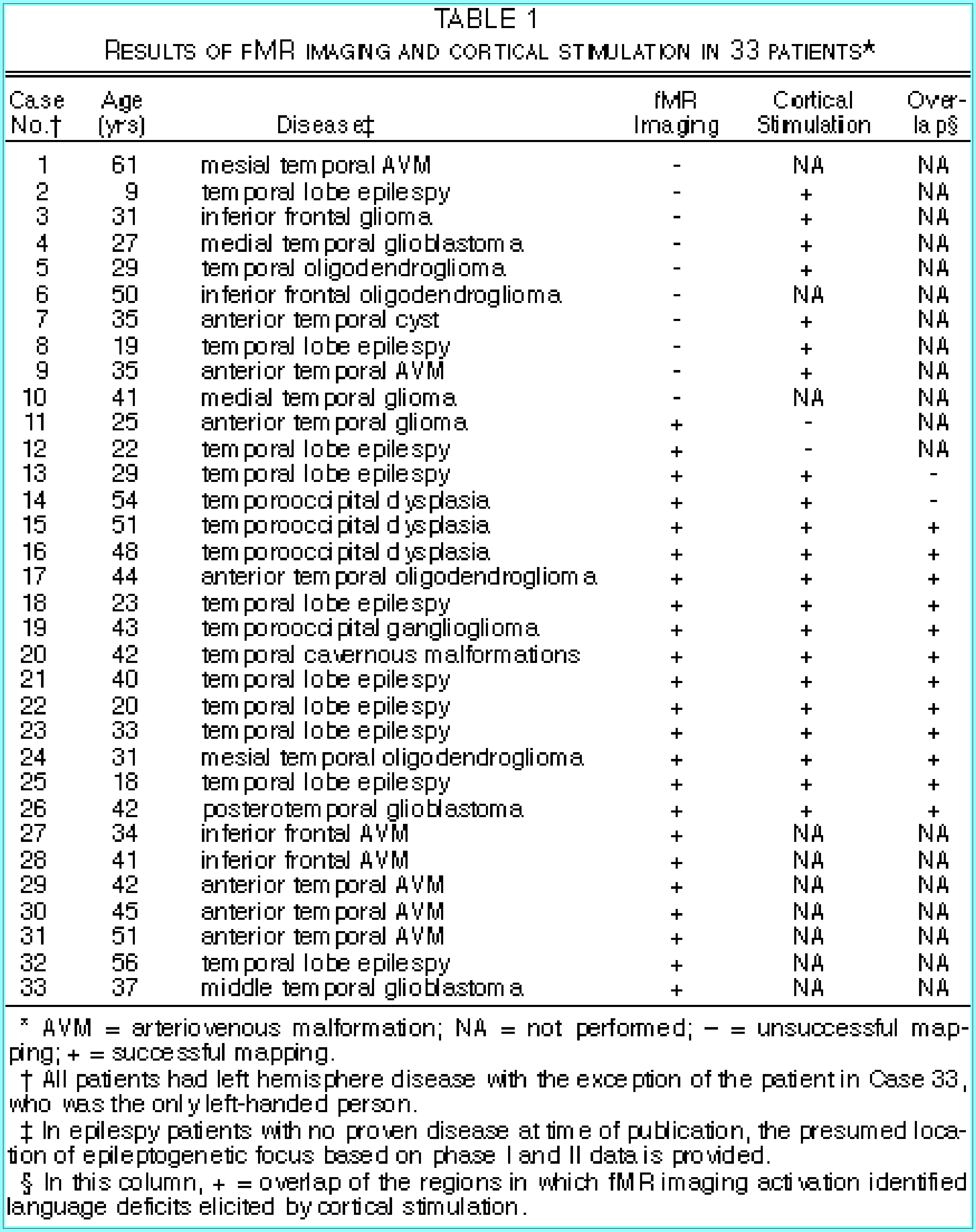

TABLE 1

RESULTS OF fMR IMAGING AND CORTICAL STIMULATION IN 33 PATIENTS*

Case No.†	Age (yrs)	Disease‡	fMR Imaging	Cortical Stimulation	Overlap§
1	61	mesial temporal AVM	-	NA	NA
2	9	temporal lobe epilespy	-	+	NA
3	31	inferior frontal glioma	-	+	NA
4	27	medial temporal glioblastoma	-	+	NA
5	29	temporal oligodendroglioma	-	+	NA
6	50	inferior frontal oligodendroglioma	-	NA	NA
7	35	anterior temporal cyst	-	+	NA
8	19	temporal lobe epilespy	-	+	NA
9	35	anterior temporal AVM	-	+	NA
10	41	medial temporal glioma	-	NA	NA
11	25	anterior temporal glioma	+	-	NA
12	22	temporal lobe epilespy	+	-	NA
13	29	temporal lobe epilespy	+	+	-
14	54	temporooccipital dysplasia	+	+	-
15	51	temporooccipital dysplasia	+	+	+
16	48	temporooccipital dysplasia	+	+	+
17	44	anterior temporal oligodendroglioma	+	+	+
18	23	temporal lobe epilespy	+	+	+
19	43	temporooccipital ganglioglioma	+	+	+
20	42	temporal cavernous malformations	+	+	+
21	40	temporal lobe epilespy	+	+	+
22	20	temporal lobe epilespy	+	+	+
23	33	temporal lobe epilespy	+	+	+
24	31	mesial temporal oligodendroglioma	+	+	+
25	18	temporal lobe epilespy	+	+	+
26	42	posterotemporal glioblastoma	+	+	+
27	34	inferior frontal AVM	+	NA	NA
28	41	inferior frontal AVM	+	NA	NA
29	42	anterior temporal AVM	+	NA	NA
30	45	anterior temporal AVM	+	NA	NA
31	51	anterior temporal AVM	+	NA	NA
32	56	temporal lobe epilespy	+	NA	NA
33	37	middle temporal glioblastoma	+	NA	NA

* AVM = arteriovenous malformation; NA = not performed; − = unsuccessful mapping; + = successful mapping.

† All patients had left hemisphere disease with the exception of the patient in Case 33, who was the only left-handed person.

‡ In epilespy patients with no proven disease at time of publication, the presumed location of epileptogenetic focus based on phase I and II data is provided.

§ In this column, + = overlap of the regions in which fMR imaging activation identified language deficits elicited by cortical stimulation.

The 23 patients in whom consistent fMR imaging activation was obtained had activation patterns similar to those seen in the study of neurologically normal patients,[27] with four exceptions noted below. A typical fMR imaging activation, obtained in a patient with temporal lobe epilepsy, is shown in Fig. 1. Strong activation was demonstrated in the posterior superior temporal sulcus with additional activation obtained in the left inferior frontal gyrus. This pattern is consistent with those obtained by Schlosser, et al., in a study of neurologically normal volunteers.[27]

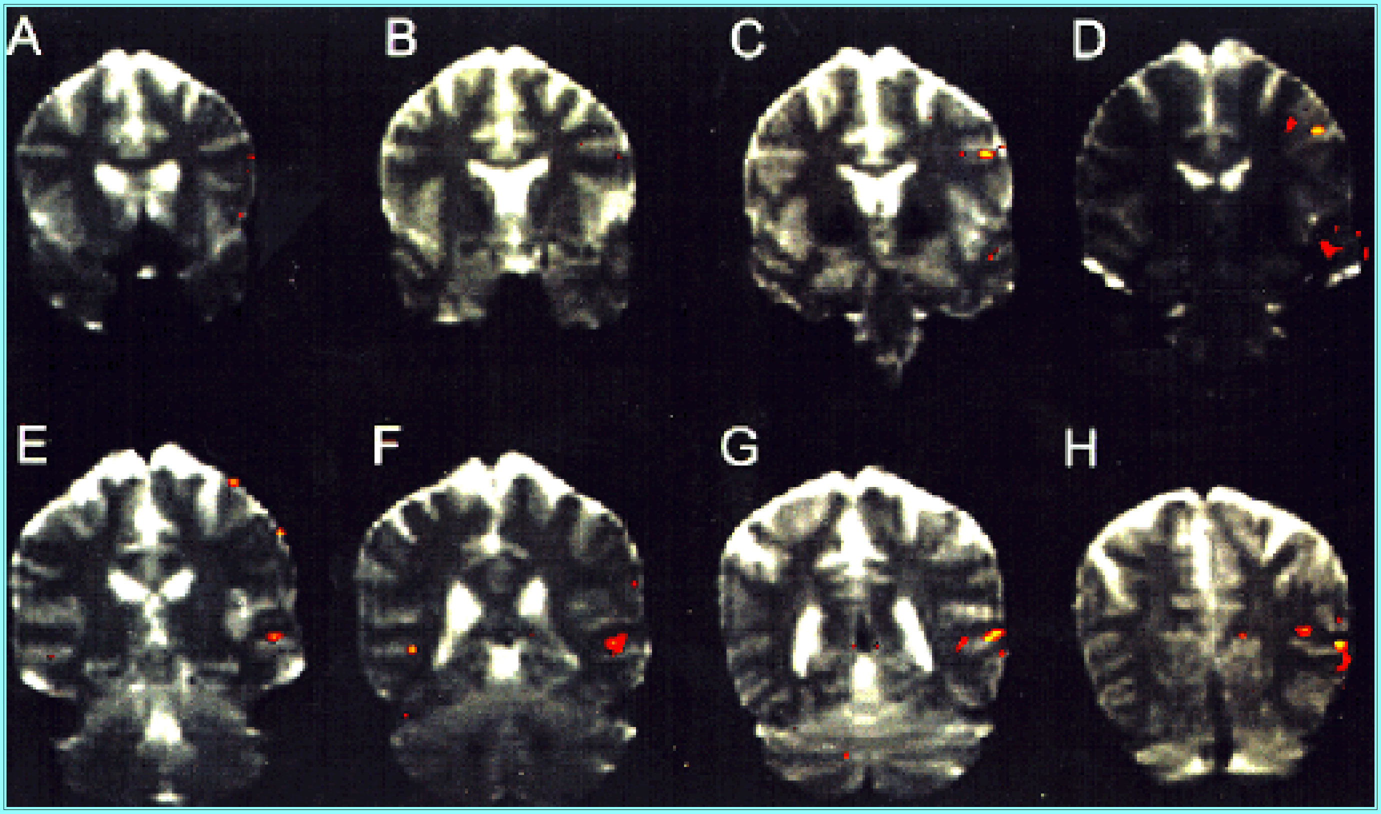

Fig. 1. A-H: Functional MR imaging activations evoked by English sentences at eight slice locations superimposed on spin-echo echoplanar images. Coronal slices are shown in the radiological convention in which the right side of the figure represents the left hemisphere. The color scale represents increasing t values from 1.96 to 5.9.

In four patients, there was an unusual pattern of activation. In two right-handed patients who harbored left posterior temporal lobe tumors, activation was shown in the right posterior superior temporal gyrus (STG) and left inferior frontal gyrus (IFG). In one right-handed patient with a long-standing left temporal lobe arteriovenous malformation, activation was demonstrated in the right STG and IFG. Lastly, in one left-handed patient who harbored a large right temporal lobe glioblastoma, activation was shown in the right IFG but left STG.

Of the 23 patients in whom consistent fMR imaging activations were obtained, 16 also underwent cortical stimulation mapping. The remaining seven patients did not undergo cortical stimulation. Five patients harbored vascular malformations and underwent surgery after induction of a general anesthetic, which made intraoperative cortical stimulation impossible. In two patients, the lesion was sufficiently far from the primary language area that cortical stimulation was not deemed necessary. Of 16 patients who underwent cortical stimulation, in two patients positive stimulation findings were not obtained (no language deficits were demonstrated at any electrode pairs or locations in the surgical field). Thus, 14 patients underwent successful language mapping in which both modalities were used. Of these 14, the images in 12 showed significant overlap between the regions activated during the auditory-comprehension fMR imaging procedure and regions where electrical stimulation produced language disruption. Examples of the results obtained in individual patients are summarized in the following section.

ILLUSTRATIVE CASES

Case 16

The findings in this case provide an example of perfect correspondence between a focal fMR imaging activation and a focal stimulation-induced language deficit. This patient suffered from left occipitotemporal lobe epilepsy, and a subdural grid was implanted for seizure localization. Figure 2 shows the fMR imaging and cortical stimulation data. The electrode site where stimulation produced language deficits is depicted in blue in Fig. 2 B-D. This pair was positioned directly over the area of cortex that was activated in the fMR imaging task. Evaluation of the cortical stimulation report for this electrode pair indicated that object-naming hesitation occurred at 6 mA and object-naming deficits at 8 mA. No other locations on the grid indicated the presence of language deficits, nor were there any other fMR imaging activations. This patient underwent a left temporooccipital resection and was left with right visual field cut, but no residual language deficits by 6 months postsurgery.

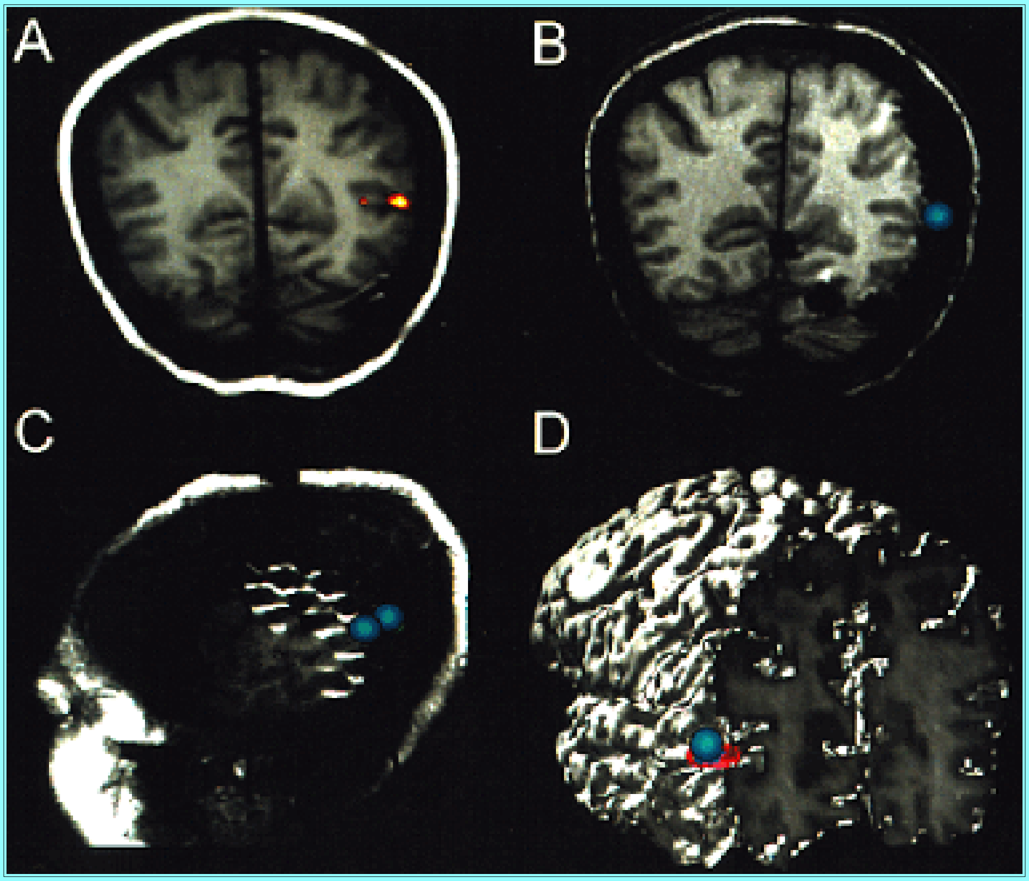

Fig. 2. Case 16. A: Posterior temporal lobe fMR imaging activation. This posterior superior temporal sulcus (STS) activation was the sole location activated by English sentences in this patient. B: Coronal slice obtained from the postimplant image that corresponds with the slice shown in 2A. Blue shaded electrodes indicate locations at which stimulation evoked deficits in object naming at 8 mA and 10 mA. C: A sagittal image obtained from the same postimplant series shown in 2B, demonstrating the same electrode pair in which object-naming deficits were evoked. Language difficulties were not found to result from stimulation of any other electrode pair on the implanted grid. D: A three-dimensional (3-D) surface rendering of the anatomical, fMR imaging and cortical stimulation data obtained in the coronal plane. The electrode pair shown in Fig. 2B is depicted in the 3-D view and directly overlies the fMR imaging activation evoked by English sentences (shaded red area).

Case 20

This case represented a more complex pattern of stimulation-induced deficits and fMR imaging activations. This patient harbored two cavernous malformations in his left temporal lobe (indicated by green shading [in Fig. 3]): one in the anterior and inferior temporal lobe and one more superior and posterior (Fig. 3A). A lateral surface grid and two multicontact depth electrodes (probes) were placed in proximity to the lesions. The posterior temporal depth electrode and lateral surface grid were stimulated extraoperatively to obtain language-function mapping data.

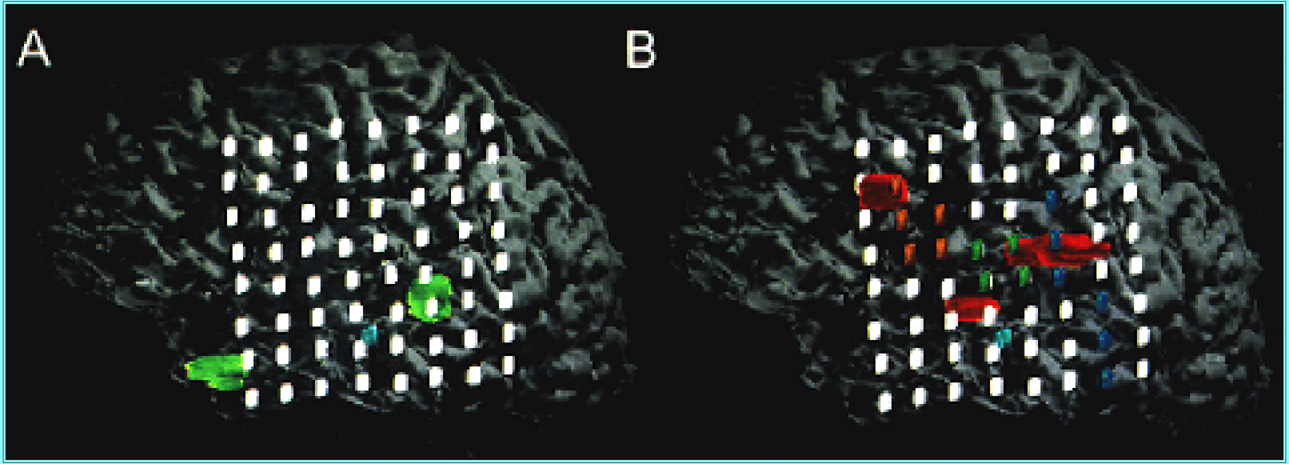

Fig. 3. Case 20. A: A 3-D surface MR imaging rendering depicting the location of subdural electrodes (white shading). Areas shaded green represent the two temporal lobe cavernous malformations described in the text. Two multicontact depth electrodes (probes) were also placed in this patient's left temporal lobe, one in proximity to each lesion. The posterior of the two probes is displayed in light blue, the anterior probe is not displayed. B: The same surface rendering displayed in Fig. 3A in which red-shaded areas represent the fMR imaging activations to English sentences. Electrode pairs in the inferior frontal region that evoked speech arrest when stimulated are shaded orange, stimulation sites in which mouth and face motor movements were evoked are shaded green, and sites in which auditory comprehension and object-naming deficits were evoked are shaded blue. Depth probe contacts in which stimulation-induced auditory comprehension deficits were evoked are shaded light blue. Electrodes in which face motor and language deficits were not evoked are shown in white. This color coding convention is used in all figures.

The results of cortical stimulation are shown on Fig. 3B. Speech arrest was obtained from electrodes in the inferior frontal lobe (orange shading). One pair of electrodes placed in an area where speech arrest was obtained was located directly above the fMR imaging activation in the inferior frontal gyrus. Language-comprehension deficits were elicited in the posterior section of the grid and on contacts of the posterior depth probe. Figure 3B shows electrode pairs on the probe where deficits in sentence completion and execution of verbal commands were evoked by stimulation (light blue shading). These electrodes lay directly under the more anterior of the two areas of temporal lobe fMR imaging activations (red shading in image). Grid locations where object-naming and sentence-completion deficits were evoked also overlapped with the fMR imaging activation. No fMR imaging activations were found in the posterior inferior temporal gyrus where prominent object-naming deficits were evoked by stimulation.

The two cavernous malformations and the surrounding tissue which showed marked gliosis were resected. Postoperatively the patient experienced object-naming deficits that resolved completely. Six weeks after surgery, his deficits had resolved.

Case 18

This case provides an example of how focal fMR imaging activation was completely contained within a larger region defined by cortical stimulation. Figure 4A shows a three-dimensional MR image surface rendering in which the grid electrodes and fMR imaging activation are depicted. Figure 4B shows an intraoperative photograph of the grid placement. The electrodes from which object-naming and sentence-completion deficits were evoked are indicated in blue. These functional deficits were evoked by stimulation at 8 mA and 10 mA.

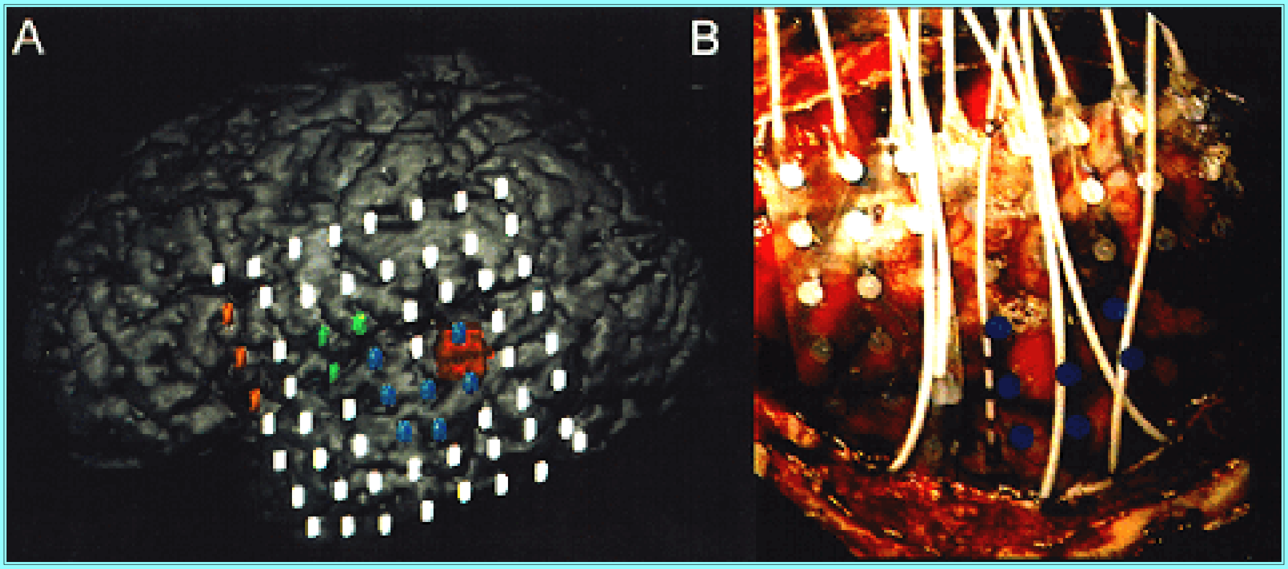

Fig. 4. Case 18. A: A 3-D surface rendering of structural MR and fMR imaging activations (red shading). All fMR image activations exceed the t threshold of 1.96. Stimulation effects are coded as in Fig. 3 (speech arrest, orange; mouth and face motor movements, green; and comprehension and object naming deficits, blue). B: Intraoperative photograph obtained during placement of the subdural electrodes shown in Fig. 2A. Electrodes shaded blue in Fig. 2A are reproduced.

During extraoperative mapping, stimulation of the electrode pair directly overlying the fMR imaging activation (shown in red) produced deficits in naming, comprehension, and reading. The patient was slow to name and could not name the last item shown until the stimulation was terminated. The patient could not provide the ending word for a simple sentence that was read to him and complained that the sentence sounded like "gibberish." When asked to read, the patient was seen to exhibit definite hesitations. During a subsequent left medial temporal resection, all sites in which stimulation evoked language disturbances (including those sites overlapping with the fMR imaging activations) were spared. In the immediate postoperative period the patient was profoundly aphasic, but he recovered completely within days after receiving a tapering dose of dexamethazone. Six months after surgery he was without deficits.

Case 22

This patient had both a subdural grid and two depth probes placed in the left temporal lobe (Fig. 5 A-C). One probe was placed in the supramarginal gyrus and the other in the superior temporal sulcus. In addition to cortical stimulation and fMR imaging mapping, evoked potentials in response to complex visual stimuli including faces, flowers, and nouns were recorded. Stimulation of electrodes in the superior temporal sulcus and on the surface of the middle temporal gyrus (the blue shading in Fig. 5B) evoked object-naming and sentence-completion deficits when stimulated at 10 mA. These electrodes surrounded cortex that was activated by the fMR imaging task. Nouns (but not faces or flowers) elicited a negative event-related potential at electrode sites in the supramarginal gyrus (Fig. 5C). These electrodes were located directly adjacent to cortex activated by English sentences.

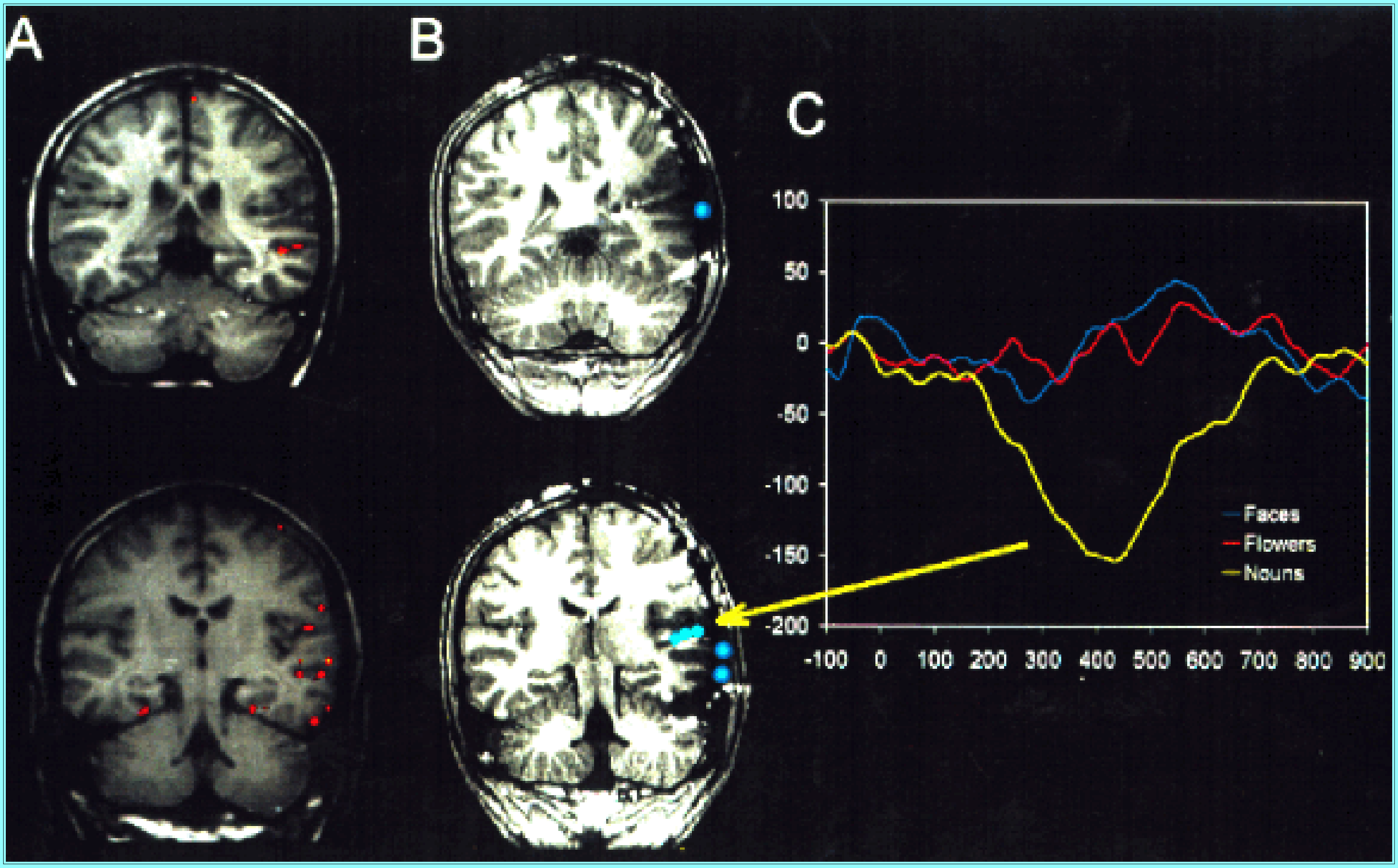

Fig. 5. Case 22. A: Functional MR imaging activation obtained from two coronal slices. B: Corresponding coronal slices in the postimplant MR image showing the location of surface electrodes and two multicontact depth electrodes. One probe lay in the superior temporal sulcus and the other was nearby in the supramarginal sulcus. Light blue circles represent the probe electrodes that evoked auditory-comprehension deficits during stimulation. The negative event-related potential displayed in Fig. 5C was recorded from the center electrode. Large blue circles on the surface of the brain represent surface electrodes where stimulation evoked auditory-comprehension and object-naming deficits. C: Graph depicting the event-related potentials evoked by visual presentations of nouns (yellow line), faces (blue line), and flowers (red line). Microvolts are represented on the vertical axis and milliseconds on the horizontal axis.

Case 15

This patient's intraoperative language mapping was performed with the assistance of a frameless stereotactic system as previously described. The surgeon marked stimulated areas that produced language-comprehension deficits with small white markers (as visible on Fig. 6D). The tip of the arm was then placed in the center of these markers. The cross hairs shown in Fig. 6B indicate the position of one such marker where the sentence-completion task was interrupted. As can been seen in Fig. 6A, these locations correlated well with activation to English sentences in the fMR imaging mapping.

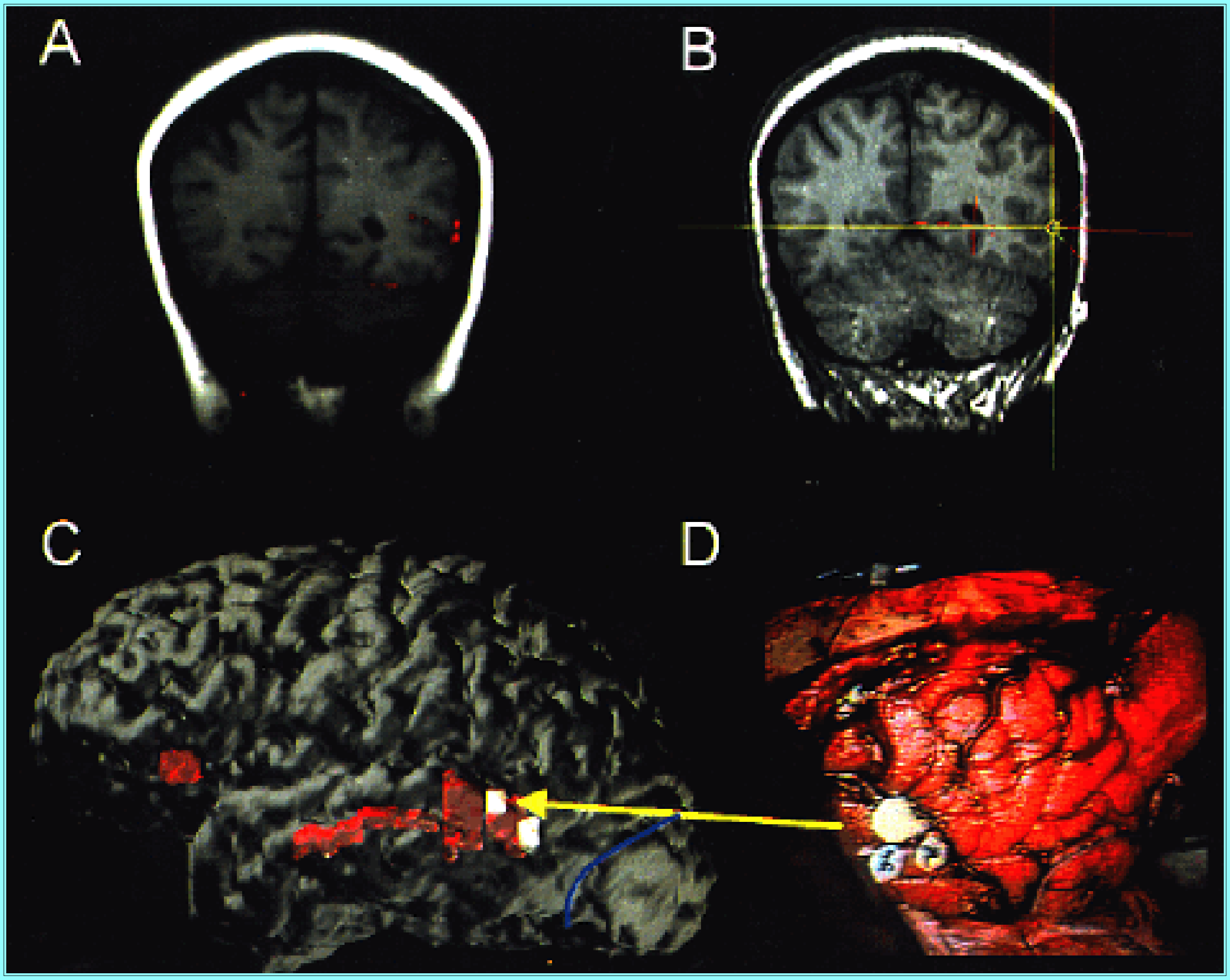

Fig. 6. Case 15. A: Functional MR imaging activations (red shading) in the STS and middle temporal gyrus elicited by English sentences are shown superimposed on a structural MR image. B. Output of the frameless stereotactic system showing the location of a site (indicated by cross hairs) where intraoperative cortical stimulation evoked auditory-comprehension (sentence-completion task) deficits. C: A 3-D surface rendering of structural MR and fMR imaging activations. White rectangles represent markers placed on the surface of the brain during stimulation in areas where sentence-completion deficits were evoked by stimulation (as seen in Fig. 6D). Stimulation was not performed anterior to the two white rectangles because this was the anterior border of the surgical exposure. D: Intraoperative photograph obtained following cortical stimulation. The three markers indicate sites at which stimulation produced auditory-comprehension deficits.

Stimulation of the cortex overlying the more anterior fMR imaging activations was not possible because the craniotomy did not expose this region. A posterior temporooccipital resection was completed using the combined cortical stimulation and fMR imaging as a guide, and the patient was without postoperative language deficit.

Case 17

This patient harbored an anteroinferior temporal lobe MR-documented abnormality that appeared consistent with a low-grade glioma. The location of language areas posterior to the tumor was critical for establishing resection margins, and thus, intraoperative cortical stimulation and fMR imaging mapping were performed (Fig. 7).

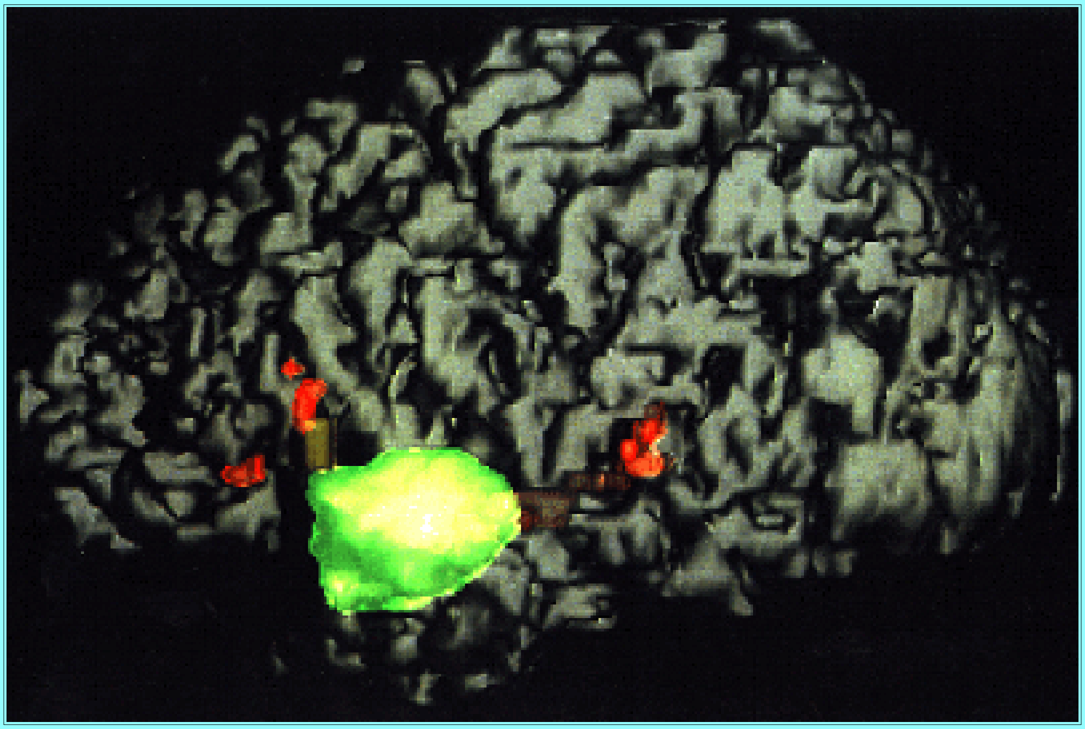

Fig. 7. Case 17. Functional MR imaging activation, intraoperative cortical stimulation results, and the location of a glioma are represented on a 3-D surface rendering of the structural MR image. Two levels of fMR imaging activations are depicted. The bright red activation represents voxels with a p value exceeding 0.005, and the dull red voxels had values between 0.05 and 0.005. A small craniotomy limited the extent of cortical stimulation. Bright red posterior temporal lobe activations were not demonstrated. The orange marker shows the location at which stimulation produced speech arrest. After this site was identified, further stimulation of the inferior frontal lobe was halted due to a focal motor seizure.

A small craniotomy was performed directly over the tumor (green shading in Fig. 7). Cortical stimulation of the cortex immediately posterior to the tumor did not result in any convincing sentence-completion or object-naming deficits. Some hesitations and mistakes were noted, but none was reproducible. The region of the posterior superior temporal sulcus in which the most significant (highest t values) fMR imaging activation was obtained was not stimulated. Stimulation of the inferior frontal lobe adjacent to the fMR imaging activation resulted in speech arrest (orange shading in Fig. 7). Stimulation just superior to this marker resulted in a focal motor seizure of the face, and thus further stimulation mapping of this area was halted. There were no language deficits noted postoperatively.

Case 26

In this patient with a small posterior temporal ring-enhancing lesion, fMR imaging mapping resulted in activation in the posterior superior temporal sulcus (STS) just anterior to the lesion, lower intensity activations in the anterior temporal, and robust activation in the inferior frontal gyrus. A large craniotomy was performed to allow stimulation of the temporal lobe and inferior frontal gyrus. Evaluation of the stimulation results revealed that comprehension deficits had occurred in cortices overlying the right posterior fMR imaging activation. Additionally, subtle but reproducible deficits in naming and repetition were found in the anterior temporal lobe that overlaid the fMR imaging activations of lesser intensity. Lastly, speech arrest was found in the inferior frontal gyrus in a location that overlapped fMR imaging activation results.

Failures

In two patients, language regions identified by both methods did not overlap, and in one patient an fMR imaging activation was obtained without any positive stimulation findings. In each case fMR imaging activation with the highest intensity (t value) was deep within the STS, 5 to 10 mm from the lateral cortical surface. In one patient, a large craniotomy allowed for intraoperative stimulation of both the inferior frontal gyrus and posterior temporal lobe. Speech arrest occurred during stimulation of the IFG; however, no frontal lobe activation had been obtained in the preoperative fMR imaging study. Stimulation of the temporal lobe produced no reproducible language deficits, but a focal activation was identified by fMR imaging deep within the posterior STS. The anterior temporal resection did not encroach on the fMR imaging activation, and language deficits were observed postoperatively.

The second patient had an implanted subdural grid and underwent mapping extraoperatively. Stimulation of electrodes overlying the middle temporal lobe produced hesitation in object naming. A focal fMR imaging activation was buried deep in the posterior STS. Stimulation of the electrodes directly overlying the posterior STS did not produce a language deficit. The patient underwent an anterior temporal lobe resection in which the superior temporal gyrus was spared without complication, and he sustained no language deficits after surgery.

In the third patient a focal fMR imaging activation was also shown deep within the posterior STS near the region identified by intracranial electroencephalography recording as the site of seizure onset. Stimulation of the lateral surface overlying the fMR imaging activation evoked no language deficits, nor did stimulation of the rest of the exposed temporal lobe. However, once the resection progressed into the deep portion of the STS, the patient's speech stopped. Postoperatively, she experienced a marked deficit in confrontational naming that resolved by 6 months postsurgery.

DISCUSSION

Cortical stimulation delivered in close proximity to the regions in which the most significant (that is, highest t values) fMR imaging activations occurred produced language deficits in 12 of 14 patients. Additionally, in those same 12 patients, all areas of cortex that, with stimulation, produced significant and reproducible language deficits were shown to be active in the fMR imaging task. This finding indicates that the task described by Schlosser, et al.,[27] provides accurate language localization. However, the spatial extent of the fMR imaging activations and the extent of the region in which more subtle stimulation-induced language disruptions occurred did not always correspond. There are a number of factors that could account for this difference.

First, the task used for the fMR imaging study and those used for cortical stimulation differed. The fMR imaging activations were evoked by a single auditory task, whereas the cortical stimulation maps were based on several tasks (object naming, sentence completion, verbal command, and reading). Repetition of this study by performing multiple fMR imaging language tasks designed to activate different aspects of language processing could produce activations in all areas in which stimulation produced deficits. However, we noted that cortical stimulation in critical posterior sites typically produced marked disruption in object-naming, sentence-completion, and verbal-command tasks together.

Second, the spatial extent of the fMR imaging activation is partly related to the statistical threshold at which the activations are plotted. Lower statistical thresholds typically reveal activations with spatially larger extents (and more false-positive results). The closest match to stimulation results occurred in focal fMR imaging activations obtained with high t values; this typically occurred in the most posterior slices. Lesser activations along the anterior STS were inconsistently related to subtle stimulation effects. The apparent spatial extent of the fMR imaging activation may also be influenced by increased HbO_2 in the draining veins and venules that may be distant from the activated tissue. The use of higher field strength (3.0 tesla) would increase the signal-to-noise ratio and produce activations with more accurate extent and less noise.

Third, some positive stimulation effects were subtle and subjective (for example, hesitation in object naming) and were not always reproducible. These subtle stimulation effects often circumscribed more focal regions in which very clear comprehension deficits could be evoked. This is typical of our experience in performing posterior temporal stimulation, particularly when stimulation occurs via implanted subdural grids. When subtle effects are observed, it is not clear whether the stimulated tissue is less critical to the tested language function, whether stimulation affected the patient's attention to the task, or whether the stimulation produced undetected after-discharges in other brain regions that interfered with comprehension.

Fourth, the stimulation level necessary to achieve language disruption was not uniform across positive electrode sites. Thus, current introduced between two electrodes that produce subtle language deficits may produce those effects by activating more distant cortices through current spread.[2,21,25,26,28] This may be particularly problematic if the cortex that is critical for the language function is located deep in a sulcus. Cortical stimulation between many electrode sites on the brain surface may disrupt the function of that deep cortex when stimulation occurs at high-current levels. One patient in our series sustained no language deficits while undergoing lateral surface stimulation; however, as the resection proceeded into the STS and a deep area shown to be active on fMR imaging was entered, the patient developed confrontational naming difficulties. This indicated that the surface stimulation did not generate a sufficient current density deep within the sulcus to detect this functional area. This aspect is an inherent limitation in lateral surface stimulation and one which fMR imaging can improve on current language-mapping techniques.

In an earlier study, the authors encountered no failures in obtaining reliable fMR imaging activation to the English-language sentences among their 14 neurologically normal volunteers.[27] Therefore ,we were dissatisfied by our failure to obtain credible fMR imaging activation in 10 of our 33 patients. Half (five) of the cases in which activation could not be evoked were attributed to imager error or gross head movement, but the remaining five cases of failure were not readily explainable. Our passive-listening task was deliberately designed to avoid explicit memory, decision, or motor components. However, although it was successful with motivated volunteers, this design provided no feedback to the examiner regarding the degree to which patients attended to and/or comprehended the sentences. Patients must devote sufficient attention to the task to generate a signal. The use of sedating anticonvulsant or pain medication can further contribute to a lack of sufficient attention. Future development of this task will need to include a behavioral indication that clarifies the patient's engagement by the task.

Finally, an important issue in the use of fMR imaging in patients undergoing temporal lobe resections is that of hemispheric dominance. We designed this study to answer how fMR imaging mapping of auditory comprehension would compare in its ability to map language within the dominant temporal lobe with the results obtained by performing cortical stimulation. The question of the comparison of the laterality of fMR imaging activations to dominance as determined by Wada testing was not specifically raised in this study. However, analysis of previous work by other authors has shown fMR imaging mapping of language to produce similar results when compared with Wada testing.[4,11,29]

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