The value of multichannel MEG and EEG in the presurgical evaluation of 70 epilepsy patients

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Abstract

Objective: To evaluate the sensitivity of a simultaneous whole-head 306-channel magnetoencephalography (MEG)/70-electrode EEG recording to detect interictal epileptiform activity (IED) in a prospective, consecutive cohort of patients with medically refractory epilepsy that were considered candidates for epilepsy surgery.

Methods: Seventy patients were prospectively evaluated by simultaneously recorded MEG/EEG. All patients were surgical candidates or were considered for invasive EEG monitoring and had undergone an extensive presurgical evaluation at a tertiary epilepsy center. MEG and EEG raw traces were analysed individually by two independent reviewers.

Results: MEG data could not be evaluated due to excessive magnetic artefacts in three patients (4%). In the remaining 67 patients, the overall sensitivity to detect IED was 72% (48/67 patients) for MEG and 61% for EEG (41/67 patients) analysing the raw data. In 13% (9/67 patients), MEG-only IED were recorded, whereas in 3% (2/67 patients) EEG-only IED were recorded. The combined sensitivity was 75% (50/67 patients).

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Conclusion: Three hundred and six-channel MEG has a similarly high sensitivity to record IED as EEG and appears to be complementary. In one-third of the EEG-negative patients, MEG can be expected to record IED, especially in the case of lateral neocortical epilepsy and/or cortical dysplasia.

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1. Introduction

The goal of epilepsy surgery is the complete resection or disconnection of the epileptogenic zone while preserving the functionally relevant eloquent cortex. A variety of diagnostic tools, including EEG, video-EEG monitoring (Jayakar, 1999), MRI (Knake et al., 2005), functional imaging (PET, SPECT and MRI) (Diehl et al., 2003) and neuropsychological testing are used to presurgically define the seizure onset zone and the eloquent cortex (Rosenow and Lüders, 2001), in addition to the irritative zone, that is the cortical region generating interictal epileptiform discharges (IED). Identification of the irritative zone by EEG recordings contributes to the definition of the epilepsy syndrome and to planning of a resective procedure or of invasive studies using subdural or depth electrodes when non-invasive studies remain inconclusive or discordant (Rosenow and Lüders, 2001). Invasive monitoring, however, carries additional risks and expenses (Hamer et al., 2002; Onal et al., 2003). The selection of candidates for invasive intracranial recordings and a precise determination of the area to sample from is crucial to the success of these evaluations (Siegel et al., 2000), and these tasks are especially difficult in those patients in whom no IED are recorded despite prolonged video-EEG monitoring.

Magnetoecephalography (MEG) has been used clinically since the early 1980s to characterize the irritative zone and in some studies the seizure onset zone (Shiraishi et al., 2005, 2001; Stefan et al., 1990, 2003; Ebersole, 1999).

In our prospective study, multichannel MEG and EEG raw traces were analysed independently to evaluate the sensitivity of both methods to detect interictal epileptiform discharges in an unselected, consecutive clinical cohort of 70 patients with medically intractable focal epilepsies. Our goal was to determine the sensitivity of MEG and EEG to detect IED, and if possible to identify patient groups that are more prone to show IED in either MEG or EEG.

2. Methods

2.1. Patients

Seventy patients were referred during the period 2/2002–5/2003 from five tertiary epilepsy centers for a simultaneous whole-head MEG/EEG recording. Patients had medically intractable focal epilepsies, had undergone a comprehensive phase 1 video-EEG evaluation, and were considered as potential candidates for invasive EEG monitoring due to inconclusive results in the phase 1 evaluation or due to a complex clinical picture. Written reports of previous investigations were available for all patients. All patients gave informed consent and the local Institutional Review Boards approved the study.

2.2. Methods

A 306-channel whole-head MEG (VectorView, Elekta Neuromag, Helsinki, Finland) was recorded simultaneously with a 70-electrode EEG. The MEG system consisted of 204 gradiometers and 102 magnetometers distributed over 102 locations in a helmet-shaped array inside the liquid helium dewar. The recordings were performed in a three-layer magnetically shielded room (Imedco, Hagedorn, Switzerland). Patients were recorded in supine position and instructed to rest or sleep. Recordings of spontaneous activity were followed by 4 min of hyperventilation (HV) and 4 min of post-HV recording. The total average recording time was 2 h. EEG was recorded using a non-magnetic 70-channel electrode cap (Elekta Neuromag) and four additional single electrodes for obtaining the electrooculogram (EOG). Electrode positions on the cap were following the international 10-10 system. EEG was obtained with a common reference montage. Prior to recording, a 3D digitizer (Polhemus, Colchester, VT, USA) was used to determine the position of fiducial landmarks, the nasion, preauricular points (tragus bilaterally), the
individual head shape and the position of the EEG electrodes and of four HPI (head position indicator) coils, used to determine the position of the head in relation to the MEG sensors before each run (Hämäläinen et al., 1993). MEG data were collected in epochs lasting 4 min each. Before each epoch, a measurement of the head-position (using the HPI-coils) was taken. MEG and EEG signals were amplified, filtered (low-pass filter of 200 Hz and high-pass filter of 0.03 Hz), analog-to-digital converted (sampling rate = 600 Hz) and were stored digitally for off-line data analysis.

A review of IED in the raw MEG and raw EEG traces was performed independently by three neurophysiologists, board certified in EEG and experienced with MEG interpretation (SK, HS, KH). Reviewers were not blinded regarding the identity of the subjects but were blinded for the results of the interpretation of the other modality. Data were included for analysis only when there was inter-observer agreement on the presence of an IED at a given timepoint in either EEG or MEG. The sensitivity of MEG and EEG was based exclusively on the presence of IED in the raw MEG and raw EEG data traces. The visually identified IED were then attributed to the lobe of possible origin. The inter-observer reliability for the localization of spike foci was 100% for all patients included. After IED had been identified in each modality, they were classified as MEG/EEG, MEG-only IED or EEG-only IED.

3. Results

Seventy consecutive patients were studied. Thirty-nine female (55%) and 31 male patients (44%), 9–56 years old (mean age: 29.5 years), constituted our study group. Three patients (4%) could not enter the study because old metallic dental work prevented obtaining usable MEG data due to excessive artefacts. In the remaining 67 patients studied, the sensitivity for detecting IED was 72% for MEG alone (48/67 patients), 61% for EEG alone (41/67 patients) and 75% for both modalities in combination (50/67 patients) (Table 1). No seizures were recorded.

3.1. Group 1: IED in MEG but not in EEG (nine patients; Table 2)

IED that occurred in MEG but not in the simultaneously recorded EEG were detected in 9 of the 67 patients (13%), which constitutes 33% of the 26 EEG-negative patients (Table 2). Two of those patients with MEG-only spikes had lateral temporal lobe (22%), five had lateral frontal (56%), and one had medial temporal lobe (11%) and one had medial frontal lobe (11%) IED in MEG. Six out of nine patients (67%) showed a lesion on MRI, including focal cortical dysplasia (4), periventricular nodular heterotopia (1) and encephalomalacia (1). The IED recorded in MEG corresponded to the MRI lesion in five of those six patients (83%). At the same time as IED in MEG, the simultaneously acquired EEG did not show IED or any other pathologic activity (slowing, loss of normal rhythms). Averaging of EEG data at the time points when MEG raw traces showed IED activity did not change the clinical interpretation of the EEG in any patient. Seven of these nine patients (78%) had also no IED in prior routine clinical EEG or during prolonged video-EEG monitoring; in the other two, IED were reported in the same location as the MEG-IED. The additional information provided by the MEG investigation influenced clinical decision making in three patients (33%), by obviating the need for invasive monitoring in one, and in the other two by better defining the position of invasive electrodes prior to iEEG monitoring. In three other patients the clinical diagnosis made prior to MEG was confirmed.

3.2. Group 2: IED in EEG but not in MEG (two patients; Table 3)

IED that occurred in EEG but not in MEG were detected in 2 of the 67 patients (3%). Both patients were suffering from frontal lobe epilepsy of the medial
Table 2
Patients with IED in MEG but not in EEG (nine patients)

<table>
<thead>
<tr>
<th>No.</th>
<th>Age (years)</th>
<th>Sex</th>
<th>AaO</th>
<th>Diagnosis</th>
<th>EEG</th>
<th>MEG</th>
<th>MRI</th>
<th>SURG</th>
<th>Histol</th>
<th>iEEG</th>
<th>CiM</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>28</td>
<td>f</td>
<td>16</td>
<td>PLE</td>
<td>No</td>
<td>r MF</td>
<td>nL</td>
<td>Yes</td>
<td>m</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>27</td>
<td>m</td>
<td>18</td>
<td>TLE</td>
<td>No</td>
<td>r LT</td>
<td>CD r TL</td>
<td>Yea</td>
<td>CD</td>
<td>–</td>
<td>Yes</td>
</tr>
<tr>
<td>3</td>
<td>13</td>
<td>m</td>
<td>7</td>
<td>TLE</td>
<td>No</td>
<td>r LT</td>
<td>CD r TL</td>
<td>Yes</td>
<td>CD</td>
<td>Yes</td>
<td>Position iEEG</td>
</tr>
<tr>
<td>4</td>
<td>19</td>
<td>f</td>
<td>14</td>
<td>FLE</td>
<td>No</td>
<td>r LF</td>
<td>CD r FL</td>
<td>No</td>
<td>–</td>
<td>–</td>
<td>No</td>
</tr>
<tr>
<td>5</td>
<td>49</td>
<td>f</td>
<td>11</td>
<td>FLE</td>
<td>No</td>
<td>r LF</td>
<td>Encephalomalacia</td>
<td>No</td>
<td>–</td>
<td>–</td>
<td>No</td>
</tr>
<tr>
<td>6</td>
<td>43</td>
<td>m</td>
<td>11</td>
<td>TLE</td>
<td>No</td>
<td>r LT</td>
<td>CD (PNH)</td>
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<td>–</td>
<td>–</td>
<td>No</td>
</tr>
<tr>
<td>7</td>
<td>56</td>
<td>m</td>
<td>21</td>
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<td>No</td>
<td>r MT</td>
<td>nL</td>
<td>No</td>
<td>–</td>
<td>–</td>
<td>No</td>
</tr>
<tr>
<td>8</td>
<td>9</td>
<td>m</td>
<td>5</td>
<td>Multifocal</td>
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<td>nL</td>
<td>No</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>9</td>
<td>18</td>
<td>f</td>
<td>0.2</td>
<td>FLE</td>
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<td>r LF</td>
<td>CD 1 FL</td>
<td>No</td>
<td>–</td>
<td>–</td>
<td>No</td>
</tr>
</tbody>
</table>

Diagnosis—diagnosis is based on the results after video-EEG monitoring; AaO—age at onset in years; IED—interictal epileptiform discharges; EEG—IED in EEG; MEG—IED in MEG; SURG—surgery performed?; Histol—histology; iEEG—invasive video-EEG monitoring performed?; CiM—change in management; PLE—parietal lobe epilepsy; TLE—temporal lobe epilepsy; r—right; l—left; m—male; f—female; MF—mesial frontal IED; MT—mesial temporal IED; LF—lateral frontal IED; LT—lateral temporal IED; CD—cortical dysplasia; PNH—periventricular nodular heterotopia; FL—frontal lobe; TL—temporal lobe; ns—non-specific; no iEEG—invasive EEG monitoring avoided; position iEEG—change in iEEG electrode positioning.

Table 3
Results of all patients with IED in EEG but not in MEG (two patients)

<table>
<thead>
<tr>
<th>No.</th>
<th>Age (years)</th>
<th>Sex</th>
<th>AaO</th>
<th>Diagnosis</th>
<th>EEG</th>
<th>MEG</th>
<th>MRI</th>
<th>SURG</th>
<th>Histol</th>
<th>iEEG</th>
<th>CiM</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>21</td>
<td>m</td>
<td>4</td>
<td>FLE</td>
<td>CZ</td>
<td>No</td>
<td>CD r SSMA</td>
<td>Yes</td>
<td>CD</td>
<td>–</td>
<td>No</td>
</tr>
<tr>
<td>11</td>
<td>16</td>
<td>m</td>
<td>12</td>
<td>FLE</td>
<td>CZ, F3</td>
<td>No</td>
<td>nL</td>
<td>No</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

Diagnosis—diagnosis is based on the results after video-EEG monitoring; AaO—age at onset in years; MEG—IED in MEG; EEG—IED in EEG; SURG—surgery performed?; Histol—histology; iEEG—invasive video-EEG monitoring performed?; CiM—change in management; SSMA—supplementary sensorimotor area; CZ—EEG electrode position showing the maximum of the IED according to the international 10/20 system; F3—EEG electrode position showing the maximum of the IED according to the international 10/20 system; FLE—frontal lobe epilepsy; r—right; l—left; m—male; f—female; CD—cortical dysplasia; nL—normal; no iEEG—invasive EEG monitoring avoided.

3.3. Group 3: IED in MEG and EEG (39 patients)

IED that occurred simultaneously in EEG and MEG were detected in 39 of 67 patients (58%). When the IED was seen in both modalities at the same time point, the spike morphology and the lobe localization was always congruent. Twenty-five patients showing IED in MEG and EEG were suffering from temporal lobe epilepsy, 10 from frontal lobe epilepsy, 2 from occipital lobe epilepsy and 1 patient each from parietal lobe epilepsy and multifocal epilepsy (Table 1). In 11 patients (32%) cortical dysplasia was identified on MRI.

3.4. Group 4: no IED in EEG and MEG (17 patients)

In 17 patients, no IED could be recorded in either EEG or MEG (25%). Seven of these patients had lesional temporal lobe epilepsy, and two had lesional frontal lobe epilepsy. In eight patients, no focal lesion could be detected on MRI.

4. Discussion

We prospectively investigated the sensitivity of combined recording of 306-channel MEG and 70-
channel EEG to detect IED in the presurgical evaluation of 70 patients with medically intractable focal epilepsies. MEG and EEG showed similar sensitivity for detecting IED. However, in one-third of EEG-negative patients, MEG recorded IED, especially those with lateral neocortical epilepsy and/or cortical dysplasia. Especially in complicated evaluations, where iEEG monitoring was being considered, the combined EEG/MEG study provided crucial information on the irritative zone which may help tailor invasive EEG studies, thereby contributing to successful resective procedures. Previous studies support our finding of an equally good or a slightly higher sensitivity of MEG as compared to EEG (Iwasaki et al., 2002, 2005; Lin et al., 2003). Other groups have reported that MEG may aid in the presurgical evaluation of patients with focal epilepsies (Stefan et al., 1990, 2000, 2003; Pataraia et al., 2002; Binnie and Stefan, 1999; Forss et al., 2000; Baumgartner et al., 2000). Previous studies, however, have used fewer MEG channels and EEG electrodes. The evolution of MEG over the last decade, especially the advent of whole-head systems, has provided additional ability to define the irritative zone (Barkley and Baumgartner, 2003; Pataraia et al., 2004; Baumgartner, 2004). Knowlton et al. (1997) studied patients selected randomly from a presurgical population using a 37-channel MEG and found a similar sensitivity of 73%. However, Stefan et al. (1990, 2000, 2003) found that the diagnostic yield increases with the number of sensors in a study, comparing the diagnostic yield of 37- and 74-channel MEG systems, suggesting that the use of whole-head systems with densely spaced arrays of sensors will contribute more to the presurgical evaluation.

Both EEG and MEG measure bioelectric neuronal currents arising in the pyramidal neurons with a temporal resolution of 1 ms or less (Barkley and Baumgartner, 2003). Although generated by the same neurophysiological process, MEG and EEG signals have some important differences: EEG is much more subject to artefacts produced by the conductivity properties of brain, CSF, skull and scalp than MEG, which theoretically should result in better spatial resolution for MEG (Cohen and Cuffin, 1983, 1991). MEG, on the other hand, is insensitive to pure radial sources, which generate no magnetic field outside the head, while EEG is sensitive to both tangential and radial sources. Therefore, MEG measures predominantly activity in the sulci of superficial cortex and is more prone to detect lateral neocortical IED, while EEG is more likely to detect IED of the medial neocortex. In patients with temporal lobe epilepsies, Baumgartner et al. (2000) found that MEG was more sensitive than scalp EEG for IED from the lateral cortex.

In our study, the sensitivity of both modalities was determined by carefully analysing the raw traces, as in routine clinical settings. More patients (9/67 patients; 13%) showed MEG-only IED than EEG-only IED (2/67 patients; 3%). Especially patients with lateral neocortical epilepsy and patients with focal cortical dysplasia seemed to benefit from the MEG investigation. The high proportion of patients with cortical dysplasia (59 patients; 56%) in the MEG-only group may be due to disturbed laminar architecture of the neocortex in the area of dysplasia, which may result in a different electromagnetic field of the dipole and possibly facilitate the recording of IED in MEG. Three MEG-only patients were already scheduled for phase II monitoring with invasive electrodes. In two of these, the positioning of invasive electrodes was influenced by the MEG results, potentially improving their chance of a seizure free outcome by reducing sampling error (Siegel et al., 2000), and in one, invasive video-EEG monitoring was omitted, avoiding costs and risks (Hamer et al., 2002). In the remaining patients, MEG/EEG confirmed results of previous presurgical investigations.

Both patients who showed IED in EEG-only had medial frontal lobe epilepsy characterized by simple partial seizures with motor symptoms in the leg, with a focus close to the central sulcus. MEG might not have detected the source generating the IED in this region as it may be radial in orientation. Of interest is that both patients had not shown IED in previous clinical EEGs and even in prolonged video-EEG monitoring; the closely spaced array of 70 electrodes might have helped to detect IED.

In more than half of the patients in our study IED were detected by EEG and MEG simultaneously. MEG-IED and EEG-IED localized to the same area in these patients, which can be interpreted as indicating that MEG and EEG depict the same irritative zone, despite the discussed differences in signal properties. However, one-fourth of the patients (25/69) did not show any IED in either modality.
Our study suggests that whole-head MEG may provide additional information for the management of patients with medically refractory epilepsies. However, we did not specifically address the effect of the MEG investigation on the clinical outcome, which ideally requires a randomized control group (placebo or sham MEG). The combined multichannel MEG/EEG approach may improve the non-invasive evaluation of epilepsy patients and further reduce the need for invasive procedures. Especially patients with medically resistant lateral neocortical epilepsies and patients in with a dyplastic cortical lesion may benefit from an MEG investigation. Larger, prospective, blinded studies of the clinical impact of MEG/EEG investigations are needed.

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