Tangential and Radial Epileptic Spike Activity: Different Sensitivity in EEG and MEG

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Objective: Observations in epileptic patients show that interictal spikes are sometimes only visible in electroencephalography (EEG) and sometimes only in magnetoencephalography (MEG). This observation cannot readily be explained by the theoretical sensitivities of EEG and MEG based on analytical models. In this context, we aimed to study the directional sensitivity of radial and tangential spike activity in numerical simulations using realistic head models.

Methods: We calculated the signal-to-noise ratio (SNR) of simulated spikes at varying orientations and with varying background activity in 12 brain regions in 4 volunteers. Different levels of background activity were modeled by adjusting the amplitudes of several thousand dipoles distributed in the cortex.

Results: For a fixed realistic background activity, we found a higher SNR for MEG spikes for spike orientations that deviated not >30° from the tangential direction. In contrast, we found a higher SNR for EEG spikes that deviated not >45° from the radial direction. When the radial background activity was selectively increased, the sensitivity of EEG for radially oriented spikes decreased; when the tangential background activity selectively increased, the sensitivity of MEG for tangentially oriented spikes was decreased.

Conclusions: Our simulations provide a possible explanation for the clinically observed differences in epileptic spike detection between EEG and MEG. Epileptic spike detection can be improved by analyzing a combination of EEG and MEG data.

Key Words: Electroencephalography, Magnetoencephalography, Epilepsy, Epileptic spike.

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Electroencephalography and MEG are used in the diagnosis of epilepsy (Barkley and Baumgartner, 2003; Funke et al., 2009; Knowlton and Shih, 2004). Both techniques are noninvasive and have a high time resolution, suitable for the detection and eventual localization of ictal and interictal spike activity in the brain. In general, EEG and MEG signals are generated by the same underlying bioelectric sources; however, there are a few theoretical and practical differences with regard to the sensitivity of the two techniques (e.g., Liehr et al., 2005; Roth and Wikswo, 1986). Perhaps the most important difference with respect to the recording of epileptic spikes is that EEG is approximately 6 to 12 times more sensitive to radially oriented sources compared with MEG (Haueisen et al., 1995; Melcher and Cohen, 1988). Distinction between radially and tangentially oriented sources is based on the local curvature of the inner skull; however, it also corresponds to the cortical anatomy, reflecting orientation of the neuron layer. Tangential brain activity originates mainly from the walls of the sulci, whereas radial brain activity originates mainly from the crown of the gyri and the bottom of the sulci.

It is well known that MEG is sensitive to tangential activity, whereas EEG is sensitive to both radial and tangential activity (Cohen and Cuffin, 1983). Thus, to some extent, it is surprising that studies in epileptic patients have reported cases in which spikes were visible in MEG but not in EEG (e.g., Baumgartner et al., 2000; Stefan et al., 2003; for a review, see Barkley and Baumgartner, 2003). Yoshinaga et al. (2002) reported that spikes were visible only in EEG in two of seven patients, while spikes were visible only in MEG in another two of seven patients. Rodin et al. (2004) reported a case in which clear spikes were visible in the MEG signal but were indistinguishable from background activity in a simultaneously recorded EEG. Iwasaki et al. (2005) reported that of 43 patients, interictal spikes were visible simultaneously in EEG and MEG in 31 patients, in MEG alone in 8, in EEG alone in 1, and in neither modality in 3 patients. In a study by Ramantani et al. (2006), more spikes were detected in the MEG compared with the simultaneously recorded EEG in 14 patients. Ramantani et al. assumed that exclusive MEG spike detection is likely influenced by overlapping background activity (especially radial background activity) in EEG. A similar argumentation was put forward earlier by Park et al. (2004).

The aim of this study was to investigate the influence of radial and tangential background activity on radial and tangential epileptic spike activity. For this purpose, we performed numerical simulations on realistic head models with radially and tangentially oriented dipolar sources distributed in various regions of the brain. We selectively changed radial and tangential background activity to test the hypothesis that increased radial background activity would contribute to higher MEG spike sensitivity in the case of tangentially oriented spikes.

METHODS

T1-weighted MRI data sets (160 sagittal slices with 1-mm resolution) of 4 healthy volunteers (2 men, 2 women; all right handed) were obtained (using the framework of another study) on a 3-T Magnetom TRIO (Siemens, Erlangen, Germany). Using these data sets, the cortical surfaces were segmented and triangulated (triangle side length, 3 mm) to serve as source spaces. For the 4 volunteers, this resulted in 18,259; 14,871; 17,035; and 14,288 nodes; a dipolar source was positioned at each node. The orientation of the electric current dipole at each node was set equivalent to the...
surface normal vector at the given node. Thus, all dipoles were oriented perpendicular to the cortical (pial) surface. We chose six cortical regions for each volunteer and each hemisphere, as indicated in Figure 1: frontal, frontotemporal, temporoparietal, central, parietal, and occipital, resulting in a total of 48 regions. In each region, a trace of six neighbor nodes (of the six respective dipolar sources) was algorithmically selected based on the orientations of the surface normal vectors at each node point. The trace of 6 dipolar sources always included 1 source with a mainly radial orientation (<10° deviation from the radial direction) on the crown of the gyrus and 1 source with a mainly tangential orientation (<10° deviation from the tangential direction) in the wall of the sulcus. The other 4 dipolar sources were chosen so that their orientations sampled the directions between radial and tangential, at intervals of approximately 15°. The inset in Figure 1 shows an example of such a dipolar source trace. The trace represents the transition from the radial to tangential direction along the cortical surface in terms of a set of node points.

For dipolar sources representing epileptic spike activity and also for dipoles representing background activity, orientation was classified as radial or tangential with respect to the local skull curvature. For this purpose, we first determined the closest node on the inner skull boundary (see the boundary element method [BEM] model construction below) for each node on the cortical surface by searching for the Euclidian minimum distance. Second, the surface normals at both nodes were evaluated, and deviation from the inner skull boundary surface normal was determined. An angle of 0° represented a radial orientation and an angle of 90° represented a tangential orientation.

We constructed a synthetic and amplitude-normalized time-activation series (Fig. 2) in MATLAB (The Mathworks, Natick, MA) based on spike time series found in the literature. For each simulation run of 1 of the 4 volunteers, this time-activation series was assigned to 1 of the 72 dipolar sources (12 regions with 6 dipoles), representing epileptic spike activity. The other 71 dipoles, which were not active epileptic sources for this simulation run, were added as sources that generate background activity.

Background activity was modeled by assigning a stochastic amplitude time series to each of the dipolar sources in the cortex (except for one source that served as a spike-generating source). The amplitude time series was generated in MATLAB (The Mathworks) based on 3 seconds (at 1,024 Hz) of Gaussian white noise and a second, very-low-frequency random signal for mimicking periods of more or less activity. We obtained a typical EEG-like background signal by filtering and multiplying the two random signals and applying a mean value filter. The entire process was performed separately for each dipole, resulting in different background time series for each dipole.

Because our simulations included selectively increased radial and tangential background activity, we classified all dipoles in the cortex in a similar manner to that for dipolar sources representing spike activity (see above). All sources with an orientation angle of <10° (with respect to the surface normal of the closest point of the inner skull layer) were defined as radial, while those with an orientation angle of >80° were defined as tangential. For our 4 models, this resulted in 784, 842, 969, and 715 radial sources and 3,246, 2,237, 3,046; and 2,411 tangential sources. The ratios between the number of tangential and radial sources were 4.1, 2.7, 3.1, and 3.4.

For each volunteer, a realistic three-compartment BEM model was derived to serve as a forward model. Skin and the inner and outer skull boundaries were segmented out of the MRI data sets, and compartment conductivities of 0.33, 0.0042, and 0.33 S/m (Geddes and Baker, 1967) were assumed. The triangle side length was set to 7 mm for the inner skull boundary, to 9 mm for the outer skull boundary, and to 10 mm for the scalp boundary (Haueisen et al., 1997).

The EEG and MEG sensor positions were taken from the equipment used in our MEG facility. The EEG sensor positions were captured for one of the volunteers with a Polhemus Fastrak (Polhemus Inc., Colchester, VT) from a 63-channel EEG cap with an extended 10 to 20 layout (EasyCap, FMS, Munich, Germany). We added 11 more electrodes to obtain a 74-channel EEG setup (Fig. 3, middle). We used this extended EEG setup for all further
computations and created a sub-setup to investigate the influence of a reduced number of EEG electrodes, using 33 electrodes from the initial 74-channel electrode setup. The reduced setup contained the following electrodes (Fig. 3, right): Fz, Cz, Pz, Fp1, FC1, CP1, O1, O9, F3, C3, P3, FC5, CP5, F7, T7, P7, F9, P9, Fp2, FC2, CP2, O2, O10, F4, C4, P4, FC6, CP6, F8, T8, P8, F10, P10 (Oostenveld and Praamstra, 2001). We digitized the following landmarks: nasion (NAS), inion (INI), left preauricular point (PAL), and right preauricular point (PAR).

The 102 MEG sensor positions were taken from the Vectorview system (Elekta Neuromag Oy, Helsinki, Finland). The average intersensor distance was 36 mm for EEG (74-electrode setup) and 41 mm for MEG (Fig. 3).

We calculated the SNR by dividing the averaged signal energy by the averaged noise energy. The averaged signal energy is the sum of the squared amplitudes of spike activity divided by the duration of the spike activity, whereas the averaged noise energy is the averaged squared amplitude of the remaining signal in time. SNR was calculated for all channels and only the maximum value was used. In cases of very-low SNR, we used the channel that showed the maximum spike amplitude in simulations without background activity, to prevent the influence of random peaks in some channels.

The MRI processing, segmentation, and creation of the forward model were performed with Curry version 4.6 (Compumedics NeuroScan, Charlotte, NC). All other computations were performed in MATLAB. Statistical testing was performed with bootstrapping and the Wilcoxon rank-sum test. Statistical significance is reported at the $P < 0.05$ level unless indicated otherwise.

RESULTS

Figure 4 shows an example of a time series with a spike visible in both EEG and MEG.

Figure 5 shows the main results for baseline background activity. The medians and 70% ranges of the normalized SNR are displayed for EEG and MEG for all simulations. The medians differed significantly between EEG and MEG for all but one bin. Bins for 0 to 9°, 10 to 27°, 63 to 80°, and 81 to 90° were significantly different at $P < 0.005$, whereas the bin for 28 to 45° was significantly different at $P < 0.05$. The bin of 46 to 62° showed no significant difference. Comparison of the results presented in Figures 5 and 6 shows that the main effect of selectively increasing radial background activity is a decrease in SNR for radially oriented spikes in the EEG; SNR in the MEG shows little change.

Figure 7 shows the influence of increased tangential background activity (150% of baseline background activity) on the SNRs. SNR values showed significant differences only for bins from 0° to 45°. The main effect of increased tangential background activity is clearly visible for the SNR of tangentially oriented MEG spike activity. Compared with the results shown in Figure 5, Figure 7 shows a lower SNR for MEG for bins between 42° and 90°. The median values in these bins were even lower than the values for EEG. In addition, Figure 7 shows reduced SNR for radially oriented spikes in EEG, although only tangential background activity was increased.

A further selective increase in radial or tangential background activity to 300% of the baseline level yielded decreased SNRs for both EEG and MEG (all median values for all bins were <0.2), yielding a qualitatively similar behavior to that shown in Figure 7.

In the second set of simulations, the spike amplitude was decreased by 20% and 40% while maintaining the background activity at baseline level (Fig. 8). As expected, the decrease in spike significantly different at $P < 0.05$. The bin of 46 to 62° showed no significant difference. Comparison of the results presented in Figures 5 and 6 shows that the main effect of selectively increasing radial background activity is a decrease in SNR for radially oriented spikes in the EEG; SNR in the MEG shows little change.

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amplitude had a stronger effect on SNR for more radially oriented sources in the EEG, and a stronger effect on more tangentially oriented sources in the MEG. Interestingly (and in line with the results shown in Fig. 7), for tangential spikes the sensitivity (SNR) of MEG degrades to such an extent that it drops below that of EEG for very weak spikes (compare the white bars in Fig. 8).

In the third set of simulations, we increased the whole background activity in steps of 25%, up to 75%. This increase resulted in a decrease in SNR, which was qualitative similar to the results shown in Figure 8. For EEG and a 75% increase in background activity, an SNR of 0.18 to 0.15 was obtained for all bins, whereas for MEG and a 75% increase in background activity, an SNR of approximately 0.1 was obtained for all bins, except the 0 to 9° (radial) bin. A detailed comparison among the six regions and the four volunteers showed no systematic or significant differences.

In the fourth set of simulations, we compared the 74-channel EEG setups with a 33-channel setup. We used reduced spike activity (80% and 60%, from the second set of simulations) and compared the electric potential distributions produced by the dipolar sources at all 72 spike locations and for all 4 volunteers, by computing the ratio of the maximum of the computed EEG amplitude between the full and reduced setups. A ratio of 1 indicates equal amplitudes for both EEG setups and typically means that a particular electrode that recorded maximal spike amplitude in the 74-channel setup was also contained in the reduced setup with 33 channels. In contrast, ratios <1 indicate the amount of decrease in maximum EEG amplitude caused by the reduced setup. Table 1 shows the mean, SD, and minimum value of the computed ratios between the maximum amplitudes in both EEG setups, presented separately for each volunteer. The average computed ratios were between 0.68 and 0.85; however, this value was significantly smaller (minimum 0.22) for single spike locations. This relatively low minimum value suggests the presence of relatively high spatial frequencies, as recently discussed (Ramon et al. 2009).

**DISCUSSION**

The present simulation study yielded two main results. First, against normal background, EEG is more sensitive to radially oriented spikes, whereas MEG is more sensitive to tangentially oriented spikes. The advantage of MEG for tangential spikes decreases if the general level of background activity is increased. Second, a selective increase in radial background activity lowers the sensitivity of EEG for radial spikes, whereas a selective increase in tangential background activity lowers the sensitivity of MEG for tangential spikes. Both of these main results hold across all brain regions.

The results shown in Figures 5-7 are generally in agreement with the hypothesis proposed by Cohen and Cuffin (1983) that MEG may enable the detection of tangential target sources that are...
obscured by radial background activity in the EEG. As noted by Rodin et al. (2004), the spikes are present in the EEG but are much too small to be independently recognized. Our simulations also confirm the assumption that these spikes, which are visible only in the MEG, have a predominantly tangential orientation (e.g., Fig. 5).

Figure 7 shows that an increase in tangential background activity can lead to a reduced SNR for radially oriented spikes in EEG. This effect may be partly because of contributions from two connected aspects: (1) the activity is not purely tangential, because all orientations that deviated <10° from tangential were taken as tangential; and (2) there were considerably more tangential than radial background dipoles, which, in combination with (1) would introduce more background activity and thus stronger effects.

The number and layout of the sensors were chosen according to the practical setups available in our laboratories. We used an EEG setup with 74 electrodes and 102 magnetometers. The intersensor distance was similar for both electrodes and magnetometers. The larger number of magnetometers was required because they are placed at a greater distance from the head surface. In addition, the MEG sensors cover a slightly larger area, especially in the frontal and temporal regions (Fig. 3). As we found no significant differences in results with respect to the six regions of the brain, we assume that the slightly greater coverage of the MEG sensor setup had no effect on the results of our study. Moreover, we can assume that the MEG sensor array provided adequate coverage of the six regions of interest used in this study.

This study has several limitations. Our forward computation model included anatomically realistic individual 3-compartment BEM models; these models can account for volume currents much better than simple spherical models but have the intrinsic disadvantage that the compartments are assumed to be homogeneous and isotropic in conductivity. Finite element method models enable detailed modeling of inhomogeneous and anisotropic conductivity distributions (Haueisen et al. 2002). We chose the BEM approach for the present study for two reasons: BEM models are currently more widely used, and model construction is easier to achieve for compartmental models. Consequently, the influence of inhomogeneous and anisotropic conductivity distributions on the sensitivity of EEG and MEG to epileptic spikes remains to be investigated.

The present simulations were performed with discrete point-like dipolar sources only. Discretization of the sources was determined by triangulation of the cortical surface with a side length of approximately 3 mm. Although more extended sources are likely for epileptic spikes and can be also modeled in EEG and MEG (e.g., Yetik et al. 2005), we focused on pointlike sources because they are widely used in standard source localization schemes.

A further limitation of our simulation study is that spikes were identical in waveform and duration. In clinical studies, spike timing is sometimes different between EEG and MEG (EEG preceding MEG and vice versa), as are spike waveforms. Such differences may be partly explained by the configuration of the areas activated in the brain. Because segmentation of the bottoms of the sulci is more complex, we included only superficial sources on the crowns of the gyri and the adjacent walls of the sulci. Further studies are needed to investigate the different sensitivities of EEG and MEG in the case of deeper sources. This is particularly important because EEG and MEG exhibit different depth sensibilities for the detection of dipolar sources.

### Table 1. Ratios of Maximum Amplitudes Between EEG Setups With 74 and 33 Channels (Fig. 3)

<table>
<thead>
<tr>
<th>Volunteer</th>
<th>Mean Ratio for Spike Amplitude 80%</th>
<th>SD</th>
<th>Min.</th>
<th>Mean Ratio for Spike Amplitude 60%</th>
<th>SD</th>
<th>Min.</th>
</tr>
</thead>
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<tr>
<td>1</td>
<td>0.79</td>
<td>0.25</td>
<td>0.23</td>
<td>0.81</td>
<td>0.23</td>
<td>0.24</td>
</tr>
<tr>
<td>2</td>
<td>0.70</td>
<td>0.15</td>
<td>0.35</td>
<td>0.68</td>
<td>0.11</td>
<td>0.42</td>
</tr>
<tr>
<td>3</td>
<td>0.82</td>
<td>0.26</td>
<td>0.22</td>
<td>0.85</td>
<td>0.23</td>
<td>0.30</td>
</tr>
<tr>
<td>4</td>
<td>0.83</td>
<td>0.16</td>
<td>0.29</td>
<td>0.85</td>
<td>0.11</td>
<td>0.39</td>
</tr>
</tbody>
</table>

EEG, electroencephalography.
CONCLUSIONS
Our results provide a possible explanation of clinical reports that spikes are sometimes more visible in EEG, although sometimes more visible in MEG. We conclude that a combination of EEG and MEG, which have different sensitivity profiles, will improve detection of interictal epileptiform activity and perhaps allow for detection in an earlier disease stage.

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