Integrating sensory and motor mapping in a comprehensive MEG protocol: Clinical validity and replicability

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Considerable evidence supports the idea of magnetoencephalography (MEG) being a valuable noninvasive tool for presurgical mapping of sensory and motor functions. In this study, we test the validity and replicability of a new experimental paradigm for simultaneous sensory and motor mapping using MEG recordings. This comprehensive sensorimotor protocol (CSSMP), where external mechanic stimulation serves as a cue for voluntary movements, allows the recording of sensory and motor cortical responses during a single activation task. The stability and replicability of MEG-derived recordings during this paradigm were tested in a group of eight neurologically normal volunteers and six patients with perirolandic lesions. We found that a common sensorimotor cortical network, engaging sensory (S1, S2) and motor (M1) areas, was reliably activated in all subjects and patients and that the results remained exceptionally stable over time. Additionally, the clinical validity of the MEG-derived maps of activation was tested through intraoperative electrocortical stimulation mapping in the group of patients. The MEG-derived anatomical maps for specific sensory (S1) and motor (M1) responses were verified, by direct cortical mapping, and confirmed with the patient’s surgical outcome. The results of this validation study show that the so-called CSSMP is a reliable and reproducible method for assessing simultaneously sensory and motor areas. This method minimizes methodological problems and improves our knowledge of the spatiotemporal organization of the sensorimotor cortical network and helps to optimize the surgical management of patients with perirolandic lesions.

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Introduction

Space-occupying lesions (tumors, vascular malformations) in the vicinity of the central sulcus are often associated with the appearance of sensory and/or motor deficits. The surgical management of these perirolandic lesions requires a detailed mapping of cortical regions involved in sensory and motor functions to avoid further deterioration of function.

Traditionally, neurosurgeons gain access to this information at the time of surgery through corticography and/or electrocortical stimulation (Pendfield and Rasmussen, 1957). Although these methods are the “gold standards” for sensorimotor mapping, they are not helpful for presurgical planning. This goal can only be achieved through noninvasive functional brain imaging techniques, namely positron emission tomography (PET; Meyer et al., 2003), functional magnetic resonance imaging (MRI; Kober et al., 2001), and magnetoencephalography (MEG; Ganslandt et al., 1997, 1999). To be clinically useful, noninvasive mapping methods must meet the following criteria: (1) high yield and applicability to a wide range of patients, including children, (2) relatively simple procedures for reconstruction of activation images, ensuring rapid turnaround of results, (3) near-perfect test–retest reliability, and (4) high degree of localization accuracy. The latter is defined as (a) close agreement with the results of invasive mapping procedures (concurrent validity), and (b) strong correlation with functional postsurgical outcome (predictive validity). In principle, MEG, otherwise known as magnetic source imaging (MSI), has the potential to meet all the aforementioned criteria because it relies on magnetic fields produced by intracellular neuronal currents (Okada et al., 1997), rather than measuring the secondary effects of neuronal activity on regional blood flow and metabolism. MEG procedures are characterized by a high degree of pragmatic utility, as demonstrated by their clinical applicability for both receptive and expressive language mapping (Castillo et al., 2001; Papanicolaou et al., 1999; Simos et al., 1998). Moreover, MEG-derived maps associated with performance of linguistic tasks have been shown to be reliable and highly concordant with the results of invasive procedures (Breier et al., 1999, 2001; Maestu et al., 2002; Simos et al., 1999; Szymanski et al., 2001).

Event-related magnetic field responses (ERFs) elicited by somatic stimuli consist of two or three successive components. While the initial component is more commonly observed follow-
ing electrical stimulation of peripheral nerves, the second, middle latency component can be reliably elicited by mechanical stimulation of fingers and/or toes. The middle latency component peaks at 40–70 or 50–80 ms after stimulation of the upper or lower limb, respectively. Both components are reliably localized in the contralateral SI area (Hochstetser et al., 2001; Wilkstrom et al., 1996), although sources in the ipsilateral somatosensory cortex may be found in some cases for the middle latency component (Hari et al., 1984). For all practical purposes, the sources of the two components overlap to a great extent in contralateral primary sensory cortex (Gallen et al., 1993; Ganslandt et al., 1999) and are used clinically as indices of the location of the primary somatosensory area (SI). Finally, the late ERF response that peaks after 90 ms poststimulus onset is thought to originate in the secondary somatosensory area (SII) and may reflect processes related to sensorimotor integration (Huutunen et al., 1996). Two main types of movement-related potentials and fields have been described: slow cortical responses associated with the preparation of voluntary movements (readiness potential; Deecke et al., 1969, 1987; Kristeva et al., 1979), and faster cortical responses time-locked to muscle excitation per se (Ikeda et al., 1992). It is the latter responses that have been studied as indices of the location of primary motor cortices in patients with perirolandic brain tumors (Ganslandt et al., 1999).

To date, studies on the clinical utility of MEG for sensorimotor mapping used different activation protocols to estimate the location of somatosensory cortex (e.g., Ganslandt et al., 1997, 1999; Ossenblok et al., 2003; Schiffbauer et al., 2002; Watanabe et al., 1993) and motor cortex independently (Kassubeck et al., 1996). However, invasive studies in humans (e.g., Fielden and Rasmussen, 1957) and histological studies in humans and other primates (DeFelipe et al., 1986) have long demonstrated the close anatomical proximity and dense functional connectivity between primary sensory and motor cortex that are located on the caudal and rostral banks of the central sulcus, respectively. In addition to this conceptual issue, there may be practical problems encountered when using independent sensory and motor-mapping protocols, mainly related to test duration and localization accuracy. The latter may become an issue because when sensory and motor responses are obtained in separate recording sessions, the intrinsic spatial error introduced by the head localization and subsequent MEG-MRI overlay procedure (on the order of millimeters) is maximized. Taking into consideration that sensory and motor cortices are anatomically adjacent, the generators of the electromagnetic responses are typically very close (anterior and posterior bank of the central sulcus). This spatial proximity introduces a methodological problem that could be by-passed using a single activation task to evoke simultaneously sensory and motor responses. MEG, by affording direct, real-time estimates of neurophysiological activity, is well suited to the task of capturing sequential patterns of excitation within distinct neuronal populations in sensory and motor cortices.

The present study was conducted to test the validity of a novel activation protocol (henceforth called the comprehensive sensorimotor-motor protocol, or CSSMP) that affords concurrent mapping of sensory and motor cortex using magnetoencephalographic recordings. Three specific questions were addressed that are directly related to the potential clinical utility of this protocol for sensory and motor presurgical mapping in patients. First, is this protocol capable of eliciting (in a single activation task) clear sensory and motor event-related fields in healthy individuals and in patients with perirolandic lesions? Second, are the results replicable over time? Third, do estimates of the location of sensorimotor cortices agree with those obtained intraoperatively?

MEG recordings were obtained in two experimental groups while they perform the CSSMP. The first experimental group involved eight healthy volunteers. The CSSMP was conducted for the purpose of developing the basic MEG sensorimotor mapping procedure and for assessing the test–retest reliability and across-subject consistency of the derived waveforms and activation maps. A second group of six patients with perirolandic lesions was tested to assess the clinical yield and validity of the CSSMP by comparing the derived sensorimotor activation maps with the results of intraoperative mapping and surgical outcome.

Materials and method

Subjects

We investigated two experimental groups. Group A of eight right-handed healthy volunteers (five males, three females) between 24 and 52 years of age (mean = 33.4 years) and group B of six right-handed patients (all of them male) between 14 and 43 years of age (mean = 21.2 years) with perirolandic brain lesions. All patients were surgical candidates suffering from seizures and presented with mild to moderate motor and/or sensory symptoms during the epileptic episodes. Their current sensory and motor neurological examination was normal. Sensation to light touch, pinprick, and joint position were intact in all limbs. Graphesthesia was intact in both hands for all of them. Before the study, all participants gave their written informed consent after the purpose of the study and the nature of the procedures involved had been explained to them.

Stimuli and task

During the MEG sessions, pneumatically driven mechanical taps (25 lb/in.²) were applied to the distal fingertips of the subject’s index finger via a balloon diaphragm (1 cm in diameter). Stimulus duration was 40 ms, interstimulus interval was randomly varied from 1.9 to 2.5 s, and stimuli were repeated 250 times for each condition. An active condition (stimulation with motor response) and a passive condition (stimulation without response) were administered to all the participants (always in this order). During the active condition, subjects were instructed to respond with a full hand extension, followed by a passive return to the original resting position, immediately after they felt a brief pressure pulse delivered by a pneumatic drum placed on the right index finger. They were told that rather than a fast reaction time, the goal of their performance should be to execute a rhythmic and uniform movement after each tactile cue. They were instructed to remain still, keeping their eyes open during the scan and trying to avoid blinking. A short practice run was performed before the MEG data acquisition to ensure optimal performance (i.e., adequate and consistent response timing), minimize biogenic artifacts, and optimize the quality of electromyographic recordings used to estimate muscle excitation latency (see below). During the passive condition, participants were told to relax their hands and monitor the presentation of the stimuli avoiding any movement. The passive condition only served as a baseline for characterizing the morphology and underlying source distribution of somatosen-
sory ERFs under identical stimulation conditions as in the active condition but without the requirement of a motor response.

**MEG recordings and analysis**

All MEG recordings were done using a whole-head neuromagnetometer containing an array of 148 magnetometer sensors (WH 2500, 4D Neuroimaging, San Diego, CA) housed in a sound-damped and magnetically shielded room. During MEG recordings, subjects were asked to stay motionless and avoid blinking or eye movements by keeping their eyes on a fixation spot placed on the ceiling. Their right hand was placed on a rolled towel at the wrist to facilitate hand movement and minimize unnecessary muscle tension. Simultaneously recorded electromyographic responses (EMG) were obtained from the right hand through an electrode placed over the motor point of the extensor digitorum muscle for the middle finger referenced to an inactive electrode placed on the dorsum of the forefoot. For further details about the EMG recordings, see Goodin and Aminoff (1992). A total of 250 ERF epochs (1400-ms duration, 150-ms prestimulus baseline) were acquired for each condition with a bandpass set between 2.0 and 40 Hz and a sampling rate of 508 Hz. Following visual inspection of individual ERF epochs, 160 and 220 MEG segments were averaged together for each condition after excluding those containing eye movements (identified by their distinct waveform morphology and surface magnetic flux distribution) or other myogenic or mechanical artifact. MEG segments associated with extreme EMG responses were also excluded (the range of acceptable peak EMG latencies was 200–500 ms after stimulus onset).

Mathematical models for the head as volume conductor and for the neural generators are employed by linear and nonlinear minimization algorithms to localize EEG and MEG signals. To solve the inverse problem, parametric methods typically assume that the sources can be represented by a few equivalent current dipoles of unknown location and moment to be estimated with a nonlinear numerical method. In this study, the intracranial generators of the observed ERFs were modeled as moving equivalent current dipoles (ECDs), at successive 2-ms intervals, by using the nonlinear Levenberg–Marquardt algorithm applied to a spherical head model determined by the local skull curvature (Levenberg, 1944; Marquardt, 1963). This method searched for the ECD that was most likely to have produced the observed magnetic field distribution given at a certain point in time (according to the Biot-Savart law). Only activity sources accounting for >92% of the field variance and with confidence volumes lower than 10 cm³ were accepted. The dipole fitting algorithm was applied to the magnetic flux measurements obtained from a group of 34–38 sensors, always including both magnetic flux extrema. ECD location was computed in reference to a Cartesian coordinate system defined by a set of three anatomical landmarks (fiducial points): the right and left external meatus and the nasion. Those fiducial points were used for the co-registration of the MRI scans and the MEG recordings. Sources (at the peak of successive ERF peaks) were superimposed on T1-weighted MRIs that were available for each subject or patient.

Two ECD parameters were extracted and analyzed for the active condition: (1) latency or delay between the onset of the mechanical stimulation and the peak of each component, and (2) amplitude or global field power of each magnetic response, expressed as the root mean square (RMS) of magnetic flux integrated across all sensors capturing the magnetic field extrema at the peak of each component.

**Intraoperative verification of MEG-derived maps**

Four patients underwent intraoperative sensory and motor mapping. Both procedures were guided using the MEG-derived maps. MEG-derived functional maps (DICOM format images) were transferred to the surgical navigation workstation (Medtronic USA) and were available as directional landmarks for intraoperative sensory and motor mapping, which was then less time-consuming. Somatosensory evoked potentials were evoked through electrical stimulation of the right median nerve at the wrist and recorded from a six-contact subdural strip electrode placed on the surface of the brain (Luders et al., 1986). For motor mapping, high-frequency electrical stimulation (50-Hz square pulse of 0.3 ms duration with alternative polarity delivered for 2–5 s) was applied to the precentral gyrus to elicit muscle contraction of contralateral extremities. Stimulus intensity was increased gradually until the maximum intensity of 15 mA was reached, positive responses were elicited, or after-discharges were noted (Luders et al., 1987). All the operations and stimulation, procedures were video recorded. The site of effective electrical stimulation was noted by the surgeon on the appropriate MR image with the aid of the Zeiss frameless stereotactic SMN system and digital images of the exposed cortex were taken. The images containing the MEG-derived maps and the marked site(s) of successful electrical stimulation (or somatosensory mapping) were then compared and the distances between both measurements was estimated, where discrepancies lower than 6 mm were considered a match.

**Results**

**Profile of sensorimotor ERFs**

Morphological differences between the averaged waveforms recorded for the passive and active conditions were evident to visual inspection in all participants (see Fig. 1). In the active condition, a sequence of five components (S1, S2a, S2b, M1, S2c) were clearly identified in all 14 participants (subjects and patients). As expected, ERFs for the passive condition contained all three initial somatosensory components (S1, S2a, S2b) but no motor components (Fig 1). No significant differences were found between conditions on latency or amplitude of each component neither between patients and normal subjects.

The earliest peak was observed in both conditions, exclusively in the contralateral hemisphere, at latencies between 36 and 48 ms (mean = 41.8 ± 4.3 ms) following stimulus onset. This response has been well described previously and probably reflects neural activity in Brodmann’s areas 3b and 1 (Hari et al., 1993). In agreement with these reports, dipolar activity sources computed at the peak of this component were reliably localized along the posterior bank of the central sulcus in all participants. Following SI activation, a second, larger component, peaking between 75 and 101 ms (mean = 80.8 ± 4.2 ms), was noted bilaterally and was localized in parietal opercular cortices (with exception of one of the patients where this response was uniquely contralateral). This component (S2a), which presumably reflected neurophysiological activity in secondary somatosensory cortices (SII), peaked earlier in the contralateral than in the ipsilateral hemisphere (mean
hemisphere difference = 12 ± 4.1). This latency lag has been reported previously and probably reflects interhemispheric signal transmission via the corpus callosum (Hari et al., 1990; Hoechstetter et al., 2000, 2001). A third component (S2b) was also noted in all the subjects with a bilateral (seven cases) or unilateral distribution (five contralateral and two ipsilateral). The mean latency of this component was 137.7 ± 17.0 ms for the contralateral peak and 142.7 ± 17.1 ms for the ipsilateral peak. Dipolar sources accounting for the peak of the S2b component were localized in close proximity to the sources of the earlier S2a response. In the active condition, exclusively, additional components were noted that preceded the hand movement. The earliest of these components was observed bilaterally in 10 out of 14 participants at a mean latency of 214.8 ± 43.5 ms (see Figs. 1 and 3), and was localized in premotor cortices (Brodmann’s area 6).

Immediately preceding the onset of the EMG response in the contralateral hand, activity was first noted in the precentral gyrus in the form of the primary motor component (M1) in all participants. Although, the M1 component peak and the onset of the EMG response occurred, on average, simultaneously (254.2 ± 33.9 vs. 255.9 ± 37.4 ms, respectively), motor cortex activity consistently preceded EMG onset. The earliest latency at which activity sources were found in the precentral gyrus preceded the onset of the EMG response, on average, by 23 ± 7.3 ms. Following hand movement (mean latency = 375.8 ± 52.7 ms), a weaker and slower component is clearly identified in all 14 participants. This component was localized in parietal opercular regions in the vicinity of SII and probably reflects neurophysiological activity associated with processing of proprioceptive input.

Fig. 1. Examples of averaged ERF waveforms for a representative healthy volunteer (S #2). The ERF for the active condition (upper panel) shows a sequence of three somatosensory evoked components (S1, S2a, S2b) and two motor responses (PrM and M1) preceding and accompanying, respectively, the onset of the electromyographic response (EMG). After hand movement, a late component is evident in the active condition arising from SII (S2c). The ERF for the passive condition (lower panel) consists only of primary and secondary somatosensory event-related fields (S1, S2a, S2b).
Peak latency and amplitude data for each component during the active condition are summarized in Table 1.

Individual variability in EMG onset latency was strongly associated with MEG-derived measures of activity in primary somatosensory cortex.

Fig. 3. Averaged waveform, isofield magnetic maps (corresponding to S1 and M1 responses), and co-registration of S1 and M1 estimated sources onto patient's MRI (patient S). The co-registration of the MEG-derived maps and the MRI shows the proximity of the estimated sensory (S1) and motor (M1) sources to a 3-cm septated cyst in the left parietal lobe involving the gray matter and underlying gray matter. The patient suffered from infrequent episodes of mental clouding and right arm numbness.

Fig. 4. (Upper panel) Averaged waveforms obtained on three separate occasions (A, B, C) for one participant (S #1) in the active condition. The hand movement latency is marked on the x-axis for each replication (a, b, and c). (Lower panel) Source locations of the S1, S2, and M1 responses superimposed on the participant’s MRI. The source of the earliest response contralateral to the stimulated hand (S1) was localized in primary somatosensory cortex in the posterior wall of the central sulcus. Subsequently, a bilateral component (S2) was localized the inferior secondary parietal–ventral cortex. Right hand movement is accompanied with a contralateral cortical response (M1) localized in the primary motor cortex.

Fig. 5. (Upper panel) Intraoperative confirmation of MEG-derived sensorimotor maps in one patient. (A) Axial view of the left posterior quadrant of the patient’s MRI showing the spatial relation of the lesion (cavernous angioma) and the localization of the sensory (dark circle) and motor activity sources (dark square) estimated at the peak of the S1 and M1 responses. (B) Placement of an electrode strip on the exposed cortical surface. (C) Schematic diagram showing the spatial relation among the lesion (Les.), the estimated S1 and M1 activity sources, and the primary sensory (S) and motor (M) cortical regions identified by SSEPs and electrocortical stimulation, respectively. (D) Intraoperative photograph showing the resected area.
motor (both peak latency and amplitude of the M1 component),
premotor (peak amplitude of the PrM component), and secondary
somatosensory cortices (peak latency of the S2a component).
Table 2 lists partial correlation coefficients computed between
each of the MEG-derived measures and EMG onset latency.
Faster EMG responses are associated with rapid activation of
secondary association and primary motor cortices, increased
magnetic flux produced by activity in premotor cortices, and
decreased magnetic flux in primary motor cortex. Combined,
these indices of neurophysiological activation that precedes
movement can account for 81% of the variability in the onset
timing of this movement \( \text{Adj. } R^2 = 0.81, F(4,15) = 16.50, P < 0.0001 \). The predictive value of these indices is demonstrated
graphically in Fig. 2.

No apparent differences were found in the morphology,
distribution, latency, or amplitude of the S1, S2a, S2b, M1,
and S2c responses between the group of healthy volunteers and
the group of patients (as indicated by the lack of significant
group effects in separate ANOVAs computed on the peak latency
and amplitude of each component). Only one patient (Fig. 3)
showed a lack of ipsilateral activation for two components (S2a
and S2b). This pattern may be due to a disruption of trans-
callosal connections, although its clinical significance remains
unclear.

### Table 2

<table>
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<tr>
<th>Subject</th>
<th>S1</th>
<th>S2a</th>
<th>S2b</th>
<th>PrM</th>
<th>M1</th>
<th>S2c</th>
<th>Muscle response</th>
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<tr>
<td>S2</td>
<td></td>
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<td>S3</td>
<td></td>
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<td>S5</td>
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<tr>
<td>S6</td>
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<td>–</td>
<td>198(59)</td>
<td>229(49)</td>
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</table>

S1: primary sensory; S2a and S2b: secondary sensory; PrM and M1: premotor and primary motor, respectively; S2c: late secondary proprioceptive response. Specific hemispheric responses ipsilateral (i) and contralateral (c) to the stimulated hand are summarized for S2a and S2b. *Values for bilateral responses (b) as PrM and S2c are reflected as the mean value of both hemispheric responses.

### Table 2

<table>
<thead>
<tr>
<th>Component</th>
<th>Standardized ß</th>
<th>t</th>
<th>P</th>
<th>R</th>
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<td>2.747</td>
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<td>M1 Latency</td>
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<td>M1 RMS</td>
<td>-0.279</td>
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Standardized regression coefficients, their corresponding \( t \) tests, and partial correlation coefficients computed among MEG-derived measures of motor, premotor, and sensory cortex activation and EMG onset latency.

**Replicability**

The procedure was repeated in a randomly selected subject three times (on different days) to test the reproducibility of the ERF waveforms and the resulting activation maps. The upper panel of Fig. 4 shows the close similarity of waveforms obtained across the three sessions (A, B, C). The lower panel of Fig. 3 shows the close proximity of dipolar sources computed at the peak of each component. Maximum ECD displacement across sessions ranged from 3–8 mm (M1) to 4–7 mm (S1).
**Table 3 Clinical and outcome data**

<table>
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<th>#ID</th>
<th>Age/gender</th>
<th>Lesion</th>
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<th>Somatosensory disturbances</th>
<th>ECS</th>
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<td>Yes</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>20/m</td>
<td>left frontal oligodendroglioma</td>
<td>SPS</td>
<td>weakness, right side</td>
<td>Yes</td>
<td>++</td>
</tr>
<tr>
<td>5</td>
<td>21/m</td>
<td>left parietal cyst</td>
<td>CPS</td>
<td>hemianesthesia, right arm</td>
<td>Yes</td>
<td>++</td>
</tr>
<tr>
<td>6</td>
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<td>left frontal cavernous hemangioma</td>
<td>SPS</td>
<td>weakness, right arm</td>
<td>No</td>
<td>++</td>
</tr>
</tbody>
</table>


*These somatosensory disturbances were part of the ictal semiology.

**External verification using intraoperative stimulation**

MEG recordings were performed in six patients (Table 3) with space-occupying lesions surrounding the central sulcus using the CSSMP before the surgery. Clinical and outcome data are shown in Table 3.

MEG-derived maps of activation were used as functional intraoperative guide and as a directional landmark for intraoperative sensory and motor mapping in four cases (Fig. 5).

In all four cases, MEG-derived localizations of primary sensory and motor cortex were verified using invasive recordings during the surgery. The overall outcome of the six patients was as follows. Seizure control was achieved in four out of six cases, with frequency of seizures reduction in the other two cases (patients 3 and 4). One patient (patient 1) showed a transient worsening of somatosensory functions in the right hand and leg after surgery. The patient progressed to a complete recovery of the functions at a presurgical level in 3 months and his leg tremor previously present disappeared.

**Discussion**

The observations of Penfield and Rasmussen who stimulated pre- and postcentral regions during the course of brain surgery have favored the notion that neurophysiological processes that take place in sensory and motor cortices are closely linked to each other (for a historical review of this issue, see Bolind et al., 2002). Accurate execution of movement that is guided by somatic input requires precise processing and transformation of incoming sensory information to produce accurate motor responses. With whole-head MEG recordings, the temporal order of activation of different areas can be monitored to reveal functional organization of the somatosensory cortical network. In this study, the interplay between sensory and motor cortex was readily observed in real time using MEG recordings in the context of a cued-motor task. In addition, the precise location of neuronal populations giving rise to the primary sensory and motor components of the ERF waveform was confirmed through invasive electrophysiology.

Our findings reinforce previous reports (Ganslandt et al., 1999; Makela et al., 2001; Roberts et al., 1998) supporting the clinical utility of MEG for sensory and motor mapping. The inter- and intrasubject replicability of the patterns of EFs and source localizations in conjunction with the external validation (through direct electrocortical recordings) of this CSSMP helps to consolidate this paradigm as a valid tool for somatosensory mapping.

The application of the CSSMP did elicit five clear responses in all the participants (S1, S2a, S2b, M1, S2c) and a premotor response in 10 out 14 participants. The sequence of three initial components (S1, S2a, S2b) was present in all participants in both conditions (passive and active). The contralateral distribution and location of S1 sources agrees with previous reports about the somatotopic representation of the index finger (Baumgartner et al., 1991; Roberts and Rowley, 1997). In some cases, we were able to visually identify ipsilateral dipolar distributions in some individuals (3 out of 14) at the S1 response latency but dipole fitting did not reach the confidence value set a priori. Indeed, tactile inputs from one hand seem to have access to the S1 cortices of both hemispheres, probably through callosal connections (Schnitzler et al., 1995). The lack of a clear ipsilateral S1 response is a common finding and the lower amplitude with respect to S2 is not a surprising fact. Recordings in monkeys have shown that receptive fields of many S2 neurons are larger than those of S1 neurons (Robinson and Burton, 1980), which directly affect the magnitude of the evoked magnetic field.

Activation in the upper lip of the sylvian fissure (S2) has widely been reported after tactile stimulation (Disbrow et al., 2001; Hari et al., 1983, 1990) and the latency and amplitude of the responses can vary in relation to the stimuli applied (Forss et al., 1994) or individual features (Elbert et al., 1995). The latency lag between the peak of this response (approximately 12 ms) in both hemispheres reinforces the hypothesis of a transcerebral input to the ipsilateral S2 (Fabri and Manzoni, 1996; Pandya and Vignolo, 1969). However, this interpretation is only supported by temporal information because neuromagnetic responses record the compound activity of all neural assemblies in one area and cannot identify the contribution of different input pathways. The second burst of activation in this area (S2b) probably reflects the intense flow of information between ipsilateral and contralateral somatosensory areas during stimuli evaluation (Forss et al., 1994; Hoechstetter et al., 2001). Recent studies (Disbrow et al., 2000, 2001) have demonstrated that in S2 and the parietal ventral area (PV), two topographically organized representations of cutaneous receptors conjunct.

Movement of the right hand and M1 activation was preceded in the majority of the cases by a bilateral component arising from the premotor cortex (PrM). This component may reflect preparatory activity. Performance of somatosensory tasks, such as those employed in the present study, requires the analysis of relevant sensory input which is closely linked to the preparation of appropriate motor commands. Our data suggest that premotor input into primary motor cortex may serve this function, although premotor activity was not detected in all participants. Further studies with higher-density neuromagnetometer arrays that afford greater overall sensitivity to underlying cortical sources are necessary to determine whether premotor input is a necessary component—and therefore invariably detected—of the brain circuit that supports cued voluntary movements.
We found M1 activation associated with hand movement in all the participants contralateral to the stimulation and moved hand. Our patients suffered from left hemisphere lesions and were right-hand dominants like the healthy volunteers. A more bilateral M1 representation has been reported for the nondominant hand in left- and right-handed subjects (Taniguchi et al., 1998). This M1 activity burst was clearly associated to the timing of the hand movement (strong positive correlation), suggesting a temporal overlap between cortical primary cortex activation and muscle engagement.

The last identified cortical response was localized in S2/PV. This response was in all cases posterior to the hand movement suggesting a proprioceptive function. M1 activation has proven to be necessary for the somatic perception of movement of our limbs (Naito et al., 2002) and the posterior presence of S2 activation reinforces the idea of a continuous flow of information between pre- and postcentral areas in sensorimotor integration. There is an intimate physiological and anatomical relationship between the pre- and postcentral cortices, as evidenced by extensive corticocortical fibers between the two regions and rich connections with other brain areas (Crosby et al., 1962; Kaneto et al., 1994).

According to the data presented above, we have summarized the possible pathway and centers where activity flows from the input (tactile stimuli) to the hand movement in Fig. 6.

The basic pattern of EFs elicited using the CSSMP has common features with previous reports adding new information relevant to the mapping procedure. The manipulation of certain experimental conditions has a clear effect in the recorded EFs (Wilkinson et al., 1996) and can explain some specific differences in our results (latencies and strength of EFs).

Ultimately, verification of any new experimental paradigm or technique for functional mapping requires a direct comparison with the “gold standard procedure,” in this case, direct electrocortical recordings. Specific lesions in the course of many diseases, such as stroke, brain tumors, and cortical myoclonus can differentially affect the activation of sensorimotor cortical networks (centers and/or afferent and efferent pathways) distorting specific cortical responses (Forss et al., 1999; Roberts et al., 2002; Uesaka et al., 1993). Identification of modified activation patterns and their comparison with patients’ clinical signs and symptoms may reveal pathophysiological mechanisms underlying the diseases. Recent studies have shown brain lesions can lead to an atypical cortical representation of sensorimotor functions (Papanicolau et al., 2001). Yates et al. (2002) have recently demonstrated that AVMs can be associated with shift in the topography of cortical function in as many as one-third of patients. Those brain lesions in the vicinity of the central sulcus may alter the surrounding brain tissue structurally by either moving or compressing it, or by infiltration or edema or by a mixture of these. In some of these cases, surgical treatment is needed, requiring a clear definition of eloquent cortex with respect to the lesion. The clinical utility of MEG-derived recordings of specific sensory (S1, S2) and motor (M1) responses had been already validated independently through electrocortical recordings (Ganslandt et al., 1999, 2002; Hund et al., 1997; Makela et al., 2001). Our results are consistent with those previous reports because MEG-derived maps of sensorimotor activation were verified through direct neurophysiological recordings in four patients. These results in conjunction with the positive outcome data of our six patients suggest that the CSSMP was a useful noninvasive approach to guide the surgical approach. The MEG proved in those cases to provide relevant noninvasive information to plan preoperatively the surgical intervention and speed up the intraoperative stimulation procedure.

Furthermore, the CSSMP introduces the possibility of tracking the flow of information between the sensory and the motor cortex in patients with structural lesions and minimizes some methodological problem. One important source of error variance in previous studies is the lack of movement control between the sensory and the motor trial, together with the necessity of independent sensory and motor data analysis and co-registration (with subject’s MRI) introducing new sources of error to the localization process. The fact that using the CSSMP sensory and motor cortical responses are simultaneously evoked and analyzed eliminates the localization error due to independent analysis and co-registration of sensory and motor trials, which can be quantified in millimeters. The CSSMP allows the fine and accurate spatial identification of two areas anatomically as close as the sensory and motor cortex.

All the participants (patients and healthy volunteers) were able to perform the task without major problems. Our patients did not present with sensory or motor deficits during the MEG examination and therefore were fully capable of performing the task. Their deficits were only apparent during the episodes associated to their epileptic conditions. Patients with permanent sensory or motor deficits must be studied under different experimental conditions. To study the effects of permanent sensory and/or motor disturbances in evoked responses was not part of the present study, though previous studies on this topic have produced interesting findings using different procedures (Papanicolau et al., 2001).

At present, no single imaging technique fulfills each of the criteria we have proposed. However, we would suggest that MEG fulfills most of these requirements and we provide evidence for this suggestion below. To date, there are far fewer centers equipped with MEG than fMRI and PET, yet, as we will now describe, its advantages are considerable for the mapping of sensorimotor function in the brain. In addition to its reliability, validity, specificity, and spatial and temporal resolution, MSI has a unique advantage of providing a direct measure of cortical function. Unlike PET and fMRI, MSI is not based on blood flow, but on the magnetic flux distributions that arise directly from brain activity. EEG studies have led the way in describing somatosensory and motor responses associated with tactile stimulation and movement execution (Deecke et al., 1969; Ito et al., 1992; Shibasaki et al., 1980) in the past. However, the principal advantage of MEG over EEG recordings as a means of detecting sensorimotor-evoked responses is that MEG provides a simpler and more accurate mechanism for the localization of the neural generators. Even with high-density EEG recordings and co-registration of sources onto structural images, the mathematical modeling of electrical currents does not achieve the spatial resolution of MEG (Ballish et al., 1991; Ilmoniemi, 1993). Although MEG is not widely available for clinical use, its experimental use in the last decade has shown it to be a promising functional mapping tool due precisely to its spatial and temporal resolution (Papanicolau, 1998).

Two specific features of the results of this study need to be mention. First, to our knowledge, this is the first time that a unique experimental paradigm elicits primary sensory and primary motor EFs and verifies the estimated sources using the gold standard technique (using invasive neurophysiology). Second, this is the first time that a clear interaction between precentral and postcentral areas is described in the context of a simple sensorimotor behavior using MEG recordings.
In conclusion, we consider that the CSSMP is a reliable and valid method to characterize sensorimotor function and helps to optimize the surgical procedure when perirolandic areas are compromised.

Acknowledgments

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References


