Functional neuronavigation with magnetoencephalography: outcome in 50 patients with lesions around the motor cortex

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The authors conducted a study to evaluate the clinical outcome in 50 patients with lesions around the motor cortex who underwent surgery in which functional neuronavigation was performed.

The sensorimotor cortex was identified in all patients with the use of magnetoencephalography (MEG). The MEG-source localizations were superimposed onto a three-dimensional magnetic resonance image, and the image data set was then implemented into a neuronavigation system. Based on this setup, the surgeon chose the best surgical strategy. During surgery, the pre- and postcentral gyrus were identified by neuronavigation, and in addition, the central sulcus was localized using intraoperative recording of somatosensory evoked potentials. In all cases MEG localizations of the sensory or motor cortex were correct. In 30% of the patients preoperative paresis improved, in 66% no additional deficits occurred, and in only 4% (two patients) deterioration of neurological function occurred. In one of these patients the deterioration was not related to the method.

The method of incorporating functional data into neuronavigation systems is a promising tool that can be used in more radical surgery to cause less morbidity around eloquent brain areas.

Key Words * magnetic source imaging * functional imaging * magnetoencephalography * neuronavigation * tumor removal

Lesions that surround the eloquent brain areas are always a challenge in neurosurgical decision making. In some cases tumors adjacent to the sensorimotor cortex are completely resectable; however, it is often difficult to depict the relationship of the lesion with the known anatomical structures. The results of neuroradiological assessment of the central sulcus are often ambiguous, especially when edema or mass lesions are present. Intraoperatively the localization of the central sulcus can be achieved by recording of the somatosensory-evoked potentials (SSEPs). Although this method is presently considered as the reference standard for the identification of the central region, it has limitations. Not in all cases is the N20/P20 wave phase-reversal pattern clearly distinct. In rare cases intraoperative localizations may err as much as one gyrus.[3,28] Furthermore, a preoperative estimation of the tumor-motor cortex relationship cannot be assessed by this method.

In recent years the technique of preoperative mapping of functionally important brain areas has made enormous advances. In addition to positron-emission tomography PET and functional magnetic resonance (fMR) imaging, magnetoencephalography (MEG) proved to be a valuable tool for the localization of intracranial neuroelectric sources.[1,4,8]. The basic principle of MEG is the recording of weak neuromagnetic signals with the aid of highly sensitive superquantum interference device detectors. Because the neuromagnetic fields are not distorted while
passing boundaries of different electrical conductivity (unlike electrical potentials), MEG offers the possibility of localizing electrical sources with high temporal and spatial accuracy.[5,27] The MEG results can be overlaid onto MR images via transformation of the MR and MEG coordinate system. For this technique, the term magnetic source (MS) imaging is used. The evaluation of the somatosensory cortex by using MEG has been a field of interest to basic researchers but also to neurologists and, lately, also to neurosurgeons, mainly, because it is feasible to incorporate functional data into frame-based and frameless neuronavigation systems. Watanabe and associates[29] described the method of using MEG and neuronavigation in 1993. Gallen and coworkers[6] reported on the usefulness of preoperative localization of the motor cortex by using MS imaging and intraoperative phase reversal. With the advent of image-guided frameless stereotaxy there was suddenly not only the possibility of using anatomical information but also of integrating functional data, which could be used to identify eloquent brain areas intraoperatively without the patient's being awake. The method and its application for a frame- and pointer-based navigation system have already been described.[7,20,21]. In this report we address the question of whether the use of neuronavigation combined with functional imaging may contribute to a better clinical outcome in patients who undergo surgery that involves areas around the sensorimotor cortex.

CLINICAL MATERIAL AND METHODS

Patient Selection

In the period between February 1995 and July 1998; a total of 61 patients in whom tumors involved the central region were examined using MEG to detect sensory-evoked fields (SEFs) and motor-evoked fields (MEFs). In all patients the relationship of the tumor with the sensorimotor cortex was assessed preoperatively by performing MEG-dipole localization and MS imaging. Eleven patients were rejected for surgery because there was evidence of tumor infiltration into the motor cortex on MS imaging. Fifty patients were eligible for surgery (16 with astrocytomas, WHO Grades II and III; 12 with glioblastomas, 13 with meningiomas, six with metastases, three with other lesions). The age ranged from 6 to 79 years (mean 48.3 years). All patients provided informed consent. In 21 patients the space-occupying lesion was located in the premotor area, and in 12 cases the tumor had partly infiltrated the motor cortex. In 17 patients the tumor was located in the postcentral area. Twenty five of the 50 patients experienced a paresis before operation.

Magnetic Source Imaging

All patients underwent SEF monitoring, and in addition, 19 patients underwent MEF monitoring. We used a MAGNES II biomagnetometer with multi 2 x 37 channels for the MEG recording. The recording was performed inside a magnetic-shielded room. For SEF recordings 200 tactile stimuli were applied to the patient's thumb, index finger, and little finger on the side contralateral to the lesion (interstimulus interval 1 second) and averaged, covering a 300-msec interval (150 msec pre- and 150 msec poststimulus); the sampling rate was 1041.7 Hz. For MEF monitoring patients were asked to perform self-paced repetitive finger tapping with the contralateral index finger every 3 to 5 seconds. The single finger movement was used to obtain a trigger signal of the surface electromyography (EMG) reading of the flexor digitorum superficialis indicis muscle. To obtain the average, 120 runs were sampled, covering a 600-msec interval. Special care was taken to avoid motion artifacts: the patient's arm was fixed and the head was embedded in a vacuum cushion, and with this precaution head movement was minimized during the recordings of the evoked magnetic fields. The somatosensory neuromagnetic peak components ranged from 20 to 100 msec and represented activity in the primary sensory cortex.[9] The MEFs showed marked activity with 100-msec latency after EMG onset[12] (Figs. 1 and 2).[30]
Fig. 1. Case 46. Averaged and overlayed signal traces after motor experiment recorded by way of movement of index finger. The average was triggered with the simultaneously recorded surface EMG shown beneath the MEG traces. ms = milliseconds; fT = fento Tesla.

Fig. 2. Isocontour map of the M100 latency after EMG onset shown in Fig. 3 demonstrating dipolar field activity. The numbers in the image represent the 37 channels of the MEG (A1-37) in one of the two sensors.

At these points in time the latencies were investigated with the dipole fit and the equivalent current dipole (ECD) model and the sphere as the head model.[10] The equivalent current dipole solution of localizing intracranial sources is commonly used in simple activation tasks, in which it is plausible to assume that there is only one dipolar source active. Magnetoencephalography results from the synchronized activity of excitatory postsynaptic potentials of more than $10^5$ pyramide cells, which are to be found in the cerebral cortex in an order of $10^5$ per mm$^2$. According to Okada,[17] a cortex area of about 1 to 5 mm$^2$ is activated by applying simple stimuli. The localization with the best correlation ($> 0.97$) between the measured field and the calculated field was used for image fusion with MR imaging (0.2 tesla; three-dimensional fast low angle shot sequence with a slab thickness of 168 mm, slice thickness 1.5 mm, TR 16msec, TE 7msec, field of view 250 mm). The image fusion was achieved with a self-developed contour fit program described previously.[14]

**Neuronavigation**

In 25 cases we used the StealthStation, a free-hand stereotactic pointing device, the position of which is registered
via light emitting diodes. The position of the pointer tip in the surgical space is displayed on the workstation's monitor with the corresponding location in the image space.[24] In these cases the MEG-marked gyrus was found by projection of the MEG dipole to the surface of the gyrus with the workstation's software. In all other procedures the Zeiss Multiple Coordinate Manipulator (MKM) neuronavigation system was used. The MKM consists of a robotic microscope integrated into a neuronavigation system. All the navigation data that are visible on the workstation can be displayed through a head-up display into the eyepiece of the microscope view as well.[13,16] This system is very useful for displaying tumor contours, as well as surgical pathways to the target, or for incorporation and visualization of functional data within the surgical space. For referencing image space and patient we used a set of at least eight to 10 fiducial markers that were attached to the patient's head. In our previously conducted phantom studies it has been shown that a minimum of eight generalized markers provided optimum accuracy to the 95th percentile for the localization error of 2.2 mm, whereas the mean localization error varied between 1.59 ± 0.29 mm for the MKM system.[25] Although the MEG measurement was obtained 1 to 2 days prior to surgery, the data transfer to the neuronavigator was performed on the evening before operation. The image data were transferred via fast ethernet by using the DICOM 3 protocol (Digital Imaging and Communications in Medicine). The referencing procedure with the MKM system takes approximately 20 minutes. Before draping, the tumor contour was superimposed onto the patient's skin, allowing an adequate skin incision to be marked as well as planing of the bone flap. After craniotomy, five additional bone fiducials were applied around the bone flap. These markers were used for new reference points in case the initial reference fiducial was lost due to technical failure of the workstation or in case an update of the neuronavigation was required after the patient underwent intraoperative imaging in the open MR imaging unit to compensate for inaccuracy due to brain shift (not part of this study). However, in these cases the functional data are no longer included. After opening of the dura, the motor cortex was identified either with the StealthStation's pointer or by direct visualization via the MKM microscope. Intraoperative recording of the SSEPs phase reversal elicited by median nerve electrical stimulation was then performed to localize the central sulcus and to verify the MEG localization. For the SSEPs monitoring, strip electrodes with four or eight electrodes were used. A Pathfinder I was used for all recordings. Stimulation parameters were: intensity 15 to 25 mA, frequency 5.1 Hz, duration 100 µsec, filter 30 to 3 kHz. The MAGNES II biomagnetometer was obtained from Biomagnetic Technologies, Inc. (San Diego, CA) and the Stealth Station was acquired from Surgical Navigation Technologies, Inc. (Broomfield, CO). The MR imager was manufactured by SIEMENS (Erlangen, Germany). The MKM neuronavigation system was obtained from Zeiss (Oberkochen, Germany); the fiducial markers from Tikom (Fürth, Germany) and Howmedica Leibinger (Freiburg, Germany); and the Pathfinder I from Nicolet Instruments (Madison, WI).

ILLUSTRATIVE CASES

Case 46

Examination. This 27-year-old right-handed woman suffered a generalized seizure for the first time in February 1998. Her prior medical history was not conspicuous. On MR imaging a right-sided frontal tumor close to the motor cortex was revealed. On admission the patient showed no focal neurological deficits. Magnetoencephalography was performed to record SEF- and MEF dipole localizations. Magnetic source imaging was performed using a three-dimensional MR imager in the low-field MR unit. The MEF dipole was located posterior to the tumor and the SEF dipole was one gyrus further posterior. Evaluation of the MS imaging studies indicated that the tumor had evolved to the anterior part of the motor cortex without having invaded it.

Surgery. A right frontal craniotomy was centered onto the tumor contour that was projected to the skin by the MKM microscope. After opening the dura the tumor and the segmented MEF and SEF dipoles could be seen through the eyepieces of the navigation microscope (Fig. 3). The tumor appeared to be anterior to the precentral gyrus. This was confirmed by the intraoperative phase reversal of the N20/P20 wave potentials posterior to the projected MEF dipole and anterior to the projected SEF dipole with the four-strip electrode placed partly under the bone. The tumor was then resected completely. An intraoperative MR image confirmed total removal of the tumor (image not shown).
Fig. 3. Case 46. A: Intraoperative view through MKM neuronavigation microscope displaying the tumor contour of the low-grade precentral astrocytoma along with the MEF dipole localization of the motor cortex projected to the brain surface (the MEF dipole is a trapezoid in the MR voxels, which is manually segmented for display in the microscope. Shown here is a cut of the segmented MEF trapezoid). The phase reversal confirmed the localization of the central sulcus between the MEF and the SEF dipole (SEF dipole not shown in this photo). B: Screenshot from the computer workstation displaying the tumor contour and MEF dipole (green triangle) that marks the motor cortex. In this case a complete tumor removal was possible because the tumor was located in the premotor area. Because this patient was right-handed and the tumor was on the nondominant right side, no transient paresis because of supplementary motor area involvement occurred.

**Postoperative Course.** The patient sustained no neurological deficits after surgery and is working full time in her old profession. Histopathological examination revealed a low-grade astrocytoma (World Health Organization [WHO] Grade II tumor).

**Case 39**

This 35-year-old right-handed man had a history of focal seizures in his left arm since aged one year. The frequency of the fits was increasing while he underwent anticonvulsive therapy. Magnetic resonance imaging revealed a nonenhancing hypointense lesion in the right central area. On admission, the patient had a 4/5 paresis in his left arm. Magnetic source imaging with SEF and MEF revealed the tumor to be localized within the motor cortex. However, because surgery was planned to obtain a biopsy sample and to gain a histopathological diagnosis and remove exophytic tumor mass, complete tumor resection was not planned from the beginning.

**Surgery.** A small craniotomy was performed around the tumor. Intraoperative visualization of the motor functional data projected the MEF dipole onto the whitely discolored tumor. Phase reversal confirmed the correct MEF and SEF localization. Only a small biopsy sample from the anterior tumor margin was obtained (Fig. 4).
Fig. 4. Case 39. A: In this patient the MEF dipole representing the motor cortex is displayed on the same gyrus as the tumor, which indicates that a resection is not possible. The white star represents the SEF phase reversal and indicates the central sulcus. B: Screenshot of the MR imaging data set as displayed on the workstation, showing the tumor contour and MEF dipole (green triangle) in the precentral gyrus.

Postoperative Course. Histological examination confirmed a low-grade astrocytoma (WHO Grade II). After surgery, the patient's left-arm paresis deteriorated to 3/5, which was continuously improving at discharge. Three months later the paresis had improved to the preoperative level.

RESULTS

A total of 50 patients underwent surgery in which combined neuronavigation MEG-derived SEF and MEF data of the sensorimotor cortex were obtained. In Tables 1 and 2, a summary of characteristics and clinical results are provided.

<table>
<thead>
<tr>
<th>TABLE 1</th>
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<td>COMPARISON OF RESULTS OBTAINED USING FUNCTIONAL NEURONAVIGATION AND SSEP/MEP MONITORING</td>
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<table>
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<tr>
<th>Outcome</th>
<th>Functional Neuronavigation</th>
<th>SSEP/MEP Monitoring</th>
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</thead>
<tbody>
<tr>
<td>improvement</td>
<td>15 (30)</td>
<td>none</td>
</tr>
<tr>
<td>unchanged</td>
<td>33 (66)</td>
<td>82 (83)</td>
</tr>
<tr>
<td>deterioration</td>
<td>2 (4)</td>
<td>17 (17)</td>
</tr>
<tr>
<td>total</td>
<td>50</td>
<td>99</td>
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* These data are taken from a study conducted by Cedzich, et al.
Sixteen patients harbored an astrocytoma (seven WHO Grade II and nine WHO Grade III); 12 patients harbored glioblastoma; 13 patients harbored meningioma; six patients had metastasis; two patients had primitive neuroectodermal tumor (PNET); and one patient harbored an angioma. Twenty one of these tumors were located in the precentral area, 17 in the postcentral region, and 12 had infiltrated the motor cortex so that only partial resection...
or obtaining a biopsy sample was possible. In the group with low-grade astrocytomas, six tumors had developed anterior to the motor cortex, and in one case the tumor was limited to the motor cortex. Of the WHO Grade III astrocytomas, six were located in the premotor area, one was posterior to the somatosensory cortex, and two invaded the motor cortex, thus allowing only a partial resection. In the group of patients who harbored glioblastomas there were two tumors in the precentral, six in the postcentral, and four in the central area. Of the 13 meningiomas, six were located precentrally, three had developed in the area of the rolandic fissure and displaced the precentral gyrus, and four were posterior to the central sulcus. Of the six metastases, four were located in the postcentral area, one was in the precentral area, and one had infiltrated the motor cortex. Of the other three tumors there were two PNETs, one of which was situated on the surface of the rolandic fissure and one very close to the motor cortex in the postcentral gyrus, and one angioma that was located in the postcentral area. Twenty five patients presented with paresis prior to surgery. Of these, 11 patients had 4/5 paresis of the contralateral arm and three had 4/5 paresis of the leg. Five patients had both 4/5 paresis of arm and leg. Two patients suffered from 3/5 paresis of the leg and 4/5 paresis of the arm. Three patients experienced 4/5 paresis of the leg. One patient had 3/5 paresis of the leg; one, 3/5 paresis of the arm; and one patient each had 2/5 paresis of the arm and 2/5 paresis of both arm and leg. The overall outcome in all our surgically treated patients with regard to the paresis was as follows: of the group with initial paresis, 15 patients (60%) improved postoperatively or within a period of 3 to 6 months postoperatively. Of the group with 4/5 paresis (arm and leg) 10 patients (47%) had complete regression of the paresis.

Two patients deteriorated, one from unrelated complications related (this patient developed a hemiparesis due to sinus thrombosis). A 6-year-old patient with an infiltrative PNET in the postcentral area developed 3/5 paresis of the contralateral arm postoperatively after suffering severe intraoperative brain swelling. Of the group in which no paresis existed prior to surgery, one patient with Grade II astrocytoma which was confined to the motor cortex, experienced transient deterioration to a 4/5 paresis of the arm after operation but presented with normal motor function 3 months postoperatively. One patient with a large Grade III astrocytoma involving the premotor supplementary area developed a severe 3/5 hemiparesis of arm and leg immediately after surgery, which then resolved within 10 days. This phenomenon of surgery-related transient motor deficits around the supplementary motor area has been well described in the literature.[22]

The distances of the SEF dipole projected to the brain surface (marking the postcentral gyrus) and the intraoperative phase reversal (marking the central sulcus) ranged from 3.6 to 8.6 mm (mean 5.9 mm, standard deviation 1.7 mm), as previously reported.

**DISCUSSION**

Since the advent of neuronavigation devices, these systems have been used mainly to acquire information concerning the intraoperative anatomy. "Functional neuronavigation" (a term we use to describe the combination of frame-based or frameless image-guided stereotaxy and functional imaging) is a new method that allows fast orientation of the relation of lesion to functional anatomy. Here we report our experience using MEG-derived information on the sensorimotor cortex and neuronavigation in 50 patients who harbored centrally located lesions. In all cases we were able to use MEG to obtain data on the primary sensory or motor cortex, which was in agreement with intraoperative SSEP recording. In a recent report by Chong and coworkers,(unpublished data) they noted that preoperative functional imaging, which reduced hospital costs by 25%, was cost-effective because it led to the avoidance of hemiparesis or hemiplegia by allowing surgeons to choose different treatment strategies in patients with tumor invasion of the motor cortex revealed by MEG. A similar result was found in our series in which 11 patients were not available for open surgery because of invasion of the motor cortex.

The main advantage of MS imaging localization of the sensorimotor cortex is that it allows preoperative assessment of the relation of a lesion to the motor cortex and, therefore, can be helpful in indicating the type of needed surgery. Furthermore, we have localized the somatosensory or the motor cortex in all cases thus far, whereas the successful performance of the SSEP phase reversal is between 91% and 94% in experienced hands[31] and only 82% when cortical activation is achieved by fMR imaging.[19]

When comparing our results with a recent study by Cedzich, et al.,[3] (Table 1) more favorable outcome seems to
have been obtained in the group that underwent surgery in which functional neuronavigation was performed. Whether this trend can be repeated in ongoing studies will have a major impact on the cost-benefit ratio regarding this expensive method. Functional neuronavigation is not limited to the incorporation of MEG data alone; it is possible to integrate results from fMR imaging, position-emission tomography, or MR spectroscopy.[11,15,23] The application of fMR imaging, in particular, is currently being investigated as an almost ubiquitous tool for the identification of the central sulcus.[18,32] Because it is more easily available than MEG, fMRI has the potential to encourage greater use of functional neuronavigation in the future. However, the question of whether fMRI imaging, which uses metabolic rather than direct neuronal activation, can replace MEG, or provide complementary and additional information remains to be investigated. In previously published reports the distances between main fMR imaging activity and the MEG dipole localization in preoperative localization studies have been shown to vary between 10 mm and 16 mm.[2,26] These differences correlate with our own investigations (unpublished data) in which we determined that the mean difference between fMR imaging and MEG in motor tasks is 14 mm. However, the measured blood oxygen level-dependent effect in fMR imaging tends to have its highest activity within or posterior to the central sulcus due to the individual venous architecture of the motor cortex. In some cases it is difficult to assess the correct relationship of a lesion and the precentral gyrus, mainly in the presence of large distortion because of the space-occupying lesion. Furthermore, Pujol and colleagues[19] found that in 18% of the patients in their study no valid fMR imaging localization could be achieved. However, fMR imaging has the potential to make functional neuronavigation more widely available in the future, and more studies are needed to compare these two methods. The unavoidable question of whether the financial implications of this complex technology warrant the clinical benefit has to be determined by future investigations. After all, the method of intraoperative SSEP phase reversal is faster and more inexpensive. We hope that our work contributes to this ongoing discussion.

CONCLUSIONS

Functional neuronavigation is a new method that has just emerged in clinical practice. Hopefully more neurosurgical centers will use functional data along with their different neuronavigation systems for better evaluation of real clinical benefit because more studies are needed. The incorporation of localization data of the sensorimotor cortex into neuronavigation is a first step in an evolving process of integrating data other than anatomical information into the surgical site.

References


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