Preoperative mapping of the supplementary motor area in patients harboring tumors in the medial frontal lobe

LINDSEY NELSON, B.S., SAMIR LAPSİWAL, M.D., VICTOR M. HAUGHTON, M.D., JANE NOYES, N.P., AMIR H. SADRZADEH, M.D., CHAD H. MORITZ, PH.D., M. ELIZABETH MEYERAND, PH.D., AND BEHNAM BADIE, M.D.

Departments of Radiology, Medical Physics, and Neurological Surgery, University of Wisconsin School of Medicine, Madison, Wisconsin

Object. Injury to the supplementary motor area (SMA) is thought to be responsible for transient motor and speech deficits following resection of tumors involving the medial frontal lobe. Because direct intraoperative localization of SMA is difficult, the authors hypothesized that functional magnetic resonance (fMR) imaging might be useful in predicting the risk of postoperative deficits in patients who undergo resection of tumors in this region.

Methods. Twelve patients who had undergone fMR imaging mapping while performing speech and motor tasks prior to excision of their tumor, that is, based on anatomical landmarks involving the SMA, were included in this study. The distance between the edge of the tumor and the center of SMA activation was measured and was correlated with the risk of incurring postoperative neurological deficits.

In every patient, SMA activation was noted in the superior frontal gyrus on preoperative fMR imaging. Two speech and two motor deficits typical of SMA injury were observed in three of the 12 patients. The two speech deficits occurred in patients with tumors involving the dominant hemisphere, whereas one of the motor deficits occurred in a patient with a tumor in the nondominant hemisphere. The risk of developing a postoperative speech or motor deficit was 100% when the distance between the SMA and the tumor was 5 mm or less. When the distance between SMA activation and the lesion was greater than 5 mm, the risk of developing a motor or a speech deficit was 0% (p = 0.0007).

Conclusions. Early data from this study indicated that fMR imaging might be useful in localizing the SMA and in determining the risk of postoperative deficits in patients who undergo resection of tumors located in the medial frontal lobe.

KEY WORDS • supplementary motor area • brain neoplasm • tumor • functional magnetic resonance imaging

The SMA is thought to play a key role in the initiation and control of both motor and speech functions.6,16 Located in the medial aspect of the superior frontal gyrus and part of Brodmann Area 6, the SMA is divided into two regions: the SMA proper and the pre-SMA. The SMA proper lies dorsal to the cingulate sulcus, between vertical lines extending through the anterior (VCA line) and posterior (VCP line) commissures perpendicular to the AC–PC line. The pre-SMA lies anterior to the SMA proper, between the most rostral point of the genu of the corpus callosum and the VCA line.23 It has been proposed that the SMA proper and pre-SMA have different anatomical and functional properties: the pre-SMA is thought to play a role in supramotor activities such as selection, preparation, and sequencing of movements, whereas the SMA proper is more involved with movement execution.5,9,10,16 Lesions of the SMA produce characteristic neurological deficits.22,24 Severe expressive aphasia, mutism, and immediate hemiparesis contralateral to the affected hemisphere have been reported following removal of tumors involving the SMA.40,22,24 Most patients fully recover from injuries to the SMA, but some may have long-lasting disturbance of fine motor skills and complex speech functions. Because of the potential neurological deficits, identifying the location of the SMA location may be helpful in minimizing injury to this area during neurosurgical procedures.

Although intraoperative brain mapping has proven to be an important tool in reducing postoperative deficits following resection of lesions involving the sensorimotor cerebral cortex, direct intraoperative mapping of the SMA is more difficult. Some authors have estimated the location of the SMA according to its normal anatomical relationship to the motor cortex during resection of tumors involving the medial frontal lobes.22 This method is imprecise, however, and does not allow for the fact that the SMA may be displaced or reorganized due to tumor growth. An accurate knowledge of the location of the SMA may be important not only in determining the surgical approach to lesions, but also in anticipating postoperative neurological deficits.

Functional MR imaging has been used in preoperative brain mapping prior to surgical excision of brain tumors4,15 and in estimating the location of the SMA. On execution of motor and speech tasks, activation in both the SMA proper and the pre-SMA can be detected using fMR imaging.5,7,17 To our knowledge, the accuracy of fMR imaging in predicting the risk of injury to the SMA during neurosurgical procedures has not been examined in detail. The purpose of this study was to test whether preoperative fMR image lo-
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calization of the SMA is more accurate than its anatomical localization in predicting the risk of postoperative neurological deficits following resection of tumors of the medial frontal lobe.

Clinical Material and Methods

Patient Population

Between May 2000 and August 2001 12 consecutive patients with frontal lobe tumors (11 gliomas and one atypical meningioma) involving the SMA were eligible to participate in this study. To localize the SMA, preoperative fMR images were obtained in every patient while each performed language and motor tasks. All tumor resections were performed using an intraoperative neuronavigational system and included the edge of the tumor, the location of which was demonstrated on preoperative T1-weighted MR images. The extent of tumor resection, which included the anatomical SMA and/or pre-SMA in every patient (Table 1), was also confirmed on postoperative MR images. Patients with tumors involving the insular cortex, sensorimotor cortex, or Broca area were not included in the study.

Functional MR Imaging Protocol

Scanning was performed using a clinical 1.5-tesla magnet equipped with high-speed gradients for whole-body EPI. The patient’s head was positioned within a standard radiofrequency quadrature birdcage coil. Pneumatic earphones were used to reduce the patient’s exposure to ambient scanner noise and to provide auditory communication. Preliminary anatomical scans included a 3D spoiled gradient–recalled acquisition whole-brain volume (TR 21 msec, TE 7 msec, FA 40˚, FOV 24 cm, matrix 256 × 256, contiguous axial sections including vertex through cerebellum 124, slice thickness 1.2 mm). Additional anatomical scans were acquired if necessary as part of each patient’s preoperative assessment.

Echoplanar fMR images were acquired in the coronal plane using 20 6-mm-thick slice locations with a 1-mm skip, thus providing approximately entire brain coverage. The EPI parameters included the following: gradient-recalled acquisition whole-brain volume (TR 21 msec, TE 7 msec, FA 40˚, FOV 24 cm, matrix 256 × 256, contiguous axial sections including vertex through cerebellum 124, slice thickness 1.2 mm). Additional anatomical scans were acquired if necessary as part of each patient’s preoperative assessment.

Functional Activation Paradigms

Language Paradigms. Expressive language function was assessed by having the patient perform an antonym word-generation task or a letter word-generation task or both during fMR imaging. The paradigm consisted of five periods of task performance interspersed with six periods of rest, each of 20 seconds duration. For word generation, the patient was asked to generate as many words as possible that began with the letter supplied by the investigator at the beginning of each task period. For antonym word-generation, the patient was asked to generate an antonym of the word projected onto a screen every other second during the task period.

Postprocessing of fMR Imaging Data

The raw data obtained during EPI was spatially smoothed in the frequency domain by using a Hamming low-pass filter and then reconstructed into individual slice location image files. Each reconstructed fMR data set was checked for patient head motion and was realigned using a 3D spatial registration algorithm. Each motion-corrected data set was then manually coregistered with the patient’s 3D spoiled gradient–recalled acquisition whole-brain volume for accuracy of anatomical reference. A signal-to-noise ratio threshold was applied to mask background voxels outside the brain from further analysis. Functional MR imaging maps were derived by cross correlation to a smoothed boxcar reference function that modeled the presumed hemodynamic response for the task performance by using a generalized least-squares fitting algorithm. This comparison was made to the EPI time courses from each unmasked voxel within the brain, and provided a t statistic functional activation map that was overlaid on the coregistered anatomical brain volume. Images of voxels with a t statistic greater than 0.005 were used for the functional activation maps.

Calculation of Distance From Lesion Edge to Activated Cluster

Each fMR image was reviewed to identify activation likely to represent SMA. Any activation in the superior frontal gyrus along the midline within the following anterior/posterior, superior/inferior, and lateral boundaries was considered to be SMA: anteriorly, 20 mm in front of a line drawn perpendicular to the AC–PC line at the AC; posteriorly, by the precentral sulcus; inferiorly, by the cingulate gyrus; and laterally, by the superior frontal sulcus. For each

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**TABLE 1**

Characteristics of 12 patients harboring tumors of the medial frontal lobe

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Pathology, Grade*</th>
<th>Hemi-</th>
<th>Anatomical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case No.</td>
<td></td>
<td></td>
<td>sphere</td>
<td>Resection Area</td>
</tr>
<tr>
<td>1 24, M</td>
<td>astrocytoma, III</td>
<td>lt pre-SMA &amp; some SMA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 40, F</td>
<td>oligodendroglioma, II</td>
<td>lt SMA &amp; pre-SMA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 23, F</td>
<td>astrocytoma, IV</td>
<td>rt SMA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 53, F</td>
<td>meningioma, atypical</td>
<td>lt SMA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 23, F</td>
<td>astrocytoma, IV</td>
<td>rt SMA &amp; some pre-SMA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 21, M</td>
<td>astrocytoma, II</td>
<td>lt SMA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 55, M</td>
<td>oligodendroglioma, III</td>
<td>rt pre-SMA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 41, M</td>
<td>oligodendroglioma, II</td>
<td>lt SMA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9 47, M</td>
<td>oligodendroglioma, II</td>
<td>rt pre-SMA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 61, M</td>
<td>mixed glial neoplasm, IV</td>
<td>lt SMA &amp; pre-SMA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11 35, M</td>
<td>oligodendroglioma, II</td>
<td>rt pre-SMA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 35, M</td>
<td>oligodendroglioma, II</td>
<td>rt pre-SMA</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Gliomas were graded according to the scale constructed by Daumas-Duport, et al.

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task the COM of an activation cluster within the SMA was determined using the 3D clustering method given the specificities of connectivity distance (7.1 mm to include clusters connected by one side), minimum cluster volume (three voxels), and minimum threshold of activation. A threshold was applied to the clustering function, which would demonstrate one or more focal activation areas. The threshold was selected to provide a probability value of less than 0.01 by the Bonferroni correction, with no attempt to produce an equivalent number of voxels between subjects.

**Determination of Tumor Edge and Consideration of Multiple Clusters**

In every patient, the distance from the edge of the region with low signal intensity on a T1-weighted image to the COM of activation was calculated (Fig. 1). If more than one fMR image cluster was present, the distance from the tumor edge to the COM of activation within each cluster was measured, and the shortest distances at the highest threshold were considered to be the most significant. The distance between the edge of the tumor and the COM of activation for both language and motor tasks was determined and tabulated separately.

**Postoperative Motor and Language Deficits**

Patients’ medical charts were reviewed for preoperative and postoperative motor and language deficits recorded by attending physicians and speech, occupational, or physical therapists. Only language or motor deficits consistent with an SMA injury were tabulated. To qualify, the deficit must have had a temporal course and the neurological character of an SMA injury. Hemiplegia or impaired movement contralateral to the side of surgery which improved rapidly was classified as an SMA injury. Immediate speech deficits, including mutism, reduced spontaneous speech, and anomia, that recovered within 40 days were considered to be due to SMA injury.

Motor deficits were rated according to the Medical Research Council of Great Britain grading scale: 5, normal power; 4, active movement against gravity and resistance; 3, active movement against gravity only with gravity eliminated; 2, active movement only; 1, trace contraction; or 0, no contraction. Language deficits were scaled from A to C: A, no deficit; B, mild deficit such as slight expressive aphasia or anomia; or C, profound deficit such as the inability to produce sentences.

In every patient, the extent of resection of SMA was evaluated by means of an MR imaging study performed within 24 hours after surgery. Resections involving primarily pre-SMA and/or SMA based on anatomical landmarks were noted and used as a criterion for patient inclusion in the study.

**Statistical Analysis**

The McNemar test was applied to gauge the interdependence of the motor and speech tasks. The Fisher exact test was then used to compare the significance of the distance between the SMA and the tumor margin with the risk of postoperative deficits in the combined motor and speech groups (24 cases total).

**Results**

Of the 12 patients in this study group, two had postoperative speech deficits and two had postoperative motor deficits. One patient (Case 4) had both a motor deficit and a speech deficit. The distances between the SMA activation site and the tumor margin are summarized in Tables 2 and 3. These measurements were obtained only in patients with SMA activations that localized to the same hemisphere in which the tumor was located.

**Speech Activation**

Of the 12 patients, two suffered postoperative language...
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deficits (Table 2). The SMA activation site in these two patients (Cases 1 and 4) was within 5 mm of the tumor edge and was located ipsilateral to left frontal tumors. The patient in Case 4 exhibited postoperative expressive aphasia that evolved into severe anoma and slow fluent speech by postoperative Day 4. Her speech deficits resolved by 10 weeks, with no evidence of a word-finding difficulty. Functional speech maps obtained in this patient demonstrated the SMA activation to be adjacent to the tumor margin (distance = 0 mm; Fig. 2). The patient in Case 1 underwent resection of a tumor involving both SMA and pre-SMA, the localization of which were based on anatomical landmarks (Fig. 3). He experienced mild expressive aphasia and anoma immediately following surgery, which gradually improved during the next two weeks. Functional speech maps obtained in this patient also demonstrated a distance between the tumor and the SMA of less than 5 mm.

Speech SMA activation was located in the left hemisphere in the majority of patients and was bilateral in two patients. In this series, only one patient (Case 8) demonstrated a right hemisphere speech SMA activation (Fig. 4). Interestingly, this right-handed patient did not develop any postoperative deficits after complete resection of a low-grade glioma that was located within the presumed anatomical boundaries of the SMA.

The patients who did not develop postoperative aphasia included four with a distance of more than 5 mm between the tumor edge and the SMA language activation site and six with SMA activation located in the hemisphere contralateral to the tumor. These findings suggest that close proximity of SMA, as demonstrated on fMR imaging, may be important in predicting postoperative speech deficits in patients with tumors of the medial frontal lobe.

Motor Activation

In addition to activating the primary sensorimotor cortex, the performance of motor tasks activated the contralateral SMA in most patients (Table 3). Exceptions included two patients (Cases 1 and 8) harboring tumors of the left frontal lobe who demonstrated activation of the right SMA with right finger movement and one patient (Case 7) with a right frontal tumor who exhibited activation of the SMA ipsilateral to the side on which the motor task was performed. Furthermore, one patient demonstrated bilateral SMA activation while performing unilateral finger tapping. To assess whether the extent of SMA injury was associated with motor deficits, the distance between the tumor edge and the ipsilateral SMA was correlated to postoperative motor function. Two of the 12 patients had a distance of less than 5 mm between the tumor edge and the COM of the ipsilateral SMA motor activation cluster. Both patients had transient postoperative motor deficits typical of an SMA injury.

The patient in Case 4 exhibited a severe right hemiparesis affecting the upper extremity more than the lower extremity. At 10 weeks, her condition improved to a motor rating of 4/5 for both the right upper and lower extremities. Her motor deficits resolved 16 weeks following surgery. The patient in Case 3 experienced a left hemiparesis (Grade 4/5) following resection of a tumor in the right hemisphere. Fifteen days after surgery she had no clinical evidence of a motor deficit.

Interestingly, the patient in Case 1, who developed speech problems after surgery, did not exhibit any motor weakness. Although SMA activation following the performance of speech tasks was located adjacent to the tumor, SMA activation with the completion of motor tasks involving either hand was situated in the opposite hemisphere (Fig. 3). Activation of this contralateral (motor) SMA most likely explains why this patient did not develop any weakness after tumor resection.
Similar to the results for speech activation, patients with SMA motor activation in the hemisphere opposite to the tumor site (Cases 1, 7, and 8) and seven patients who had more than a 5 mm distance between the SMA motor COM and the tumor edge did not develop any postoperative motor deficits.

Statistical Significance

The McNemar test was applied to determine the interdependence of motor and speech tasks, resulting in a probability value of 0.16. Thus, we considered the motor task and speech task results as independent events and compared postoperative deficits in patients with an SMA–tumor distance of less than 5 mm with deficits in patients with a distance greater than 5 mm. The difference between the two groups was found to be statistically significant (p = 0.0007), thus suggesting that the risk of developing postoperative deficits correlated with the SMA–tumor distance. Furthermore, when patients who demonstrated both an SMA activation in the hemisphere opposite to the tumor site and an SMA–tumor distance of more than 5 mm were included in the analysis, the difference between the two groups remained significant (p = 0.0001).

Discussion

Neurosurgeons routinely use various landmarks and anatomical information such as sulcal and gyral morphology in guiding surgical excision of intrinsic brain lesions. For tumors near somatosensory, motor, or speech cortex, intraoperative brain mapping has improved the risk of surgical injury to these areas. Having used intraoperative mapping, Haglund, et al.,8 reported that when language sites in the temporal lobe were located within 2 cm of surgical resection, risk of developing a postoperative speech deficit was significantly higher. Similar observations have also been made for tumors involving somatosensory and motor cortex.15 For tumors that are located close to the SMA, however, such measurements have not been performed. This is due to technical difficulties in direct intraoperative mapping of the SMA and the fact that only a fraction of patients with tumors in the SMA region develop postoperative speech and motor deficits. Although most patients recover from injuries to the SMA, we believe that better localization of this area may be beneficial in surgical planning and preoperative patient education.

Neurological Deficits After Injury to the SMA

The nature of motor and language deficits after injury to the SMA has been well characterized. The SMA, considered to be “hierarchically superior” to the primary motor cortex, is more active in sequential movements than in simple movements.26 In addition, the SMA is presumed to be involved in the initiation and integration of motor function. It has connections to all components of the motor system including the bilateral motor cortex, basal ganglia, cingulate gyr, contralateral SMA, cerebellum, thalamus, and spinal cord.14,19 Motor deficits resulting from resection of the SMA vary in character and in course. Documented SMA motor deficits occurring in the first few days after surgery include hemiplegia, neglect, and impaired movement of the contralateral extremities. Patients exhibit relative ease of movement in performing automatic tasks, but show an impaired ability to move spontaneously. Motor recovery occurs within the first 2 weeks; however, fine motor tasks that require high-speed, advanced, or bimanual skills may remain impaired for 2 to 6 weeks. It is possible, but not well documented, that some fine motor skills may be indefinitely affected.24

Speech disturbances due to injury of the SMA also have a characteristic nature and course. The initial deficit is mutism, which recovers rapidly after injury. Aphasia due to in-
jury to the SMA often occurs in patients treated for lesions involving the dominant hemisphere. Speech deficits following injury to the nondominant SMA is not as common, but has been observed. Although language performance appears to recover in patients suffering from injury to the SMA, subtle long-term deficits may persist including difficulty in understanding more complex languages spoken at fast speeds. Reduced verbal learning, reasoning, and fluency have also been detected in patients with injuries to the SMA. Because of these lasting subtle speech and motor deficits, preoperative localization of SMA may be important in predicting postoperative deficits and in educating patients undergoing resection of tumors in this area.

Functional MR Image Mapping of the SMA

Functional MR imaging may be an alternative tool to intraoperative mapping for detection of functional brain centers prior to neurosurgical procedures. This imaging modality has been previously used accurately to map sensory, motor, and speech areas and to predict surgical risk in patients with tumors in these regions. Activation of the SMA has also been studied using fMR imaging. The SMA activation depends on the nature of the task, whether it is planned or executed automatically, or whether the task is automatic or newly acquired. The most caudal activation of SMA has been documented with the performance of finger-tapping or foot-movement paradigms, which were used in this study. Similarly, speech activation has been documented in both SMA proper and pre-SMA for word-generation tasks. Because SMA activation can be detected with the aid of fMR imaging, we hypothesized that fMR imaging can be used to predict the risk of SMA injury in patients who undergo excision of tumors of the medial frontal lobe.

In the present study, the SMA was identified reliably in every patient and the distance between SMA activation and the tumor margin was found to be important in predicting postoperative motor and speech deficits. All patients who suffered a transient postoperative deficit had an SMA–tumor distance of less than 5 mm. The deficits following resection of the SMA were typical of SMA injury, and recovery occurred within a few months of surgery. Furthermore, none of the patients with SMA activation located in the hemisphere opposite to the tumor site demonstrated any neurological deficits, despite the fact that all tumor resections, which were based on anatomical landmarks, involved all or part of the SMA. From these observations one can infer that not only the SMA–tumor distance, but also the hemispheric dominance of SMA activation may be important in predicting postoperative deficits in patients who undergo tumor resection in this area.

Except for one patient (Case 8) with right frontal SMA activation, the performance of speech tasks resulted in the activation of the left SMA in every patient. This finding explains the low incidence of speech disturbance observed in the resection of lesions involving the nondominant SMA. There was, however, more variability in the SMA activation with the completion of motor tasks. Although motor paradigms resulted in activation of the SMA of the opposite hemisphere in most patients, three patients experienced ipsilateral and one patient bilateral SMA activation with motor tasks that involved the limb opposite to the tumor site. This variation was most evident in patients in Cases 1, 7, and 8 who demonstrated activation of SMA in the hemisphere opposite to the tumor site. Whether due to plastic reorganization of the SMA as a result of tumor growth or inherent differences in brain organization, the significant variation in SMA activation strongly suggests that the location of the functional SMA cannot be predicted solely on anatomical landmarks in patients with tumors of the medial frontal lobe.

The application of fMR imaging for preoperative mapping of the SMA prior to resection of tumors of the medial frontal lobe has been reported previously. Kramik, et al., retrospectively evaluated motor deficits in 23 patients who had undergone resection of tumors involving the medial frontal lobe. These authors concluded that the risk of developing postoperative weakness increased when surgical resection included the SMA as demonstrated on preoperative fMR image mapping. Our findings confirm those discussed in this report and further emphasize the value of fMR imaging in preoperative mapping of the SMA in patients with tumors in the medial frontal lobe brain. Furthermore, data from the present study are the first to indicate a correlation between postoperative neurological deficits and SMA–tumor distance in such patients.

Limitations of the Study

There are several potential sources of inaccuracy in this study. First, our patient population did not contain enough subjects with an SMA–tumor distance from 5 to 10 mm. The distance of 5 mm was chosen to signify patients at high risk based on the observation that all patients with post-
operative deficits had an SMA–tumor distance of less than 5 mm. Second, activation that occurred outside the normal anatomical borders of SMA and pre-SMA was not considered in this study. It is possible that some patients may exhibit plastic reorganization of brain function around the tumors, resulting in activation outside the normal cytoarchitectural boundaries of SMA similar to that reported in patients with epilepsy. Third, the distance measurement from the tumor edge to the center of SMA activation may have varied depending on the threshold selection for the activation maps and differences in the number of activated voxels across cases. Because the size of the activated region was not controlled, the COM measurement was used to minimize the confounding effect of threshold on distance measurement. The choice of COM measurement consistently overestimated, to varying degrees, the distance between the tumor and activation. For example, a region of uniform activation of 10 mm in diameter adjacent to the tumor border was recorded as a 5 mm distance to the tumor edge may be important in predicting postoperative motor and speech deficits in patients who undergo resection of tumors located near the SMA.

Conclusions

Functional MR imaging is useful in the preoperative mapping of the SMA prior to resection of tumors in the medial frontal lobe. The distance between the SMA and tumor edge may be important in predicting postoperative motor and speech deficits in patients who undergo resection of tumors located near the SMA.

References


Manuscript received December 12, 2001. Accepted in final form July 1, 2002. Address reprint requests to: Behnam Badie, M.D., Department of Neurological Surgery, University of Wisconsin, 4K/805 Clinical Science Center, 600 Highland Avenue, Madison, Wisconsin 53792. email: Badie@neurosurg.wisc.edu.