Preoperative localization of hand motor cortex by adaptive spatial filtering of magnetoencephalography data

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Object. The goal of this study was to examine the sensitivity and specificity in preoperative localization of hand motor cortex by imaging regional event-related desynchronization (ERD) of brainwaves in the β frequency band (15–25 Hz) involved in self-paced movement.

Methods. Using magnetoencephalography (MEG), the authors measured ERD that occurred before self-paced unilateral index finger flexion in 66 patients with brain tumors, epilepsy, and arteriovenous malformations.

Results. The authors applied an adaptive spatial filtering algorithm to MEG data and found that peaks of the topographic distribution of β-band ERD sources reliably localized hand motor cortex compared with electrical cortical stimulation. They also observed high specificity in estimating contralateral hand motor cortical representations relative to somatosensory cortex. Neither presence nor location of tumor changed the qualitative or quantitative location of motor cortex relative to somatosensory cortex.

Conclusions. An imaging protocol using ERD obtained by adaptive spatial filtering of MEG data can be used for extremely reliable preoperative localization of hand motor cortex. (DOI: 10.3171/JNS/2008/109/8/0228)

KEY WORDS • adaptive spatial filtering • beamforming • brain tumor • functional mapping • magnetoencephalography • motor cortex • neurosurgical mapping

Preoperative localization of functionally eloquent brain tissue helps guide neurosurgical planning and tailors the extent of resection, allowing for improved functional outcomes. Various techniques are available to map functional cortical organization, including direct ECS, blood oxygen level–dependent fMR imaging, and ESI. Electromagnetic source imaging refers to the reconstruction of the spatiotemporal dynamics of brain sources from MEG data. When combined with MR imaging data, preoperative functional localization with ESI can be integrated with neuronavigational systems to provide intraoperative guidance to the surgical team.12,17,18,40,44,45 Electromagnetic source imaging mapping is important in preoperative planning and complements intraoperative mapping by delineating areas of function noninvasively and in advance, reducing the time needed for intraoperative mapping. Using ESI, relevant somatosensory, auditory, and occasionally motor cortices have been mapped preoperatively to aid surgical navigation. Preoperative ESI mapping of somatosensory cortex has been validated by comparing it with intraoperative mapping.10,11,14,15,26,27,37,38,44,45,55

Clinical ESI mapping procedures commonly use single or multiple ECD fitting procedures of stimulus-evoked magnetic field responses. These procedures have proven successful at mapping somatosensory and auditory cortices.2,9,10,12,15,37,38,44,45,55 Movement-related cortical electrical potentials and magnetic fields have been studied extensively, using EEG/ECoG and MEG, respectively, and both have shown robust, prominent deflection in the sensorimotor area contralateral to the limb movement.3,19–21,24,28,41–43,50–52 However, although ECD procedures have been successfully applied to movement-evoked magnetic fields, they appear to have both low specificity and sensitivity, and are thus unsuitable for clinical mapping of the location of motor cortex using ESI.3,9,19,20,23–25,54 Therefore, there is a clear need for alternate procedures to localize motor cortex.

Several studies have shown that voluntary movement results in desynchronization in the α (~ 10 Hz) and β (~ 20 Hz) frequency bands of brainwaves recorded from the
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Sensorimotor cortex by using EEG and ECoG \(^{1,6,7,29–36,49–51}\) This ERD typically starts at ~500 msec prior to movement onset over the contralateral Rolandic region and becomes bilaterally symmetrical immediately before movement execution. The β-band ERD is more discrete and topographically specific compared with α-band ERD \(^{1,6,7,29–36,49–51}\). The ERDs can be interpreted as an electrophysiological correlate of activation of cortical areas involved in the production of motor behavior. Power changes in the α and β bands during brisk finger extension and hand grasping can also be observed in MEG and can be localized to the precentral sulcus corresponding to hand motor cortex using adaptive spatial filtering methods.\(^{13,39,40,50,51}\) Localization of movement-related magnetic fields using β-band ERD has been shown to be consistent with single ECD localization of motor cortex using the motor field.\(^{50,51}\) However, few reports have examined the relative location of hand motor cortex with respect to hand somatosensory cortex and the overall sensitivity of using β-band ERD localization for preoperative localization of motor cortex.

In this paper, we further explore the localization of hand motor cortex using β-band ERD, measured with MEG subjected to adaptive spatial filtering methods. First, we examined the sensitivity of this procedure in locating hand motor cortex in a group of individuals. Second, we examined the specificity of the procedure to localize contralateral hand motor cortex. Third, we examined the location and distance of hand motor cortex relative to hand somatosensory cortex (as measured by ECD localization) along 3 orthogonal axes in hemispheres affected and unaffected by the presence of a brain tumor. Finally, we report the relative location of hand motor cortex assayed by ECS and demonstrate that localization of hand motor cortex relative to somatosensory cortex through MEG β-band ERD is consistent with these ECS data.

Methods

Patient Population

We retrospectively analyzed the MEG data in 66 patients with brain tumors or epilepsy or AVMs who underwent resection between 2003 and 2005. The patients ranged in age from 12 to 83 years (mean age 39.8 ± 14.2 years). Five patients were left-handed and 1 was ambidextrous. There were 30 females and 36 males. Clinical data are shown in Table 1. Many of the patients were referred to the Department of Neurological Surgery at the University of California, San Francisco, because the tumors were located near areas of eloquent cortex, necessitating preoperative and intraoperative mapping procedures.

Preoperative Clinical Neuroimaging

High-resolution MR images were acquired using a 1.5-T unit to provide necessary anatomical detail for surgical planning and intraoperative neuronavigation. The protocol typically included the following: a T1-weighted, 3D spoiled gradient recalled echo sequence with a 34-msec TR, 3–8-msec TE, 30° flip angle, 1.5-mm slice thickness, 256 × 256 × 128 matrix, and a 260 × 260-mm field of view with coverage that included the nasion, per-auricular points, and external fiducial markers; and a T2-weighted 3D fast spin echo sequence with a 3-second TR, 105-msec TE, 1.5-mm slice thickness, and 256 × 128 × 128 matrix. The MR images were transferred to the MEG workstations, and coregistration was performed based on anatomical and external fiducial landmarks. Errors due to coregistration were ~1–3 mm. After fusion with the ECD estimates for the location of somatosensory cortex, MR images were transferred to the neuronavigation system in the operating room.

Magnetic Source Imaging

Data Acquisition. Magnetic fields were recorded in a shielded room using a whole-head MEG system (Omega 275, VSM MedTech Ltd.) consisting of 275 axial gradiometers and 29 reference sensors used for computing synthetic third-order gradiometer measurements. The MEG signals were digitized at a sampling rate of 1200 Hz.

Tasks. Each individual lay on a comfortable bed. To elicit somatosensory cortical activation, painless tactile stimulation of the index finger was given using a compressed air-driven diaphragm clip (15–20 psi). Epochs of 500-msec duration with a 100-msec prestimulus interval were collected for 256 trials. For the motor task, individuals performed self-paced unilateral index finger flexion or abduction once every 3–4 seconds for a total of 100–250 movements. In most individuals, we recorded EMG responses from the dorsal interosseous or flexor digitorum muscles and the onset of EMG response for each trial was marked. Some individuals pressed a button by flexing their index fingers, and the button press was used to mark the onset of movement. Somatosensory and motor tasks were performed using both left and right fingers.

Data Analysis. The MEG data obtained during the somatosensory task were time-locked to the stimulus onset and averaged. The average somatosensory evoked field was bandpass filtered from 2 to 40 Hz, and the peak corresponding to the earliest response occurring ~40 msec following stimulus onset was localized by fitting an ECD corresponding to contralateral somatosensory cortex. The localization algorithm used an iterative least-squares minimization to compute the strength and location of a single dipole in a spherical volume of uniform conductivity that could account for the sensory data. Dipole fits were accepted based on a goodness-of-fit values > 0.95 and having 95% confidence volume of reconstructions < 0.1 cm³. The dipole parameters indicated the location of somatosensory cortex corresponding to the index finger.

The MEG data obtained during the motor task were bandpass filtered in the (15–30 Hz) β-band. Sensor data covariance was computed in a window beginning ~600 msec before the onset of movement, designated as the active period. Sensor data covariance was also computed for a 600-msec baseline control period 1–2 seconds after movement onset. Details of the adaptive spatial filtering algorithm used to analyze the β-band ERD are described elsewhere.\(^{39,46,47}\) In brief, an estimate of the source power at each voxel in the brain based on the MEG data are computed for the active and control time periods using a forward-field computed assuming a multiple local-sphere...
TABLE 1

Distribution of histological diagnoses in patients who underwent MEG* 

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>astrocytoma (Grade 2 or 3)</td>
<td>22</td>
</tr>
<tr>
<td>oligoastrocytoma (Grade 2 or 3)</td>
<td>9</td>
</tr>
<tr>
<td>oligodendroglioma (WHO Grade II or III)</td>
<td>13</td>
</tr>
<tr>
<td>glioblastoma multiforme</td>
<td>9</td>
</tr>
<tr>
<td>AVM</td>
<td>5</td>
</tr>
<tr>
<td>meningioma</td>
<td>1</td>
</tr>
<tr>
<td>ganglioglioma</td>
<td>2</td>
</tr>
<tr>
<td>epilepsy surgery</td>
<td>2</td>
</tr>
<tr>
<td>pathology report unavailable</td>
<td>3</td>
</tr>
<tr>
<td>total</td>
<td>66</td>
</tr>
</tbody>
</table>

* WHO = World Health Organization.

Intraoperative Motor Cortex Stimulation

We report the ECS mapping results from a group of 4 individuals in whom the hand motor cortex was localized. Clinical data on these individuals are reported in Table 2. Only somatosensory evoked magnetic field data were obtained in these patients. These patients underwent craniotomies while awake. Neuronavigation was performed using a Stealth Neuronavigation workstation (Sofamor Danek) that was used to plan a well-centered craniotomy and to expose functional cortical areas as much as needed to achieve a radical but function-preserving resection. For ECS mapping, an Ojemann cortical stimulator with a handheld bipolar electrode that had a 5-mm spacing between the tips was used. The stimulation protocol was a 1-second duration long train of square-wave, biphasic pulses of 1-msec duration at a frequency of 60 Hz. The stimulus currents that produced a motor response usually ranged from 2 to 16 mA. The current was increased by 1–2 mA until an observable response was obtained. Extreme care was taken to minimize the effects of after-discharges. Sites at which a positive response could be elicited were recorded using the neuronavigational system, and the coordinates were saved in axial, coronal, and probe-trajectory orientations. Hand activation was elicited in 5 sites in these 4 patients. The location of hand motor cortex (via ECS) relative to hand motor cortex obtained preoperatively was analyzed for these 5 sites.

Spherical volume conductor model making use of the sensor data covariance. Source power estimates are obtained at a 5-mm resolution across the entire brain for the active and control periods, and a pseudo-F ratio is calculated. Negative values of the pseudo-F ratio indicate desynchronization and positive values indicate synchronization. This process of adaptive spatial filtering was done using a commercially available synthetic aperture magnetometry software package (VSM MedTech Ltd.) and integrated with custom-built in-house software package (NUT-MEG). Locations of peaks of the ERD images were used to indicate the location of hand motor cortex. For each individual, the ERD/event-related synchronization images as well as the somatosensory ECD locations were overlaid on the presurgical high-resolution MR images as described above. Statistical analysis of distance between ERD image peaks and somatosensory ECD peaks was performed using t-tests. A 1-way analysis of variance was also performed between distance with affected and unaffected sides as one factor and the axis as another factor.

Results

The average power spectrum computed for active (a 600-msec window prior to movement onset) and baseline (a 600-msec window during no finger movement or preparation) periods for right and left index finger (digit 2) flexions are shown for each of MEG sensor in the array in Fig. 1A and B, respectively. The observed decrease in power during the active period (black curves) in the β-band is referred to as ERD. Figure 2 shows the location of this movement-related β-band ERD obtained from adaptive spatial filtering of MEG data in 1 individual with a right inferior frontal glioma. Full-width/half-maximum localizations for left-hand and right-hand movement are shown overlaid on a 3D rendering of the individual’s own cortical surface extracted from 3D MR imaging. Contralaterally dominant, albeit bilateral, activation of motor cortices can be observed. Figure 3 shows similar activation in a different patient with a brain tumor where we also plotted the location of the peak of activation and the location of equivalent current dipoles corresponding to somatosensory cortex. In this individual we overlay activations on serial axial images to highlight the lack of normal anatomical landmarks and the importance of providing individual functional information overlaid on images for patients’ brain tumors. The location peaks were found to be insensitive to whether the temporal window was 400 or 600 msec preceding movement onset, measured either by thresholding the EMG responses or a button press. Results were also highly reproducible to within

TABLE 2

Clinical data obtained in patients who underwent MEG and ECS hand motor cortex mapping

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Handedness</th>
<th>Diagnosis*</th>
<th>Tumor Location</th>
<th>Intraop Activation/Site</th>
<th>Distance to Preop Motor Peak (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>57, F</td>
<td>rt</td>
<td>oligodendroglioma</td>
<td>lt frontal</td>
<td>finger motor</td>
<td>0.4</td>
</tr>
<tr>
<td>2</td>
<td>63, M</td>
<td>rt</td>
<td>oligoastrocytoma</td>
<td>lt frontal</td>
<td>forearm motor</td>
<td>1.6</td>
</tr>
<tr>
<td>3</td>
<td>32, M</td>
<td>rt</td>
<td>infiltrating astrocytoma</td>
<td>rt frontal</td>
<td>forearm motor &amp; hand motor</td>
<td>1.6 &amp; 0.7</td>
</tr>
<tr>
<td>4</td>
<td>15, F</td>
<td>rt</td>
<td>oligoastrocytoma</td>
<td>rt frontotemporal</td>
<td>lt hand motor</td>
<td>1.1</td>
</tr>
</tbody>
</table>

* All tumors were Grade II according to the WHO grading system.
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Fig. 1. Power spectra of MEG sensors during premovement active (black curves) and no-movement baseline (red curves) periods.  A: Power spectra for a 600-msec active window (black) preceding right index finger (RD2) flexion compared with the power spectra for a 600-msec baseline window (red).  B: Power spectra for a 600-msec active window (black curves) preceding left index finger (LD2) flexion compared with the power spectra for a 600-msec baseline window (red curves).

Fig. 2. Images obtained from adaptive spacial filtering of MEG data.  A: Localization of β-band desynchronization preceding movement onset in an individual performing left index finger flexion. Full width at half-maximum of the adaptive spatial filter output is overlaid on a 3D rendering of the individual’s cortical surface extracted from the structural MR imaging.  B: Localization of β-band desynchronization due to the right index finger flexion in the same individual, showing contralateral hand motor cortical activation.
a few mm, assayed by splitting the data sets into 2 halves and comparing the localization results.

Such localization of movement-related β-band ERD was performed in both hemispheres in all individuals included in this study; their clinical characteristics are listed in Table 1. For right-hand movements, successful activation maps in the perirolandic region were observed in 65 of 66 individuals, yielding a sensitivity rate of 98.5%.

The procedure was unsuccessful in yielding activation in only 1 individual due to severe dental artifacts. Activation was restricted to contralateral (left hemisphere) cortex in 52 of 66 individuals. Only 2 individuals had activation restricted to the ipsilateral hemisphere and the remaining 11 individuals had bilateral hemispheric activation. For left-hand movements, successful activation maps were obtained in 62 of 63 individuals, yielding a sensitivity rate.
of 98.4%. Again, the failure in 1 individual was due to severe dental artifacts. Activation was restricted to contralateral (right hemisphere) cortex in 42 of 63 individuals. Again, only 2 individuals had activation restricted to ipsilateral cortex alone, and the remaining 18 of 63 individuals had bilateral hemispheric activation. These findings are summarized in Table 3 and Fig. 4. If we define specificity as the ability to yield activation that corresponds to contralateral motor cortex, we obtain specificity rates of 94% in the left hemisphere and 95% in the right hemisphere. Therefore, the overall sensitivity and specificity of localization of hand motor cortex from movement-related β-band ERD observed in MEG is extremely high. These results contrast sharply with our recent publication showing overall low specificity and sensitivity of equivalent current dipole localization procedures for mapping the hand motor cortex.25

We also examined the spatial location of the hand motor cortex relative to somatosensory cortex by comparing the coordinates of the peaks of contralateral hand motor cortex obtained from the spatial filtered ERD images with the location of somatosensory evoked field dipoles. Figure 5 shows the location of hand motor cortex relative to hand somatosensory cortex (both corresponding to the second digit) for both the hemisphere affected by the presence of the tumor or AVM and the hemisphere unaffected by the presence of a brain tumor or AVM. Locations are plotted in the 2 orthogonal planes defined by the mediolateral, AP, and inferosuperior axes. Data from the left and right hemisphere are shown separately as unfilled circles and filled squares, respectively. Data across all individuals in the study indicate clearly that hand motor cortex is medial and superior to hand somatosensory cortex. In contrast, it can be seen that hand motor cortex is located medially and superior to somatosensory cortex. In contrast, it can be seen that hand motor cortex does not have a consistent AP location relative to somatosensory cortex. Although these procedures have been successfully used to localize hand motor cortex, the sensitivity and specificity of this procedure is insufficient for consistent clinical utility.10–23,25 Problems of nonlinear optimization with respect to somatosensory cortex. The average distances between β-band ERD peaks and somatosensory evoked field dipole locations among individuals were computed along the AP, mediolateral, and inferosuperior axes and compared between unaffected and affected hemispheres. These data are shown in Fig. 6. Significant differences (p < 0.01) from 0 were only found for measurements in the medial and superior directions for both β-band ERD peak sites.

Two examples of the location of hand motor cortex assayed by ECS relative to preoperative hand motor cortex assayed by MEG β-band ERD are shown in Fig. 7. An analysis of all the hand motor ECS sites showed that the distance from the preoperative localizations were within 1.6 cm, with the farthest distances corresponding to forearm ECS sites. Taking into account the distance between forearm and finger representations, the full width at half-maximum of the motor cortical reconstructions, and the current spread due to the ECS, these results provide significant validation of our preoperative localization method. Consistent with the β-band ERD imaging data, the ECS data also indicate that the relative location of hand motor cortex is medial and superior to hand somatosensory cortex, and that the AP location is variable.

### Discussion

We report that preoperative MEG β-band ERD—obtained using adaptive spatial filtering methods—provides a consistent, sensitive, and specific index of activation of hand motor cortex in both hemispheres in a heterogeneous group of patients who had undergone resection of a brain lesion. The location of hand motor cortex as mapped using β-band ERD relative to somatosensory cortex as mapped using MEG ECDs is consistent with the location of hand motor cortex determined by intraoperative ECS.

Early MEG studies of movement used ECD modeling procedures on movement-averaged magnetic fields.3–5,18,20,23,34 Although these procedures have been successfully used to localize hand motor cortex, the sensitivity and specificity of this procedure is insufficient for consistent clinical utility.10–23,25 Problems of nonlinear optimization

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**TABLE 3**

*Sensitivity and specificity analyses*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Rt Hand Motor (no. of cases)</th>
<th>Lt Hand Motor (no. of cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>attempted</td>
<td>66</td>
<td>63</td>
</tr>
<tr>
<td>unsuccessful</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>contralat activation alone</td>
<td>52</td>
<td>42</td>
</tr>
<tr>
<td>ipsilat activation alone</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>bilat w/ ipsilat dominant</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td>bilat w/ contralat dominant</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>sensitivity</td>
<td>65/66 (98.5%)</td>
<td>62/63 (98.4%)</td>
</tr>
<tr>
<td>specificity</td>
<td>62/66 (93.9%)</td>
<td>60/63 (95.2%)</td>
</tr>
</tbody>
</table>

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**Fig. 4.** Bar graphs showing the sensitivity and specificity of hand motor cortical localization obtained by adaptive spatial filtering of movement-related β-band desynchronization.
and uncertainty about the number of dipoles are common and well-known problems in ECD fitting procedures. Tomographic methods, such as spatial filtering, are alternatives to ECD procedures. Among adaptive spatial filtering methods, beamforming has the highest spatial resolution with no localization bias. As indicated in Results, this approach clearly improves the sensitivity and specificity in localization of motor cortex from movement-related magnetic field data.

Indices of cortical activation during voluntary movement have been extensively studied using EEG, MEG, and ECoG. These procedures rely on the detection of regional changes in frequency spectra of cortical activity. Cortical basic rhythms are believed to be generated by thalamocortical inputs, and the inhibitory effects of the basal ganglia on the thalamus are considered essential for α and β rhythm modulation, including the β-band ERD that we observed here by using MEG. However, the exact physiological significance of ERD is still unclear and needs further investigation.

In a previously published report, β-band ERD in MEG was reported to be absent in patients in the cortices ipsilateral to a brain tumor, presumably due to the presence of edema or tumor. In that study, patients were found to have β-band activity localized only to the contralateral hemisphere and shifted in the affected side. We found this not to be the case in we were able to localize β-band ERD even in the affected side of patients with tumor and AVM. These differences may be related to the task paradigm, the number of trials used for analysis, and the grade and extent of the tumor.

Previous studies have also suggested a hemispheric asymmetry in hand movement–related activation.
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Our data do not support a strong hemispheric asymmetry that is related to handedness. We observe predominant contralateral activation for movement in both hands. The only manifestation of hemispheric asymmetry was a higher incidence of bilateral activation during left-hand movement in right-handed individuals. Although this bilateral activation was not consistent, the incidence rate of bilateral activation with ipsilateral dominance was 12% for the right hand and 16% for the left hand.

The distances between hand motor cortex, localized by ECS and adaptive spatial filtering of β-band ERD, and hand somatosensory cortex, localized by MEG ECD, are comparable to those reported in other studies. In contrast to the previous studies, in the present paper we examine the consistency in the direction of motor cortex from somatosensory cortex in each individual. This directional vector will allow clinical sites that do not routinely conduct MEG motor studies to infer the location of hand motor cortex relative to the location of hand somatosensory cortex.

The preoperative procedure for localization of hand motor cortex reported here is enabled by the superior temporal resolution of MEG that allows us to examine a brief time period preceding movement onset. Such a dynamic localization of motor cortex is not possible with any other currently available noninvasive functional imaging modality such as fMR imaging. Here, we show that the motor cortical localization is distinctly different from that of somatosensory cortex. Such a distinction is not possible with fMR imaging because of its poor temporal resolution, as a consequence of which fMR imaging activation maps during motor tasks also include activation of somatosensory cortex. Furthermore, in a patient with a brain tumor, often the vasculature of the brain regions in and around a tumor are altered, resulting in vascular confounds contributing to the fMR imaging signals and the corresponding activation maps.

Conclusions

Adaptive spatial filtering methods provide adequate spatial resolution for reconstruction of such movement-related spectral power changes. Taken together, the procedures outlined in this paper demonstrate the increasing capability of preoperative spatiotemporal functional brain mapping using MEG that can be used for clinical applications in neurosurgery.

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