CHAPTER 2

Magnetoencephalographic study of posterior tibial nerve stimulation in patients with intracranial lesions around the central sulcus

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ABSTRACT

Objective
To study interhemispheric differences of somatosensory evoked field (SEF) characteristics and the spatial distribution of equivalent current dipole (ECD) sources in patients with unilateral hemispheric lesions around the central sulcus (CS) region.

Methods
In seventeen patients with perirolandic lesions, averaged somatosensory responses after posterior tibial nerve (PTN) stimulation at the ankle were recorded with magnetoencephalography (MEG). Dipole source solutions in the affected (AH) and unaffected (UH) hemisphere were analyzed and compared for latency, ECD strength, root mean square (RMS) and spatial distribution in relation to clinical findings.

Results
Three main SEF components, P45m, N60m, and P75m were identified in the hemisphere contralateral to the stimulated nerve. Dipole strength for the P45m component was significantly higher in the AH compared with the UH. SEF characteristics in the AH and UH showed no significant differences with respect to component latency or dipole strength of the N60m and P75m component. Inter-dipole location asymmetries exceeded 1.0 cm in 71% of the cases.

Comparison of the PTN evoked responses (P45m and N60m) in patients with motor deficits and patients without deficits showed that these responses are enlarged in the AH when perirolandic lesions are present. Patients with motor deficits also showed an increased response for P45m in the UH.

Conclusions
The results of posterior tibial nerve SEFs suggest spatial and functional changes in the somatosensory network as a result of perirolandic lesions, with a possible relationship with clinical symptoms. The results can provide further basis for the evaluation of cortical changes in the presence of perirolandic lesions.
INTRODUCTION

For presurgical planning or intra-operative neuronavigation, somatosensory evoked responses to electrical stimulation of the median nerve at the wrist or pneumatical stimulation of the fingers, can be applied to localise the primary somatosensory cortex (SI) in patients with intracranial lesions (5,43,48). In magnetoencephalography (MEG), the early component (N20m) of the median nerve somatosensory evoked field (SEF) can be localized to the contralateral SI using a single equivalent current dipole (ECD) model (11,12,18,23,32,40). Intra-operative recordings have shown this localization to be very reliable (12,40).

In contrast to median nerve SEFs, there are only a few MEG studies of lower limb stimulation (8,13,20,31,38,40). MEG allows better spatial localization than EEG, because it is less distorted by the tissue layers between the electrical source and recording sensors (19,41) but intra-operative recordings of the lower limb area in humans are difficult due to the fact that the lower limb representation is located deep within the principal sulcus. MEG studies on SEF responses following posterior tibial nerve (PTN) stimulation at the ankle in normal controls, report four main components, at 37 ms, 45 ms, 60 ms and 75 ms (13,20). The underlying sources of these components were identified around the foot area of the primary somatosensory (SI) cortex contralateral to the stimulated nerve, with dipole orientations rotating as a function of post-stimulus-latency (13). However, the spatiotemporal SEF characteristics of PTN stimulation in the presence of intracranial lesions are largely unknown.

In recent studies, MEG has been specifically applied to investigate the changes in cortical response to sensory stimulation in patients with unilateral pathological processes (33,37). It is conceivable that different lesions affect the somatosensory network in different ways. Therefore, knowledge about the structural as well as functional changes of the network in the presence of intracranial lesions has a potentially clinical significance for presurgical planning (4).

The objective of this study was to investigate interhemispheric differences in SEF components following PTN stimulation in patients harbouring perirolandic lesions in relation to clinical findings. To our knowledge, this is the first systematic study with respect to PTN-SEF characteristics in a population with perirolandic lesions.

METHODS

Patients

From the patients with intracranial lesions, referred to the department of Neurosurgery of the VU University Medical Center, seventeen consecutive patients with unilateral intracranial lesions around the central sulcus (CS) region eligible for treatment (eight female and nine male, age range 34 - 69 years; mean ± SD: 48.1 ± 11.6 years ) with a Karnofsky Performance Scale score ≥ 70, age ≤ 70 and successful MEG test-procedure.
All patients had a neurological and radiological examination and volumetric data of the lesions was calculated from the MR segmentation images (Vector Vision Planning, BrainLAB AG, Heimstetten, Germany). The study was approved by the Medical Ethics Committee of the VU University Medical Center and informed consent from the participants was obtained prior to inclusion.

MEG Recordings
Stimulation was applied to the ankle and delivered to the skin surface by two nickel electrodes (Electrical Stimulator: Grass, USA; model S48). The stimulation frequency was 2 Hz and electric pulse duration was 0.2 ms. Stimulation intensity was adjusted individually, starting at a low value (3-4 mA) and progressively increased until clear twitches of the toe were observed. During stimulation, subjects were lying or seating comfortably with eyes open, inside the three-layer magnetically shielded room (Vacuum Schmeltze Gmbh, Germany).

MEG was recorded with a system of 151 first-order axial gradiometers (VSM MedTech Ltd., Canada), with a helmet shape detector array covering the whole head. For the SEF recordings a pre-stimulus baseline time of 100 ms was used. About 500 epochs were measured with a sampling frequency of 1250 Hz. Data were online lowpass filtered at 400 Hz. Structural magnetic resonance imaging (MRI) scans were acquired with a 1.5 T MR scanner (Siemens Sonata, Erlangen, Germany) using T₁-weighted magnetization prepared rapid acquisition gradient echo (MPRAGE) sequence. In cases with known contrast-enhancement of the lesion, gadolinium contrast was used.

Matching of functional and anatomical data
Co-registration of MEG and MRI scan was performed using fiducial markers on the nasion and left- and right preauricular points. The markers were contained in specially developed marker sockets (BrainLAB AG) and kept in place until both MEG and MRI measurements had been performed to minimize the errors involved in data co-registration. In MEG small coils energized by AC currents and in MRI vitamin E capsules were used as markers. MRI registration was performed after MEG registration, with MRI markers in the same sockets and positions as the MEG coils, enabling matching of the datasets with an estimated precision of 2 mm (7).

The fiducial points were used to define a nasion, left ear, right ear (NLR) coordinate system. In NLR the midpoint between left and right pre-auricular points defines the origin. The x and y axes in the plane formed by the three fiducials, with the x-axis directed through the nasion (positive values towards nasion) and y axis perpendicular to the x axis (positive values towards the left ear). The z axis is perpendicular to the x-y plane, with positive values upward.

Source localization procedure
Trials or channels with artefacts (eye movements, muscle activity) were excluded. A conventional single equivalent current (moving) dipole was fitted in a least-squares sense
to the average SEFs using a homogeneous spherical volume conductor model which is usually sufficient to obtain a satisfactory solution (26). A single moving dipole model was used as dipole model because one of our goals was to compare source strengths. The stationary multiple dipole model, often yields nearby and opposing dipoles of unrealistically large amplitudes. The spatial coordinates (x, y, z positions), ECD strength (Q; nanoamperemetre, nAm) and the root mean square (RMS; femtotesla, fT) of a best-fitting single ECD were estimated for each SEF component. SEF components were selected in the time interval of 30 to 130 ms post-stimulus with residual errors of fitted dipoles < 25 %. Since field patterns of clear SEF deflections in the 130 ms poststimulus window frequently show a clear dipolar pattern, ECDs explaining at least 75% of the field variance were used. The expected dipole location in the affected hemisphere compared with homologous dipole sources in the unaffected hemisphere was used as a measure of spatial displacement in the affected hemisphere. For computing these inter-dipole distances, dipoles after right side stimulation in the left hemisphere were translated to the right hemisphere by inverting the sign of the y-coordinate (|y|). Then the distance could be calculated by taking the square root of the sum of the squares of the dipole differences of x, |y| and z.

Statistical Analysis
Latencies, ECD strengths, RMS and spatial coordinates of the dipoles were compared and tested statistically, using paired two-tailed t-tests. Statistical significance was determined at an alpha level of 0.05 and data are presented as mean ± standard deviation. The relationship between tumor volume and SEF characteristics was measured by correlation analysis. All statistics were performed using SPSS software (SPSS, Inc., Chicago, IL).

RESULTS
Table 1 summarizes the clinical data of the patient group. Nine patients had an astrocytoma (six World Health Organization [WHO] grade II, three WHO grade IV), two patients had an oligodendroglioma, two a cavernoma, one a meningioma, one an arteriovenous malformation (AVM), and one multiple sclerosis (MS), initially suspected to be a glioma. One patient had a lesion without tissue diagnosis with radiological features of a low-grade glioma (LGG). Lesions were located on the right side in eight cases, on the left in nine cases. Lesion volume ranged from 2 – 110 ml (mean ± SD: 35.5± 27.7 ml). Five patients had neurological deficits consisting of slight to moderate muscle weakness. The remaining twelve patients presented with seizures. Two patients had no surgery, one had a biopsy procedure (case 4) and fourteen had surgery. The postoperative neurological status was unchanged in 8 (53 %), 2 (13 %) had a transient motor deficit, 3 (20 %) had a new permanent mild deficit and 2 (13%) improved.
Table 2 lists the first three SEF components in the short- and middle latency range and the number of patients in which the SEF contained this component. The corresponding
Table 1. Clinical data patient group.

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Location, Lateralization</th>
<th>Lesion volume (ml)</th>
<th>Symptoms</th>
<th>Postop.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>43 / F</td>
<td></td>
<td>astrocytoma II</td>
<td>frontoparietal, R</td>
<td>32</td>
<td>seizures</td>
<td>permanent mild deficit</td>
</tr>
<tr>
<td>2</td>
<td>41 / F</td>
<td></td>
<td>AVM</td>
<td>frontotemporal, L</td>
<td>36</td>
<td>weakness L-arm/leg</td>
<td>no surgery</td>
</tr>
<tr>
<td>3</td>
<td>64 / M</td>
<td></td>
<td>oligodendrolioma</td>
<td>frontal, L</td>
<td>61</td>
<td>seizures</td>
<td>transient deficit</td>
</tr>
<tr>
<td>4</td>
<td>35 / F</td>
<td></td>
<td>MS</td>
<td>parietal, L</td>
<td>21</td>
<td>weakness R-leg</td>
<td>improved</td>
</tr>
<tr>
<td>5</td>
<td>52 / M</td>
<td></td>
<td>astrocytoma IV</td>
<td>frontotemporal, L</td>
<td>25</td>
<td>weakness R-arm/leg</td>
<td>unchanged</td>
</tr>
<tr>
<td>6</td>
<td>42 / M</td>
<td></td>
<td>astrocytoma IV</td>
<td>frontal, L</td>
<td>85</td>
<td>seizures</td>
<td>unchanged</td>
</tr>
<tr>
<td>7</td>
<td>60 / M</td>
<td></td>
<td>cavernoma</td>
<td>parietal, R</td>
<td>2</td>
<td>seizures</td>
<td>unchanged</td>
</tr>
<tr>
<td>8</td>
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<td></td>
<td>astrocytoma II</td>
<td>frontal, R</td>
<td>48</td>
<td>seizures</td>
<td>unchanged</td>
</tr>
<tr>
<td>9</td>
<td>38 / M</td>
<td></td>
<td>astrocytoma II</td>
<td>parietal, L</td>
<td>110</td>
<td>weakness R-arm/leg</td>
<td>new mild deficit</td>
</tr>
<tr>
<td>10</td>
<td>68 / M</td>
<td></td>
<td>astrocytoma IV</td>
<td>frontal, L</td>
<td>19</td>
<td>seizures</td>
<td>permanent mild deficit</td>
</tr>
<tr>
<td>11</td>
<td>69 / F</td>
<td></td>
<td>meningioma</td>
<td>frontoparietal, L</td>
<td>25</td>
<td>weakness R-arm/leg</td>
<td>improved</td>
</tr>
<tr>
<td>12</td>
<td>47 / M</td>
<td></td>
<td>astrocytoma II</td>
<td>parietal, R</td>
<td>35</td>
<td>seizures</td>
<td>unchanged</td>
</tr>
<tr>
<td>13</td>
<td>49 / F</td>
<td></td>
<td>oligodendrolioma</td>
<td>frontoparietal, R</td>
<td>21</td>
<td>seizures</td>
<td>transient deficit</td>
</tr>
<tr>
<td>14</td>
<td>48 / F</td>
<td></td>
<td>astrocytoma II</td>
<td>parietal, R</td>
<td>32</td>
<td>seizures</td>
<td>unchanged</td>
</tr>
<tr>
<td>15</td>
<td>34 / M</td>
<td></td>
<td>astrocytoma II</td>
<td>parietal, R</td>
<td>26</td>
<td>seizures</td>
<td>unchanged</td>
</tr>
<tr>
<td>16</td>
<td>35 / F</td>
<td></td>
<td>LGG</td>
<td>parietal, R</td>
<td>23</td>
<td>seizures</td>
<td>no surgery</td>
</tr>
<tr>
<td>17</td>
<td>54 / M</td>
<td></td>
<td>cavernoma</td>
<td>frontal, L</td>
<td>2</td>
<td>seizures</td>
<td>unchanged</td>
</tr>
</tbody>
</table>

*a* f, female; M, male; AVM, arteriovenous malformation; MS, multiple sclerosis; LGG, low-grade glioma; R, right; L, left.

Table 2. Somatosensory evoked field characteristics.

<table>
<thead>
<tr>
<th>Deflection</th>
<th>N</th>
<th>Variable</th>
<th>AH*</th>
<th>UH*</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>P45m</td>
<td>17</td>
<td>Latency (ms)</td>
<td>47.9 ± 4.6</td>
<td>47.6 ± 5.9</td>
<td>0.765</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Q (nAm)</td>
<td>20.6 ± 14.6</td>
<td>15.2 ± 8.0</td>
<td>0.021</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RMS (fT)</td>
<td>33.8 ± 19.5</td>
<td>26.7 ± 11.6</td>
<td>0.020</td>
</tr>
<tr>
<td>N60m</td>
<td>14</td>
<td>Latency (ms)</td>
<td>67.1 ± 13.6</td>
<td>67.0 ± 14.3</td>
<td>0.980</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Q (nAm)</td>
<td>23.1 ± 16.7</td>
<td>23.9 ± 14.6</td>
<td>0.834</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RMS (fT)</td>
<td>34.4 ± 19.4</td>
<td>31.8 ± 13.7</td>
<td>0.531</td>
</tr>
<tr>
<td>P75m</td>
<td>7</td>
<td>Latency (ms)</td>
<td>88.3 ± 15.1</td>
<td>80.9 ± 9.1</td>
<td>0.318</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Q (nAm)</td>
<td>26.1 ± 28.3</td>
<td>24.2 ± 17.4</td>
<td>0.895</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RMS (fT)</td>
<td>37.5 ± 40.6</td>
<td>37.6 ± 27.9</td>
<td>0.995</td>
</tr>
</tbody>
</table>

*N, number of patients showing corresponding deflection; AH, affected hemisphere; UH, unaffected hemisphere; Q, equivalent current dipole strength; nAm, nanoamperemetre; RMS, root mean square; fT, femtotesla. * mean ± standard deviation.*
mean latency, ECD strength (Q) and RMS for the affected (AH) and unaffected (UH) hemisphere are also listed. All patients had a first component with a mean latency of 47.9 and 47.6 ms in the AH and UH respectively. Fourteen patients also had the second component with a latency of 67.1 ms in the AH and 67.0 ms in the UH. Seven patients in the affected group and seven in the unaffected group had all three components. The mean latencies of all three components showed no statistical significant difference between groups. With respect to the first SEF component (P45m), a statistical significant (P < 0.05) enlarged ECD strength and RMS were observed in the AH compared to the UH. The second (N60m) and third (P75m) SEF component showed no statistical difference in ECD strength and RMS.

Dipole coordinates (x, y, z) and inter-dipole distances between homologous dipoles are shown in Table 3. The spatial characteristics of all three SEF components showed no interhemispheric statistical significant differences. No systematic displacement direction of the SEF components was found. However, homologous dipoles did show a considerable inter-dipole distance. Location asymmetries exceeding 1.0 cm were observed in 12/17 (71%) patients for the first SEF component, in 12/14 (86%) patients for the second and 4/5 (80%) for the third component. The mean residual error of the dipoles was 10.5%.

Analysis of the subgroup of five patients with motor deficits in relation to the patients without neurological deficit showed significant differences for the P45m and N60m component with respect to ECD strength in the AH, showing enlarged dipole strengths in the patients with motor deficits (Table 4). In patients with motor deficits the UH exhibited an increased ECD strength compared to the UH in patients without motor deficits. No relationship was found between tumor volume and SEF characteristics.

### Table 3. Spatial characteristics of dipole source solution.

<table>
<thead>
<tr>
<th>Deflection</th>
<th>AH</th>
<th>UH</th>
<th>Location Difference (D)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X (cm)</td>
<td>Y (cm)</td>
<td>Z (cm)</td>
</tr>
<tr>
<td>P45m</td>
<td>-0.58 ± 0.71</td>
<td>0.97 ± 0.44</td>
<td>9.56 ± 0.93</td>
</tr>
<tr>
<td>N60m</td>
<td>-0.39 ± 1.03</td>
<td>0.89 ± 0.50</td>
<td>9.34 ± 1.00</td>
</tr>
<tr>
<td>P75m</td>
<td>-0.47 ± 0.73</td>
<td>1.13 ± 0.81</td>
<td>8.77 ± 1.28</td>
</tr>
</tbody>
</table>

a AH, affected hemisphere; UH, unaffected hemisphere; D, inter-dipole distance between homologous dipoles. Data are given in mean ± standard deviation. b Number of patients (%) with location asymmetries exceeding 1.0 cm

### Table 4. Dipole strength and clinical motor function.

<table>
<thead>
<tr>
<th>Deflection</th>
<th>Variable</th>
<th>Motor deficit (N = 5)b</th>
<th>No deficit (N = 12)b</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>P45m</td>
<td>Q_AH</td>
<td>33.4 ± 22.1b</td>
<td>15.3 ± 5.4</td>
<td>0.015</td>
</tr>
<tr>
<td></td>
<td>Q_UH</td>
<td>22.2 ± 8.1</td>
<td>13.9 ± 5.7</td>
<td>0.030</td>
</tr>
<tr>
<td>N60m</td>
<td>Q_AH</td>
<td>34.9 ± 22.4</td>
<td>16.6 ± 8.2</td>
<td>0.043</td>
</tr>
<tr>
<td></td>
<td>Q_UH</td>
<td>29.8 ± 17.1</td>
<td>20.6 ± 12.9</td>
<td>0.277</td>
</tr>
</tbody>
</table>

a Q, equivalent current dipole strength; AH, affected hemisphere; UH, unaffected hemisphere. b mean ± standard deviation.
Illustrative Cases

Patient 4

A 35-year-old woman had suffered from progressive weakness of her right leg, and discrete motor disturbances of her right hand. An anatomic MRI scan showed a left-sided, medioparietal lesion, partially cystic, with ring-like contrast-enhancement after gadolinium and slight perilesional edema. Before treatment the PTN dipole localization showed activation within the lesion for the first SEF component (Figure 1A) and localization at the lesion margin for the second SEF component (Figure 1B).

Because an attempt to resect the lesion was judged inappropriate given the high risk of increased neurological deficit, a neuronavigation-assisted biopsy was performed with aspiration of cystic fluid. The histological diagnosis was consistent with a demyelinating disorder. Postoperatively the weakness of her right leg improved and she was referred back to her neurologist. Initially, the diagnosis of multiple sclerosis (MS) could not be confirmed on clinical grounds, but when the patient later presented with an optic neuritis, the diagnosis of MS was established and she was treated with steroids. Follow-up MR imaging showed a small remnant of the atypical MS-lesion (Figure 1C).

Figure 1. Summated SEF waveforms after right-sided PTN stimulation in patient 4 with corresponding magnetic field maps (A, anterior; P, posterior; L, left; R, right) for the first (41.6 ms) and second (54.4 ms) components in the affected hemisphere are depicted. The double peak after the stimulus onset is due to filtering the stimulus artefact. A – C, magnetic source images (MSI) showing a partially cystic mass, with ring-like enhancement and posterior tibial nerve dipole localization in the lesion (A) and at the margin (B). Follow-up T2-MRI revealed a small remnant of the MS lesion (C).
**Patient 11**
Figure 2 shows summated SEF waveforms, corresponding magnetic field maps and magnetic source images (MSI) after left and right PTN stimulation in a 69-year-old patient with a left-sided frontal meningioma presenting with slight motor weakness of the right arm and leg. The MSI show the typical orientation of the first component, directed toward the mesial wall of the hemisphere and the second component with a more lateral direction. Enlarged dipole strengths were observed for the first and second component in the affected hemisphere.

![Figure 2. Summated SEF waveforms after left and right PTN stimulation in Patient 11 with corresponding magnetic field maps (A, anterior; P, posterior; L, left; R, right) for the first (C1) and second (C2) component and MSIs. Note the latency differences and larger amplitude in the affected hemisphere.](image-url)
**Patient 12**

Figure 3 illustrates location asymmetry of homologous dipoles in a 47-year-old patient with seizures due to a right-sided parietal astrocytoma, WHO grade II. Mass effect of this postcentral tumor causes the localization of the first ECD to be displaced more anteriorly and laterally with an inter-dipole distance of 1.36 cm.

![Figure 3](image1.png)

**Figure 3.** MSIs of Patient 12 after right (A) and left (B) posterior tibial nerve stimulation, showing location asymmetry of homologous dipoles. Mass effect of the postcentral tumor causes the localization of the first ECD to be displaced more anteriorly and laterally with an inter-dipole distance of 1.36 cm.

![Figure 4](image2.png)

**Figure 4.** MSIs of Patient 15, showing the first two components in the affected (right) and unaffected (left) hemisphere. Dipole orientation, latency and localization are shown in relation to the right-sided postcentral astrocytoma, WHO grade II. The first component on the right side suggests a safe distance between tumor and somatosensory cortex; however, the second component shows activation at the margin of the lesion. The inter-dipole distance between the first components is 1.19 cm and 2.33 cm between the second component.
**Patient 15**

Figure 4 shows that dipole localizations of the first and second component at different areas relative to the lesion have potential clinical value in a 34-year-old patient with a right-sided parietal astrocytoma, WHO grade II. The first SEF component in the affected hemisphere with a latency of 48.0 ms is located anteriorly compared to the second SEF component with a latency of 88.8 ms, which is located at the tumor-margin. Intra-operative electrocorticography confirmed the tumor localization adjacent to the postcentral gyrus.

**DISCUSSION**

In the present study we compared interhemispheric differences in the activation and localization of the cortical somatosensory network to posterior tibial nerve stimulation in patients with unilateral perirolandic lesions. We found significantly increased dipole strength for the P45m component in the affected hemisphere of patients with unilateral intracranial lesions. Within the affected hemispheres, there was an additional significantly elevated dipole strength for the N60m component in the presence of motor deficits. Patients with motor deficits also showed an increased P45m response in the contralesional hemisphere. No interhemispheric differences in the latencies of the SEF waveforms could be observed, only dipole location asymmetries.

**SEF Characteristics**

MEG has been used mostly for localizing neuronal activity and the SEF characteristics and dipole strength after PTN stimulation have not received much attention in patients with intracranial pathology. In agreement with findings in normal controls, we found cortical activation patterns after PTN stimulation on the mesial wall of the contralateral hemisphere with the dipole directed horizontally to the contralateral hemisphere. Studies have shown that activation of the foot area shows rotating field patterns as a function of time, not only after tibial, but also after peroneal and sural nerve stimulations (13,17,20). Stimulation of the right PTN, for example, shows a counterclockwise rotation, which is explained by two approximately orthogonal dipoles with fixed locations and orientations but with varying relative strengths as a function of time. Although we did not study rotations of the PTN, the middle-latency component was oriented mostly in opposite directions compared to the first component.

Activity within or at the border of the lesion was found in three cases (18 %). Comparable findings were described by Schiffbauer et al. in a larger patient group, especially in the presence of low-grade gliomas (39). However, the clinical significance of these findings is subject to discussion. First, the source localization error of MEG in combination with possible conductivity heterogeneity of intracranial lesions can affect dipole localization.
Secondly, the prediction of functional deficits after total resection when MEG sources are within the lesion remains to be established.

Location asymmetries of more than 1.0 cm were observed in more than 70% of the patients for each component. Although cortical displacement was not studied in detail, these location asymmetries are mostly due to the space-occupying effect of the lesions and their associated edema, which is in agreement with previous studies (5,34). Location asymmetries less than 1.0 cm were especially observed in the two cases with a small cavernoma in which there was virtually no cortical displacement. However, others have reported interhemispheric spatial differences of SEF components in the presence of cortical lesions without cortical displacement and hypothesized an altered cortical somatosensory network in the presence of lesions (3,9,14,34).

In studies on the topography of SEF following PTN stimulation in normal subjects, the main deflections (N37m, P45m, N60m and P75m) were identified in the hemisphere contralateral to the stimulated nerve, in the foot area of SI, mainly area 3b (13,17,20). Our findings show latencies corresponding with P45m, N60m and P75m, but the N37m component was not identified. The first component in our group had a mean latency of approximately 48 ms which is in agreement with the findings of Mäkelä et al. (29). Bilateral absence of the N37m response is unlikely to be related to the intracranial lesion but probably results from an insufficient dipolar pattern around 37 ms to calculate the ECD with a residual error smaller than 25 %. In addition, differences in the experimental settings with regard to number of sensors, pulse duration, stimulus frequency, interstimulus interval, number of trials and filter settings may also be influential.

We found certain variability in the number of SEF components, but this was equally distributed between the affected and unaffected hemisphere with a high intra-subject interhemispheric consistency. This finding has not been described for PTN activation, but has been shown earlier for median nerve activation in normal controls (45).

**Interhemispheric Differences**

In agreement with Roberts et al. (37), who studied median nerve SEFs in neurosurgical patients, we observed an increased dipole strength in the affected hemisphere and no latency differences for the SEF components between the affected and unaffected hemisphere after PTN stimulation. The conclusion of Roberts et al. of increased neuromagnetic responses in patients with brain tumors was based on the absence of systematic displacement of dipole y-coordinates between the hemispheres, which could have affected the measured responses. However, the x- and z-coordinates were not taken into account. Since the estimated ECD strength value is greatly affected by the distance from the sphere center, it is possible that systematic displacement of the dipole location towards the surface could affect the ECD strength (47). Since there was no significant difference in the x- and z-coordinates in our group, this could not have influenced the observed ECD strength differences.

Some authors advocate the study of the dipole strength to study excitatory and inhibitory influences of cerebral lesions (9,33,37,47). Since the dipole strength value represents the
sum of excitatory and inhibitory postsynaptic potentials, neuronal lesions can alter the synchronisation process after somatosensory stimulation. In patients with stroke, hyperexcitability of the primary somatosensory cortex in the affected hemisphere has been found in the presence of cortical and cortico-subcortical lesions and is possibly related to a reduction of intracortical inhibition (6,33), in contrast to subcortical lesions, which show enhanced inhibition (25). Whether or not this applies to brain tumors is unclear. It has been suggested that increased dipole strength in patients with tumors close to the CS is a result of hyperactive and more synchronized neurons in surrounding tissue due to altered concentrations of inhibitory and excitatory neurotransmitters (37). Patients with motor deficits not only had increased responses in the AH, but also a substantially increased P45m response in the UH compared with the UH of patients without motor deficits. In patients with stroke motor cortex disinhibition (or hyperexcitability) has also been described in the unaffected hemisphere (25,42) and is presumed to be related to suppression of transcallosal inhibition. Others suggest increased contralesional responses as a result of recruitment reflecting cerebral plasticity (2). Our study has a relatively small and heterogeneous patient group, which makes it difficult to assess the underlying mechanism and relevance of the interhemispheric differences found. Future studies with respect to the differential effects of location and type of lesion on cerebral reorganization are needed to elucidate the mechanisms involved in cortical reorganization.

Lesion volume as a possible contributing factor to increased neuromagnetic responses was not demonstrated in our study, which is in accordance to others (33,44).

In healthy subjects, SEF characteristics after median nerve stimulation have a high inter-subject variability in combination with an intra-subject interhemispheric consistency (45,46). The somatosensory cortex of the leg is known to be highly variable between subjects and therefore affects theoretically the inter-subject variability of the tibial nerve data (13) to a large extent. This study lacks the presence of a control group, but since intra-individual characteristics are more consistent it is conceivable that despite a high inter-subject variability of the PTN data (which reduces the chance of finding significant interhemispheric differences), the results have potential clinical value.

**Clinical Relevance**
The dipole strength has been described as a valuable quantitative index of cortical response to somatosensory stimuli in patients with different neurological diseases (33,47). In our study, patients with motor deficits showed larger dipole strengths in the affected hemisphere compared with patients without motor deficits. If SEF characteristics are related to clinical motor symptoms, MEG might be used as a potential quantitative measure of lesion involvement in the motor pathways. However, in patients with intracranial lesions like in other conditions such as epilepsy, multiple sclerosis and stroke, various abnormalities of SEFs and dipole strength may exist (9,22,27,30), but the clinical relevance still has to be established.

The clinical usefulness of somatosensory evoked magnetic responses in preoperative surgical planning and intra-operative guidance using neuronavigation has been shown to
be valuable and accurate in many reports (11,12,16,21,28,35,40) with respect to activation of the median nerve or digits. We found only find three reports, describing experiences with lower limb activation in functional neuronavigation (1,28,40). Alberstone et al. found that tibial and median nerve magnetic source imaging was an important tool in the preoperative assessment of patients with intracranial lesions and adjusted their surgical strategy in case of a close relationship of the tumor with the localization of the dipole (1). Mäkelä et al. (28) found that PTN-SEFs with electrical stimulation were useful for tumors in the vicinity of the central sulcus region in 10 out of 12 patients, not only for preoperative planning, but also for intra-operative orientation and facilitate of brain mapping. Schiffbauer et al. (40) found successful localization of the somatosensory representation of the toes in 82% of patients with supratentorial intra-axial brain lesions, by using compressed air-driven diaphragm clips attached to the toes in patients. It is unclear however if the unsuccessful cases were related to tumor localization close to the CS. The presence of intracranial lesions in our patient group did not affect successful dipole localization and the results can yield important information regarding the spatial relation and displacement of the somatosensory cortex of the lower limb in relation to the lesion. Furthermore, both latter studies only used ECDs in the 30-70 ms latency range (28,40). As shown by Figure 4, it is important to identify not only the first component but also middle-latency components that may show activation in SI, otherwise incorrect localising information might give the impression that the tumor is at a safe distance from SI. The presence of dipole location asymmetries observed with different SEF latencies, could have clinical significance in the evaluation and treatment of patients harbouring intracranial lesions. Therefore, for neurosurgical applications and surgical risk assessment it is recommended not only to evaluate the early-latency component but middle-latency components with activation in SI as well.

The use of MEG for cortical localization is a matter of debate as a result of its lower spatial resolution compared to functional MR imaging (fMRI) techniques (11,24,40). However, in the presence of intracranial lesions in or adjacent to the central sulcus, the fMRI results can show significantly lower activation in the affected hemisphere, reducing its reliability (10,15,18). Additional activation in multiple nonprimary areas may confound the results of fMRI as well (24). Both techniques have their qualities and limitations and probably information from both modalities will yield the best functional information to avoid neurological deficits (18,36).

The accuracy of PTN stimulation with respect to intraoperative evoked potential recordings was shown to be reliable in earlier studies (1,28,40). Our present results can be used for further studies elucidating the somatosensory network changes in the presence of intracranial lesions in combination with clinical findings.
CONCLUSIONS

Posterior tibial nerve evoked magnetic responses in patients with unilateral supratentorial lesions around the central sulcus show significantly increased neuromagnetic responses in the affected hemisphere, especially in the presence of motor deficits. Dipole location asymmetries for homologous SEF components are frequently observed in the presence of intracranial lesions near the CS region. The results suggest spatial and functional changes in the somatosensory network as a result of intracranial lesions, with a possible relationship with clinical symptoms. Because fMRI results can be less reliable in the presence of perioral lesions, functional localization of the somatosensory cortex of the lower limb using PTN-SEFs could facilitate clinical decision making in patients with intracranial lesions.
REFERENCES


