Combined EEG/MEG Connectivity Analysis in presurgical epilepsy diagnosis

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Motivation

- Non-invasive source analysis is a promising tool in presurgical epilepsy diagnosis [1]
- Combined EEG/MEG (EMEG) source reconstruction has already proven to outperform single modality EEG or MEG source analysis epilepsy [1]
- For EMEG source analysis, skull conductivity calibration using additional somatosensory evoked potentials and fields (SEP/SEF) data is necessary [2]
- Skull conductivity has been shown to vary inter and intra individually and to mainly affect EEG activity [2]

- Epilepsy is increasingly seen as a network disease[3]
- EEG/MEG have been widely used for connectivity analysis to identify networks of neuronal activities [3, 4]
- The term '*connectivity*' can refer to different phenomena depending on the context and the purpose [4]

- As a first step, for connectivity analysis in epilepsy, we analyzed the interictal epileptic discharges (IEDs) using combined electroencephalography (EEG) and magnetoencephalography (MEG), we then investigated the connectivity network of a focal epilepsy case

The patient

- A 27 years old female
- Symptomatology: Electrical feeling on the left hand / The hand become toning then it causes tonic movements to the mouth (20 times per month)

- Non-invasive electrophysiological recordings
  - ❑ SEP/SEF data for calibration purposes / Resting state simultaneously EEG/MEG
  - ❑ Number of detected epileptic spikes by a board certified epileptologist: 328
- Diagnosis: Focal Cortical Dysplasia (FCD) type IIB (right postcentral gyrus)
- The patient underwent in a Radio-frequency thermo-coagulation (RFTC) and the Engel outcome was ID (Generalized convulsions with antiepileptic drug withdrawal only)

The SIMNEURO pipeline for presurgical epilepsy diagnosis

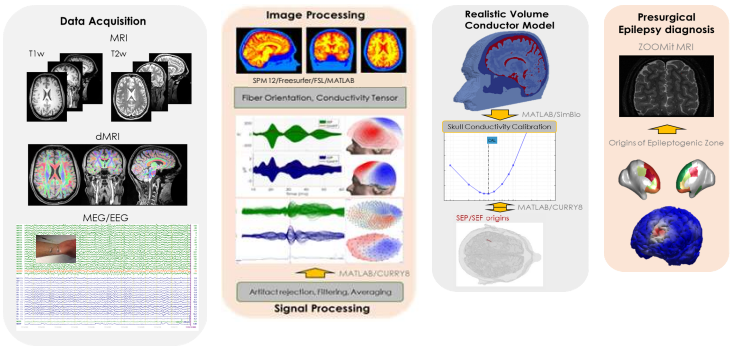
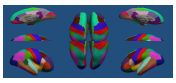


Figure 1. Pipeline for connectivity in epilepsy using EMEG source analysis. The pipeline starts from the raw data (functional and image), continuous with the preprocessing of both types of data. Next step is the calibration procedure achieving the optimal skull conductivity value and ends up with a source reconstruction of the averaged spikes and the connectivity analysis in the source space.

Skull-Conductivity Calibrated Realistic Head Model [2]

- T1w- and T2w- MRIs were used for the construction of a six compartment (skin, skull compacta, skull spongiosa, CSF, gray and white matter) head model
  - ❑ Registration was performed using FSL and image segmentation conducting SPM12– Fieldtrip combination with image processing techniques in MATLAB
  - ❑ Eddy current correction and diffeomorphic approach was applied for nonlinear correction of susceptibility artifacts[6] of the dMRI enabling modeling white matter anisotropy (WMA) [5]
- Adapted hexahedral mesh (node shifting of 0.33) with WMA conductivity tensors and source space of 2mm on gray matter far away from neighbour tissues [2]
- Finite element model simulations using Venant source modeling (AMG-CG, SimBio) [6]
- A calibration procedure[3] was performed for the selection of optimal skull conductivity

Connectivity Pipeline



- Combined EEG/MEG sLORETA for every time point of the averaged spikes
- Cortical parcellation based on the Desikan-Killiany (DTK) atlas
- Selection of the highest anatomical regions
- Window-based time-varying effective connectivity using the multivariable (MVAR) metric: generalized Partiacial Directed Coherence (gPDC) [7, 8]
- Network evaluation at a time point with low SNR [1] and in the upstroke of the spike peak [1]
- Quantification of the directed flows
  - ❑ Outflow: The strength of caused flow directed out of a brain region
  - ❑ Inflow: The strength of caused flow directed into a brain region

Results

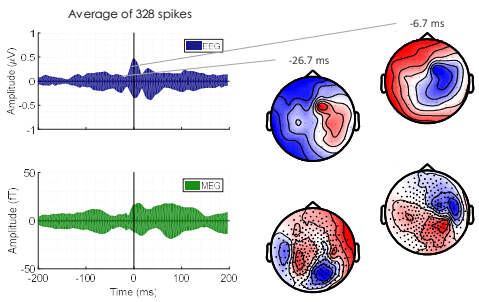
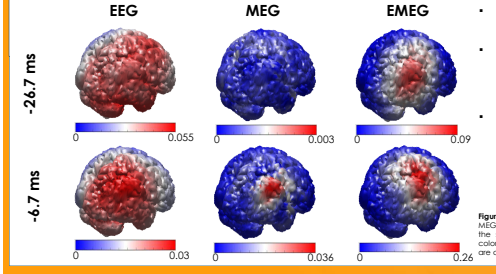


Figure 2. The butterfly plots of averaged spikes for EEG (in blue) and MEG (in green) are presented in combination with the scalp topographies for the time points -26.7 ms and -6.7 ms. The horizontal axis shows the time (in ms) while the vertical axis represents the amplitude of the signals (EEG in μV and MEG in fT). The vertical black line indicates the spike peak.

Preprocessing of EEG/MEG

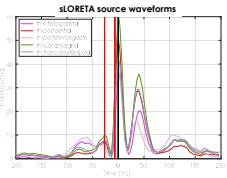
- Constant baseline correction
- Band-pass filtering at 1 – 100Hz (Notch filtering at 50Hz)
- Artifact rejection and elimination of EEG/MEG using trial SNR-based threshold approaches[3] and visual inspection
- EEG/MEG averaging across the marked spikes



- EMEG source reconstruction was focal and close to the FCD in both time points
- EEG source reconstruction occurred quite spread in the right hemisphere for the first time point while it became less covered for the second time point
- MEG source reconstruction was far away from the FCD for the first time point, but it was very focal and with the highest amplitude at the upstroke of the spike peak

Figure 3. Source reconstruction of the averaged spikes for EEG, MEG and EMEG. Standardized LORETA (sLORETA) was applied at the specific time points (-26.7 ms and -6.7 ms. The cortex is colored based on the occured current density. The color limits are different for every depicted case.

The source waveforms and connectivity patterns



- Criterion of selection

$$s_i > mean(\boldsymbol{S}) + std(\boldsymbol{S}) \; for \; i = 1, \ldots, 101 \; a.a.$$

where $\boldsymbol{S}$ is the reconstructed source time series array of (101 a.a. x 120 timepoints) and s_i row element of the $\boldsymbol{S}$

Figure 4. The sLORETA-based source waveforms with the highest activity. The vertical axis shows the strength for the waveforms while the horizontal axis represents the time interval in ms. Two vertical red lines demonstrate the selected time points for which the connectivity analysis was performed. The vertical black line shows the spike peak.

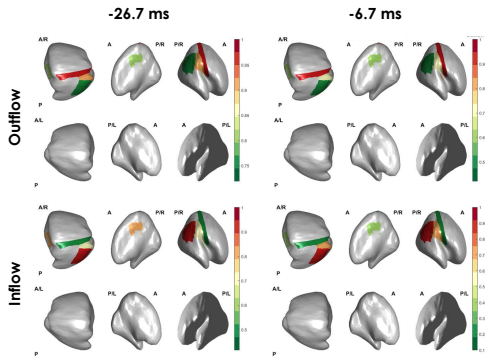


Figure 5. The outflow and inflow indices of EMEG sLORETA-based network are presented for both examined time points. Six different views demonstrate all the parcels of cortex that are involved in the connectivity analysis. A colormap from green to red represents the value of the outflow/inflow index. A red region denotes that the a number of flows direct out (or in) of the specific node while a green region the opposite.

The resected region

- The order of the multivariable model was selected based on the AIC criterion
- The window size was equal to 50 ms with an overlap o 10 ms
- The right postcentral gyrus had the highest out flow value (i.e. hub node) while the same anatomical area received the lowest amount of flow (i.e. leaf)
- The FCD belong to the hub node of the investigated network indicating that when the specific area caused seizures, other anatomical areas in the vicinity of the FCD were disturbed

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Conclusion and Outlook

- Realistic volume conductor head models, as presented here, are essential for source analysis minimizing the modelling errors
- An Individual calibration procedure is necessary
  - ❑ to stabilize the uncertainty of skull conductivity variations
  - ❑ to enable the EMEG source analysis
- EMEG source analysis show more reliable results, especially for low SNR scenarios
- Time-varying effective connectivity revealed the temporal directed paths of information flow from/to the FCD and the neighbor anatomical areas
- Convergence evidence pointed to the resected FCD indicating that the use of combined EEG/MEG with realistic head modeling benefits the presurgical epilepsy diagnosis