Combined EEG/MEG can outperform single modality EEG or MEG source reconstruction in presurgical epilepsy diagnosis

Ü. Aydin[1], J. Vorwerk[1], M. Dümpelmann[2], P. Küpper[3], H. Kugel[4], J. Wellmer[5], C. Kellinghaus[3], J. Haueisen[6], S. Rampp[7], H. Stefan[7], C.H. Wolters[1]

[1]Institute for Biomagnetism and Biosignalanalysis, Westfälische Wilhelms-Universität Münster, [2]Epilepsy Center, Universitätsklinikum Freiburg, [3]Department of Neurology, Klinikum Osnabrück, [4]Department of Clinical Radiology, Universitätsklinikum Münster, [5]Ruhr-Epileptology Department of Neurology, Universitätsklinikum Knappschaftskrankenhaus Bochum, [6]Institute for Biomedical Engineering and Informatics, Technische Universität Ilmenau, [7]Epilepsy Center, Department of Neurology, Universitätsklinikum Erlangen, Germany

Introduction

Epileptic activity should be localized as close as possible to the spike onset to avoid propagation. However, the low signal-to-noise-ratio (SNR) limits the confidence in source reconstructions at these early time instants. In this study we investigated if combined EEG/MEG (EMEG) could increase the reliability in localizations compared to single modality EEG or MEG with a special focus on early points in time.

It is also important to decide whether to localize each interictal spike separately, or to average all spikes first (grand-average) and then localize. The former might give an estimate on the size of the irritative zone while the latter benefits from improved SNR. Many papers suggested the size of the irritative zone as an indicator of the focality and the chance of seizure freedom after surgery. Therefore, we chose a compromise here between both approaches by using subaverages and compared its performance with single and grand-averaged epileptic spikes.

Electrophysiological measurements

A patient suffering from pharmaco-resistant focal epilepsy has been measured with simultaneous EEG (80 Electrodes), MEG (275 gradiometers) and afterwards with low density EEG (21 Electrodes) and stereo-EEG (sEEG with 167 contacts).

Spike detection

BESA Research[1] has been used to mark epileptic spikes. First, 10 clear left temporal epileptic spikes were selected and averaged using a temporal source montage. Then, the averaged signal was used in template search to find spike candidates. After visual inspection 200 left temporal spikes have been selected for further analysis.

Head model and source space construction

- T1 and T2 weighted MRIs were used to segment skin, skull compacta, skull spongiosa, cerebrospinal fluid, gray and white matter in a pipeline that includes FSL[2], Freesurfer[3] and CURRY 7[4]. Diffusion tensor MRI has been used to model white matter anisotropy (Fig. 1).
- Measured somatosensory evoked potentials and fields were used in an iterative fashion to calibrate patient specific skull compacta and spongiosa conductivities following Aydin et al. (2014), which showed the need for calibrating realistic head models to enable combined EEG/MEG source analysis.
- We constructed a 2 mm source space, constrained inside the gray matter, with a custom written Matlab[5] code. It was ensured that all source space points were sufficiently away from other tissues, thus satisfying the Venant condition (Vorwerk et al. 2012).
- A geometrically adapted hexahedral mesh with 1 mm resolution was constructed with Vgrid, and the SimBio[6] software was used for calculating the EEG and MEG leadfield matrices from the finite element mesh (Wolters et al. 2007).

Subaveraging procedure

Ten subaverages starting from 5 (Av5) as multiples of 5 until 50 (Av50) were constructed with random drawing from the spikes using Matlab. Each subaverage group consists of 200 subaveraged signals. It was insured that none of the spikes appear twice in the same average.

Source reconstruction

The leadfield matrices, calculated with SimBio, and the source space were imported to CURRY 7, and moving dipole scans for EEG, MEG and EMEG were calculated from -33 to 0 ms (EEG peak).

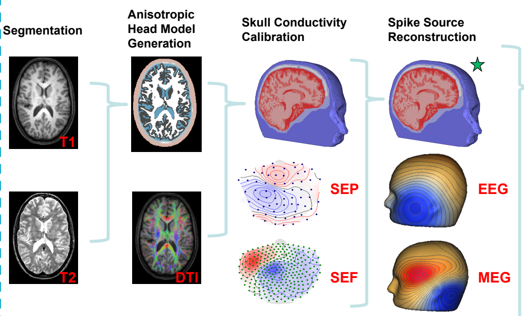

Fig. 1: Head model construction and source reconstruction pipeline. Green star indicates the conductivity calibrated model.

Results

- EMEG performed better than EEG or MEG alone at the spike onset (Fig. 2; -33 ms).
- Source reconstructions at earlier time points were closer to seizure onset zone and at the spike peak they propagated to the pole of the temporal lobe (Fig. 2).
- The MEG peak was ~7 ms before the EEG peak. Moreover, the peaks of the posterior sEEG leads were preceding anterior sEEG leads and the low density EEG by ~7.5 ms.
- EEG and MEG source reconstructions alone were able to highlight just a subset of the spiking sEEG leads: anterior regions with EEG and posterior regions with MEG. EMEG results, on the other hand, were covering almost all relevant sEEG leads (Fig. 2; -23 ms).
- Localizations obtained with higher subaverage numbers differed considerably from single spikes and subaverages of 5 (Fig. 3).
- The spread of the dipole clusters became smaller with increasing SNR (Fig. 4).

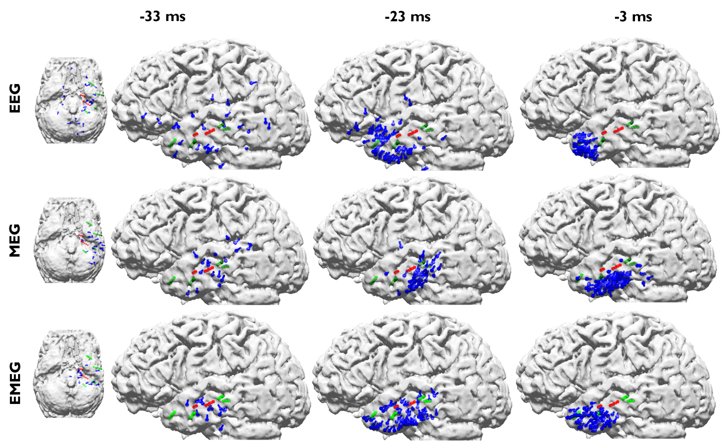

Fig. 2: EEG, MEG and EMEG dipole scan peaks of Av10 for different time instants (0 ms is the EEG spike peak). The bottom view is only given for -33 ms due to lack of space. Blue dipoles illustrate the noninvasive reconstructions, both green and red spheres show the sEEG leads where frequent interictal activity can be measured, and red spheres alone show seizure onset leads.

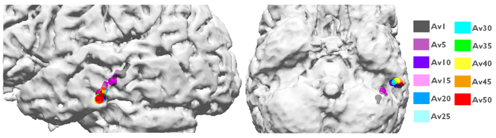

Fig.3: The centroid dipoles determined from the dipole scan peaks of MEG for different subaverages. Av1 indicates single spike reconstructions.

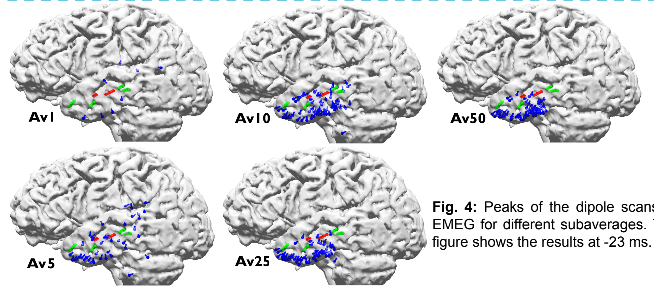

Fig. 4: Peaks of the dipole scans of EMEG for different subaverages. The figure shows the results at -23 ms.

Conclusions

- EEG and MEG are not competing, but contain complementary information. Combined EEG/MEG source analysis can increase accuracy and confidence of localizations.
- Localizing at spike onset instead of spike peak could help avoiding mislocalizations due to propagation, and the complementarity of EEG and MEG improves the localization of the noisy signals at these early time points in combined EEG/MEG scenarios.
- The SNRs of single spikes at the onset are not always sufficient for reliable localizations and therefore averaging should be performed.
- Subaveraging might achieve accuracies with regard to localization and spread of the activity that neither single nor grand-averaged spike localizations can achieve. However, the size of the dipole scatter depends highly on SNR and should thus be interpreted with care.

Acknowledgements: This work has been supported by DFG projects WO1425/2-1 and STE380/14-1, the Priority Program 1665 of the DFG (WO1425/5-1), and by the Medical Faculty of Ruhr University Bochum, by a FoRUM research grant (K062-11). We would like to thank Dr. Marcel Heers for his valuable support in setting up patient measurements and Dr. Michael Scherg for fruitful discussions.

References:
- Aydin et al., (2014) Combining EEG and MEG for the reconstruction of epileptic activity using a calibrated realistic volume conductor model. PLoS ONE.
- Vorwerk et al., (2012) Comparison of Boundary Element and Finite Element Approaches to the EEG Forward Problem. Biomed Eng Tech.
- Wolters et al., (2007) Geometry-adapted hexahedral meshes improve accuracy of finite-element-method-based EEG source analysis. IEEE Trans Biomed Eng.

[1] http://www.besa.de
[2] http://www.fmrib.ox.ac.uk/fsl
[3] http://surfer.nmr.mgh.harvard.edu
[4] http://www.neuroscan.com/curry.cfm
[5] http://www.matlab.com
[6] https://www.mrt.uni-jena.de/simbio and http://fieldtrip.fcdonders.nl/development/simbio

Contact: umit.aydin@uni-muenster.de

funded by the DFG