Prediction of neurological deficits and recovery after surgery in the supplementary motor area: a prospective study in 26 patients

Clinical article

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Object. Resection of lesions involving the supplementary motor area (SMA) may result in immediate postoperative motor and speech deficits that are reversible in most cases. In the present study the authors aimed to determine the critical involvement of SMA in the lesioned and healthy hemispheres in this functional recovery. They hypothesized that compensatory mechanisms take place following surgery in the SMA, and that these mechanisms can involve either the lesioned or the non-lesioned hemisphere. In addition, they hypothesized that a correlation will be present between the functional MR imaging (fMR) imaging–related activation in the SMA and the occurrence of a functional deficit during intraoperative cortical stimulation.

Methods. Twenty-six patients scheduled for resection of space-occupying lesions involving, or in the vicinity of, the SMA were recruited. Patients underwent an fMR imaging examination that included finger-tapping and verb-generation tests to assess for motor and language functions. Intraoperatively direct cortical stimulation (DCS) of the SMA region was performed while patients were monitored for language and motor functions using tests similar to those used for the fMR imaging. Task dysfunction during DCS assessed the critical involvement of the SMA in the tested functions. Neurological evaluations were performed prior to surgery and at 3 time points within a month following surgery. A region of interest–based approach was used to evaluate fMR imaging blood oxygen level–dependent activation level and asymmetry in the SMA. These measurements were later compared with the intraoperative DCS and neurological findings.

Results. Functional MR imaging showed greater activation and dominance of the SMA in the lesioned hemisphere in patients who exhibited no motor or language dysfunction during DCS. In addition, patients with the highest activation of the SMA in the lesioned hemisphere for language and motor tests showed stronger coupling of this region with ipsilateral motor and language networks. In contrast, activation in the nonlesioned hemisphere did not correspond with DCS results.

Conclusions. The authors’ findings demonstrate the necessity of activation in the vicinity of the lesioned SMA for functional compensation in motor and language tasks. It is possible that more effective functional coupling of the SMA with motor and language areas in the same hemisphere prevents dysfunctions following surgical intervention. Importantly, fMR imaging activation in the unaffected SMA was not sufficient for development of functional compensation and, if anything, indicated decompensation. (DOI: 10.3171/2010.6.JNS1090)

Key Words • supplementary motor area • cortical stimulation • functional magnetic resonance imaging

The SMA is a key structure for the planning and initiation of simple and complex behaviors.1,16,29 First described by Laplane et al.,13 unilateral resection of the SMA region may result in immediate postoperative motor and speech deficits commonly referred to as the SMA syndrome. Such deficits characteristically resolve within several weeks or months.2,5,8,12,21,22 The mechanisms underlying the recovery process of SMA syndrome, however, have not been elucidated.

Brain reorganization of motor and language functions resulting from a brain lesion were previously studied in vivo using functional imaging techniques. Brain plasticity has been suggested as one possible mechanism in which the transfer of language representation from the dominant to the nondominant hemisphere results in the recovery of language function. Positron emission tomog-
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raphy and fMR imaging studies obtained in patients who had recovered from aphasia after a left-hemisphere stroke have demonstrated an association between the degree of language recovery and the amount of right-sided activation in homologous regions. Patients with glioma involving language areas were shown to have language activation in the nondominant hemisphere. Other possible compensatory mechanisms involve the recruitment of the lesioned hemisphere; improvement of motor function was associated with recruitment of areas ipsilateral to the lesioned hemisphere. In addition, in ischemic perinatal stroke movement therapy induced increased motor-related activations (using fMR imaging) in the primary motor cortex of the lesioned hemisphere.

In the present study, we have investigated the activation of the SMA in patients scheduled to undergo surgery for lesions in this region. Supplementary motor area–specific language and motor functions were evaluated preoperatively by fMR imaging, and this was followed by the same evaluation paradigms during awake craniotomy with DCS during surgery.

All patients underwent neurological evaluation, including assessment of motor and language functions, before surgery, during surgery, and at 3 points after surgery. The imaging and clinical data were then retrospectively analyzed to assess mechanisms that may help to predict postoperative dysfunction and subsequent recovery observed after surgery.

Our aim was to determine whether the main compensatory mechanism following surgery in the SMA region involves recruitment of the contralateral nonlesioned hemisphere, or whether it involves recruitment of regions ipsilateral and adjacent to the lesion. Special emphasis was given to the relationship between the activation level and dominance in the lesioned and nonlesioned SMA, as well as to any DCS-induced functional deficit(s) during surgery.

Method

Participants

Informed consent was obtained from all patients in accordance with the guidelines of the institutional review board at Tel-Aviv Medical Center.

The initial study group comprised 32 patients who were scheduled to undergo a resection of various lesions within, or adjacent to, the SMA region between March 2005 and March 2009. Data in 6 of the 32 patients were excluded from analysis: 3 patients refused to undergo an awake surgery and 3 others were not cooperative during surgery due to confusion (2 patients) or transient general seizures prior to DCS (1 patient). Data in 26 patients (8 females, mean age 39.3 years, range 21–68 years, 4 left handed) were thus included in the final analysis of the results. With regard to language, 4 patients had nondominant hemisphere lesions, 19 patients had dominant hemisphere lesions, and 3 had bilateral language representation.

Seventeen patients had seizures as their presenting symptom, 5 exhibited some degree of motor deficit, and 3 experienced various degrees of speech impairment.

The pathological diagnoses associated with the lesioned SMA included 12 high-grade gliomas, 9 low-grade gliomas, 2 metastatic lesions, 1 cavernoma, 1 cortical dysplasia, and 1 meningioma (Table 1). Seven patients who had undergone a previous operation for their lesion were included in the general analysis, as well as in a separate subgroup analysis.

Neurological Evaluation

Neurological evaluation of motor and language functions was obtained at different time points: 1) in the preoperative hospitalization period, 2) immediately postoperative (within 5 hours), 3) at discharge from the hospital (within 3–5 days postoperatively), and 4) 2 weeks following surgery.

Motor function was recorded and graded on a scale of 0–5 (0 = plegia, 3 = moves against gravity, 5 = full strength). Language function was evaluated by several components: comprehension, free speech, naming, and repetition.

Preoperative fMR Imaging

Image Acquisition. Data acquisition was performed using a 3-T MR imaging unit (GE Signa Excite) with a resonant gradient echo planar imaging system. Functional images were acquired using a single-shot echo planar T2*-weighted sequence with the following parameters: TR/TE 3000/35 msec, flip angle 90°, field of view 20 × 20 cm, 40 slices with 3-mm thickness and no gap, matrix 96 × 96. Functional tests were accompanied by a 3 anatomical scan using T1-weighted spoiled gradient-recalled acquisition sequence (1 × 1 × 1 mm).

Stimulus delivery and response acquisition were controlled using Presentation software (version 0.80, Neurobehavioral Systems). Stimuli were projected with an LCD projector (NEC, VT660 K) onto a screen positioned in front of the patient’s forehead and viewed through a tilted mirror.

Functional MR Imaging Paradigms. The functional scans were acquired 3–26 days prior to the operation. Motor and language paradigms were used. The motor paradigm consisted of a finger-tapping task. The task requires to plan sequences of finger movements and has been shown to activate the SMA. Patients were visually instructed to perform sequences of 3 finger tappings separately with each hand.

In a “simple” trial, the same finger was tapped 3 times. In a “complex” trial, a sequence of more than 1 finger was performed. The finger-tapping paradigm was of a block design fashion consisting of 6 tasks and 13 rest-related blocks. Each block started with a visual instruction presented on a screen for 3 seconds indicating the hand that should be used. Each block consisted of 6 sequences: each sequence was visually presented for 1 second followed by a blank picture presented for 1 second. An interval that consisted of a blank picture was presented between the blocks for 6 or 9 seconds (Fig. 1).

The language paradigm consisted of a visual verb-generation task. Patients were asked to covertly generate
a verb describing an action related to a presented picture. The pictures were presented in blocks of 21 seconds with rest periods at intervals of 18–21 seconds. An activation block included 7 pictures presented for 2500 msec each, with an interstimulus interval of 500 msec. The entire test included 4 task blocks.

**Data Analysis.** Functional MR imaging data analysis was performed using BrainVoyager software (version 1.10.4, Brain Innovation). Preprocessing included 3D motion correction and linear trend removal. High-pass filtering was used. The first 6 functional volumes, before signal stabilization, were excluded from analysis. Functional 2D data were manually aligned and coregistered with the 3D anatomical data. Functional analysis was performed using a GLM in which the activation blocks were defined as the predictors. To account for a hemodynamic response, predictors were shifted by 6 seconds.

Region of interest analysis was applied to evaluate activations magnitude and laterality between hemispheres in the pre-SMA and SMA proper. These regions were defined according to a previously described method.36 In brief, an imaginary line was determined that was vertical to the AC–PC plane and crossed the AC. This line, termed the VCA line, differentiates the 2 subregions with the SMA proper located posterior and the pre-SMA anterior to the VCA line. The ROI analysis was applied to the left and right pre-SMA and SMA proper using a box-shaped volume of 21-voxel diameter. Each box was bordered by the brain midline in its medial border (Fig. 2). For each patient, the superior boundary was set to include the functional activation.

For each of the selected ROI beta weights, which refer to the fMR imaging activation level, were computed using GLM. We selected the beta weight measure to determine the contribution of the paradigm design to the fMR imaging signal. In the standard GLM, beta weights refer to the number in by which each predictor is multiplied to best predict the criterion. In fMR imaging data, each of the task conditions is defined as a predictor in the GLM model, and the beta weights reflect the level in which each of the predictors explain the signal from a specified region.

In doing so, we aimed to characterize the level of task-related activity in each region selected. In the motor task, beta weights were extracted separately from blocks that included finger tapping of the hand contralateral to the lesion, and of the hand ipsilateral to the lesion. In

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Dominant Hand</th>
<th>Presenting Symptom</th>
<th>Pathology</th>
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<td>1</td>
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<td>2</td>
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<td>3</td>
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<td>rt</td>
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<td>melanoma metastasis</td>
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<td>ODG</td>
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<td>6</td>
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<td>7</td>
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<td>23, M</td>
<td>rt</td>
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<td>ganglioglioma Grade II</td>
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</table>

* GB = glioblastoma; ODG = oligodendroglioma.
the language task, beta weights were extracted from the verb-generation task. For language function, we applied quantitative measures of the LI using the total number of activated voxels for each region of interest [LI = (Vlesion − Vnonlesioned) / (Vlesion + Vnonlesioned)], where Vlesion and Vnonlesioned represent the number of activated voxels for the lesioned and nonlesioned hemisphere, respectively. This approach yielded LIs for the SMA proper and for the pre-SMA that ranged between +1 for strong lesioned hemispheric dominance and −1 for strong nonlesioned hemispheric dominance. For each ROI, voxels were collected using all conditions and were compared with rest condition with a probability value less than 0.05. Language dominance in Broca area was determined for each patient. This evaluation was performed as part of the clinical fMR imaging assessment of language and motor functions. The evaluation was based on visually and auditory verb-generation tests, which are routinely used for the purpose of language mapping, and have a high agreement with Wada testing (Fig. 2).23

The rational for choosing the LI for language function only and not for the motor function stems from the observation that in motor function there is less clear and consistent lateralization with regard to the SMA.26 Conversely, in language functions it was shown that a postoperative language deficit was related to resection of areas within the SMA of the dominant hemisphere for language, which showed fMR imaging–related activations.11 In addition, somatotopic studies have also shown higher SMA dominance in the hemisphere dominant for language.7

Functional Connectivity Analysis. To reveal the network of activation that might be affected by a lesion in the SMA, we used whole-brain functional coupling analysis, where the reference ROI was the activation in the SMA proper and the pre-SMA of the lesioned hemisphere. Time courses within this area were obtained separately for each patient from activation maps during the finger-tapping and verb-generation paradigms and were then used as a regressor in a voxel-based whole-brain correlation analysis.

Intraoperative Cortical Stimulations

All patients underwent awake surgery after the administration of local anesthetics to the supraorbital region and the incision site. No sedation was administered until the end of resection. Surgical navigation was used in all cases to localize the skin incision and the craniotomy site. Prior to opening the dura mater, image acquisition of the operation site was performed using a 3D ultrasound-based navigation system (SonoWand, Mison) that was coregistrated to the navigation system.

Direct cortical stimulation was performed using the Ojemann cortical stimulator (Radionics, Inc.).4 Current intensity was modified by increasing the amplitude in 2-mA increments, from a baseline of 4–10 mA or until a functional response was elicited. If seizures were observed, ice water was irrigated over the brain, without sedative medications to allow subsequent functional mapping and evaluation of the patient.

Evaluation of language function was based on naming and verb-generating tests in response to a visually presented noun and by free conversation. Motor function evaluation was based on a patient’s performance accuracy of uni- and bimanual finger-tapping tasks. Patients were instructed to perform a sequence of 3 numbers to which they had to tap the correct finger. The evaluation of motor function was documented according to the number of errors in tapping as well as on slowness and hesitations in performance. Once a dysfunction was observed, the location was documented by capturing the anatomical and radiological (navigation) location on the cortex. Throughout the operation, each patient was reevaluated by the same clinical team.

Prior to cortical stimulation, patients performed all of the functional tests to establish a baseline level to control for stress-related effects. Stimulations in the vicinity of the tumor resection area were performed prior to tumor resection, and evaluation of functional status was carried out throughout the procedure. Direct cortical stimulation was used to identify the primary motor area (MI) and only then was the SMA stimulated for the investigational purpose.

Language Evaluation

In addition, following stimulations and during the resection process free speech was examined via free conversation with the clinical team.

Statistical Analysis

Statistical analyses were done using STATISTICA software (StatSoft, Inc. [2001], version 6). An independent-samples t-test was used to compare the fMR imaging measurements between patients who exhibited dysfunction during DCS and those who were unaffected by DCS.

Results

All patients exhibited motor-related activations during the fMR imaging finger-tapping paradigm and language-related activations during the fMR imaging verb-generation paradigm (Fig. 3).5
Beta Weights as Predictors for Motor Dysfunction During DCS

Beta weights were extracted from the simple finger-tapping block, which were performed by the hand contralateral to the lesion and which were examined during DCS. Comparison between beta weights was obtained from patients who were affected by DCS and patients who were not while performing a motor task (14 patients, mean beta weight 1.24, and 12 patients, mean beta weight 0.84, respectively). This comparison revealed significantly higher fMR imaging activation in the SMA proper of the lesioned hemisphere in patients who were not affected by DCS ($t_{[2,24]} = -2.18; p < 0.04$). No significant effects were found when beta weights were extracted from the SMA proper of the intact hemisphere, nor from the pre-SMA of the lesioned and nonlesioned hemispheres. A trend for increased activation for the nonlesioned pre-SMA was found in patients in whom there was no DCS-induced motor dysfunction ($p = 0.06$) (Figs. 4 and 5 upper).

Functional Connectivity Analysis With the SMA Proper of the Lesioned Hemisphere in Motor Function

To elucidate the network of activation that may participate in the recovery process of the lesioned hemisphere, we performed a whole-brain voxel-based correlation using time courses obtained from the SMA proper. Figure 5 demonstrates the results obtained in 4 patients who had the lowest and highest beta weights in the SMA proper ipsilateral to the lesion. The data suggest that the SMA proper of the lesioned hemisphere was functionally coupled to the primary motor area only in patients in whom a high preoperative activation was shown in the SMA proper. In the 2 patients with the lowest activation in the SMA proper and DCS-induced motor dysfunction, there was no evidence of such functional coupling at the same threshold (Fig. 5 lower).

Laterality Index as a Predictor for Language Dysfunction During DCS

Because SMA dominance is influenced by language lateralization, and specifically by Broca area dominance,7 we performed a separate analysis for patients with left-side lesions. Twenty-two patients had left Broca area dominance, 1 had right-side dominance, and 3 patients had bilateral dominance. We did not perform a separate analysis for patients with right-side lesions as of the 7 patients who had right lesion only 1 exhibited language dysfunctions during DCS.

In patients with left-side lesions (19 cases), comparison between patients who were affected and those who were not affected by DCS during language naming and verb generation showed a significant difference in LI value, which was obtained from the pre-SMA using the verb-generation task ($p < 0.04$) (Fig. 6 upper). Patients who had demonstrated language dysfunction during the operation had more negative LI values, which reflect relatively higher activation in the nonlesioned right hemisphere than in the lesioned left hemisphere (mean LI $-0.34$). No such difference was found in the SMA proper. Analysis of SMA laterality in all patients (Fig. 6 lower) yielded a similar pattern of results, with stronger dominance of the nonlesioned hemisphere in patients with DCS-induced dysfunctions ($p = 0.06$). Together, these findings suggest that reorganization of the nonlesioned nondominant hemisphere was not sufficient to prevent DCS-induced language dysfunction.

Beta weights extracted from the pre-SMA and the SMA proper of the nonlesioned and lesioned hemisphere during the verb-generation task did not differ significantly
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between patients who were affected by DCS and patients who were not affected (Fig. 6).

Functional Connectivity Analysis With the Pre-SMA in Language Function

Whole-brain voxel-based correlation, using time courses obtained from the left pre-SMA, was employed in 4 patients with the lowest or highest LI values in the pre-SMA among patients with left-side lesions (Fig. 7 upper). The left pre-SMA showed a trend for increased functional coupling with the IFG and the MFG among patients who also showed preoperative high activation in the left pre-SMA, and no functional deficit during DCS (Fig. 7 lower). This suggests that activation in the left pre-SMA might be important to sustain the language network.

Functional MR Imaging Results as a Predictor for Postoperative Neurological Deficit

No significant correlation was found between preoperative fMR imaging measurements and postoperative neurological outcome. Since only 6 patients had a postoperative deficit, we cannot rule out the possibility that the small sample size prevented us from identifying a correlation between fMR imaging measurements and outcome.

Analysis Excluding Nongliomas

Because our patients had various types of lesions, which might involve different types of resection, additional analysis was conducted with the exclusion of the patients without gliomas. This analysis yielded a similar trend to the findings of the previous analysis in motor and language functions (Figs. 8 and 9, respectively). The re-
Results did not, however, reach statistical significance ($p = 0.146$ for motor, $p = 0.1$ for language), perhaps due to the small group size.

Patients who Underwent a Prior Operation

A separate analysis was performed on data obtained in the 7 patients who had undergone a prior operation in the SMA region before entering the study. The time from the initial operation to enrollment to the study ranged from 1 to 5.4 years. The aim of this analysis was to examine the effects of prior surgery on functional organization in the SMA area. For motor function, analysis of the effect of DCS showed a trend of difference between patients who were affected by DCS and those who were not. Patients who were not influenced by DCS had significantly higher beta weights in the pre-SMA of the lesioned hemisphere, and those who were affected by DCS had lower beta weights in the lesioned hemisphere. No significant difference was found in the SMA proper.

For language function, patients with a DCS-induced dysfunction had a significantly lower LI value in the SMA proper, indicating stronger lateralization for the lesioned hemisphere. No such effect was found in the pre-SMA.

Results of Direct Cortical Stimulation

Direct cortical stimulations of the SMA region caused motor dysfunction in 14 of 26 patients. In 12 of the 14 patients, the SMA lesion was on the left side (10 were right handed), and in 2 of the patients the SMA lesion was on the right side (1 was right handed). For language functions, 10 of 26 patients experienced DCS-induced dysfunction. Nine patients had a lesion in the left hemisphere (all were right handed) and only 1 right-handed patient had a lesion in the right hemisphere.

Intraoperative seizures occurred in 7 patients and were immediately controlled with ice-water irrigation. All seizures resolved within minutes and did not interfere with the patient’s cooperation for the functional intraoperative evaluation (for details see Table 2). The 1 patient who became uncooperative after a seizure was excluded from analysis as previously noted.

Patients With Immediate Postoperative Neurological Deficit

Six patients experienced an immediate postoperative new neurological deficit (5 in language and 1 in motor function). In 2 patients the deficits resolved within hours and in 3 patients within 2 weeks. In 1 patient the dysfunction slowly improved but the patient never regained his baseline language function. Of the 5 patients with postoperative language dysfunction, 2 patients also experienced language dysfunction during DCS, while in 3 no such DCS-induced dysfunction was observed.

All 5 patients with postoperative language dysfunc-
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The patient who exhibited immediate motor neurological deterioration had motor SMA dominance ipsilateral to the lesion and did not exhibit any deterioration during DCS. Six patients presented prior to surgery with a neurological deficit and improved within 3–5 days of surgery, except for 1 patient who presented with motor preoperative dysphasia that persisted after surgery.

**Supplementary Motor Area Dominance and DCS Results**

None of the patients with a lesion in their dominant SMA (LI > 0.2) experienced DCS-induced language dysfunction. Among the patients with lesion in their nondominant SMA (LI < −0.2), 50% (6 of 12) experienced DCS-induced language dysfunction, and of the patients with bilateral language activation in the SMA (−0.2 < LI < 0.2) 50% (4 of 8) experienced language dysfunction during DCS.

**Discussion**

The extent of resection significantly affects survival in patients with high- and low-grade gliomas. Long-term tumor control and delayed malignant transformation are also associated with maximal resection of low-grade gliomas. An aggressive surgical approach is justified, however, only if it does not cause new permanent neuro-
logical deficits. Gross-total resection in the SMA region can result in motor deficits, language deficits, or both. In such cases, although deficits are usually transient, the preparation of the patient and family for the possible postoperative outcome is important.

In an attempt to determine the main compensatory mechanism due to space-occupying lesions in the SMA region, we evaluated the recruitment of the contralateral nonlesioned hemisphere, as well as regions ipsilateral to and in the vicinity of the lesion, using fMR imaging and DCS. Direct cortical stimulation of the SMA resulted in dysfunction in about half of the patients (both in motor and language functions), which allowed us to evaluate the difference between the groups. We suggest that DCS does not cause functional dysfunction if a compensatory network exists, possible by the recruitment of the nonlesioned SMA or areas in the vicinity of the lesion. When DCS results in some functional deficit, such a compensatory mechanism does not exist or is insufficient to sustain the relevant function.

In the current study we found that stronger activation/dominance of the lesioned SMA was present in patients without DCS-induced dysfunctions. This may indicate a “higher” functional reserve in these regions that could compensate for electrical and mechanical disruption of these areas. We have demonstrated in patients with extreme laterality/dominance values (using whole-brain functional coupling with the SMA region) that in patients with no DCS-induced dysfunction there is also a trend for increased connectivity of the lesioned SMA with other brain areas related to the function examined during the fMR imaging paradigm. Specifically, increased coupling of the lesioned SMA with the M1 (primary motor area) was found during the finger-tapping paradigm and with language-related regions (IFG and MFG) during the verb-generation paradigm. Reduced coupling with these regions was found in patients in whom DCS-induced dysfunction was observed. It is possible that such functional coupling of the SMA with motor and language areas in the same hemisphere can explain the resilience of SMA to surgical destruction.

While looking at the relation between the fMR imaging activation level and DCS-induced motor dysfunction (Fig. 5), it may seem that the results are driven from extreme values. The reason we included all patients in the overall analysis, although the results in some seem quite extreme (as, for example, the patients in Cases 26 and 12) is that they did not meet the criterion to be defined as outliers ≥ 3 SDs. In a further analysis in which these 2 patients were excluded, there was still a trend (p = 0.1) for increased beta value for the mean DCS-induced dysfunction in the lesioned SMA proper (mean 1.123) compared with no dysfunction (mean 0.866).

Observations in patients who had undergone a previous operation showed a similar trend. Some dissimilarity, however, existed between the analysis of this group
and the analysis of the entire group. While in the general analysis the beta weights in the SMA proper of the lesioned hemisphere best predicted DCS-induced motor dysfunction, in the subgroup analysis beta weights in the pre-SMA of the lesioned hemisphere best predicted motor dysfunction during DCS. In language function, the LI extracted from the SMA proper best predicted DCS-induced language dysfunction, and not from the pre-SMA, as was the case in the entire group of patients. These findings suggest that previous surgery in the SMA area may cause some functional reorganization. Additional studies focusing on such subgroups are needed to confirm this hypothesis.

**Brain Plasticity and Space-Occupying Lesion**

The essential role of the lesioned hemisphere in functional reserve is supported by observations in stroke patients in whom movement improvement was accompanied by increased task-related fMR imaging activations in the primary motor cortex and in the SMA of the ischemic hemisphere. Increased excitability in these regions was also measured using transcranial magnetic stimulation, which depicts changes at the synaptic level. In the Broca area, language transfer from the left to right inferior frontal gyrus was recently documented in the presence of low-grade gliomas in an adult patient. Although this patient was not aphasic following resection of the left IFG, his language functions were significantly impaired.

Based on our findings, we suggest that the appearance of fMR imaging–related activations contralateral to the lesion do not necessarily represent sufficient functional reserves. In accordance with this concept, increased activation in the intact hemisphere was prominent in patients with poor motor recovery following stroke. In addition, transfer of SMA activity from the lesioned hemisphere to the intact hemisphere was not sufficient to prevent the occurrence of postoperative functional deficit following SMA resection. Thus, preoperative recruitment of the

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**TABLE 2: Summary of results in 26 patients**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Lesion Side</th>
<th>Pre-SMA LI</th>
<th>SMA Proper LI</th>
<th>Broca Side</th>
<th>DCS Deficit</th>
<th>Neurological Status</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td>Language</td>
<td>Motor</td>
<td>Function</td>
<td>Function</td>
<td>Immediate Postop</td>
</tr>
<tr>
<td>1</td>
<td>rt</td>
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</tr>
<tr>
<td>2</td>
<td>lt</td>
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</tr>
<tr>
<td>3</td>
<td>rt</td>
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<tr>
<td>4</td>
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</tr>
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<td>5</td>
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<td>rt</td>
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<td>dysphasia</td>
</tr>
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<td>healthy</td>
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<td>no change</td>
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</table>

* Dominant SMA for motor function was defined based on fMR imaging activation during hand movement in the hand contralateral to lesion. — = missing data.
intact hemisphere prior to surgery does not prevent postoperative dysfunction and may indicate that some functional deficit already exists. A possible explanation for the increased activation in the intact hemisphere following stroke may reflect the removal of transcallosal inhibition from the damaged hemisphere. Although a causal relationship cannot be ascertained between preoperative shift to the intact SMA and postoperative functional deficit, it is possible that some causality exists between these 2 observations. Nevertheless, it was demonstrated that SMA transfer to the intact hemisphere was associated with a faster recovery. Because our patients showed only short-term functional deficits, we did not examine the neural correlates related to the long-term recovery process. It is possible that activation of the intact SMA is not sufficient to prevent DCS-induced dysfunction but may be beneficial for long-term recovery.

The functional coupling analysis provides a possible explanation for the critical role of the SMA in the lesioned hemisphere. We suggest that decreased activity of the lesioned SMA may also indicate insufficient function of brain regions to which it connects. As the SMA has extensive cortical connections with motor and frontal areas, damage to the SMA may also influence the ability of the whole hemisphere to sustain the function. It is possible that DCS-induced dysfunction is caused by reduced connectivity of the SMA with the entire hemisphere; thus, no recruitment of brain areas relevant for the functions can be accomplished during DCS. In such a case, functional dysfunction during DCS may indicate a deficit of the functional reserves within the hemispheres and may not be indicative of the function of the specific area stimulated.

In interpreting the results of this study, one should take into account the influence of space-occupying lesions on the reliability of the blood oxygenation level–dependent signal. Ulmer et al. reported on a case in which language dominance (as determined by fMR imaging) was inconsistent with the intraoperative mapping results. Schlosser et al., however, have demonstrated that the blood oxygenation level–dependent signals in patients with tumors affecting the frontal lobe were comparable with normal control individuals. Validation of the fMR imaging signal in the vicinity of lesions was also performed by demonstrating high correspondence between the results of fMR imaging and Wada testing or DCS.

Conclusions

We suggest that fMR imaging activation in the nonlesioned SMA should not be automatically interpreted as compensation, allowing safe wide resection of the lesion. The consequences of misinterpreting tumor-induced fMR imaging changes as cortico reorganization are hazardous. It is possible that in some cases the fMR imaging appearance of lesion-induced cortical reorganization from one hemisphere to the other, or from one region of brain to an adjacent site, could indicate genuine reorganization. However, caution should be taken in interpreting the fMR imaging results in such cases.

Disclosure

This research was supported by the Adams Super Center for Brain Studies. The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Ram, Rosenberg, Fried, Hendler. Acquisition of data: Rosenberg, Nossek, Liebling, Fried, Shapira-Lichter. Analysis and interpretation of data: Rosenberg, Nossek. Drafting the article: Rosenberg, Nossek. Critically revising the article: Ram, Shapira-Lichter, Hendler. Reviewed final version of the manuscript and approved it for submission: all authors. Statistical analysis: Rosenberg. Administrative/technical/material support: Rosenberg. Study supervision: Ram, Hendler.

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References

Prediction of deficits and recovery after SMA surgery


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