Fusion of EEG/MEG source analysis and high-resolution MRI in presurgical Epilepsy

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Introduction

The specificity of EEG, MEG and combined EEG/MEG (EMEG) source analysis in presurgical epilepsy could be significantly increased by incorporating other available information from fMRI or PET, from seizure semiology, or from MRI sequences sensitive to structural changes and lesions. It has been reported that in up to 73% of MRI negative cases, histology shows an underlying Focal cortical dysplasia (FCD) (Lee et al. 2005).

In this study, we introduced and applied EMEG source analysis of epileptic discharges to determine a region of interest (ROI) and used a novel sequence to acquire high resolution ($0.5 \times 0.5 \times 0.5 mm^3$) MRI data of this restricted ROI with the aim of detecting cortical malformations that were not visible in lower resolutions (Aydin et al., 2017).

Methods

Analysis strategy

The analysis strategy we introduced is shown in Fig. 1 and each step is explained below (for more details: Aydin et al., 2017).

1. Acquisition of T1 weighted, T2 weighted and Diffusion Tensor MRIs.
2. Acquisition of simultaneous EEG/MEG.
   - In supine position with EEG (80 Electrodes) and MEG (275 gradiometers; OMEGA2005, CTF, VSM MedTech Ltd., Canada).
   - Six 8 minutes long resting state runs were acquired.
   - One 7 minutes long run with electrical median nerve stimulation of the wrist was acquired to be used in patient specific skull conductivity calibration.
3. Construction of the finite element head model and solving the forward problem.
   - A 7 compartment head model: skin, skull compacta, skull spongiosa, dura mater, cerebrospinal fluid, gray and white matter.
   - Diffusion tensor MRI was used to model white matter anisotropy.
   - Patient specific skull conductivity calibration was done using somatosensory evoked potentials and fields in an iterative fashion (Aydin et al., 2014).
   - Geometrically adapted hexahedral mesh with 1 mm resolution was constructed (Wolters et al. 2007).
   - SimBio[1] software was used calculate leadfield matrices from the finite element mesh.
4. Interictal epileptic discharges were marked by an experienced epileptologist and averaged.
5. Source analysis was done using sLORETA as implemented CURRY 7[2] software after importing the leadfield matrices calculated with SimBio in step 3.
6. A second set of MRI data (Zoomed MRI) was acquired with a MAGNETOM Prisma 3.0T (Siemens Medical Solutions, Erlangen, Germany) to utilize ZOOMit function.
   - ZOOMit employs localized excitation utilizing 2D selective RF pulses with parallel transmission (Blasche et al. 2012) and allows to 'zoom' to a field of view, restricting excitation to a desired area even within brain tissue without aliasing artifacts that occur when the field of view is smaller than the imaged object.
   - Cubic voxels with 0.5 mm edge length for the determined ROIs were acquired.
   - The 'zoomed' regions were selected based on converging evidence from EMEG source analysis, seizure semiology, and morphometric MRI analysis following an epilepsy specific protocol (Wellmer et al. 2013).

Patient history and presurgical evaluation prior to source analysis

- Here introduced analysis strategy was used in presurgical evaluation of a 49-year-old female suffering from pharmaco-resistant focal onset epilepsy for 47 years. The patient used 8 life-time antiepileptic drugs, but was still suffering from 100 to 200 seizures per month.
- Diagnostic 3T MRI indicated a right frontal FCD in 3D-FLAIR sequence (1 mm^3 resolution).
- Discordantly, the seizure semiology, involving tingling feeling at the right anterior torso, ascending feeling of nausea, then loss of consciousness and tonic or hypermotor movement of right arm and leg, was pointing to left frontocentral regions.

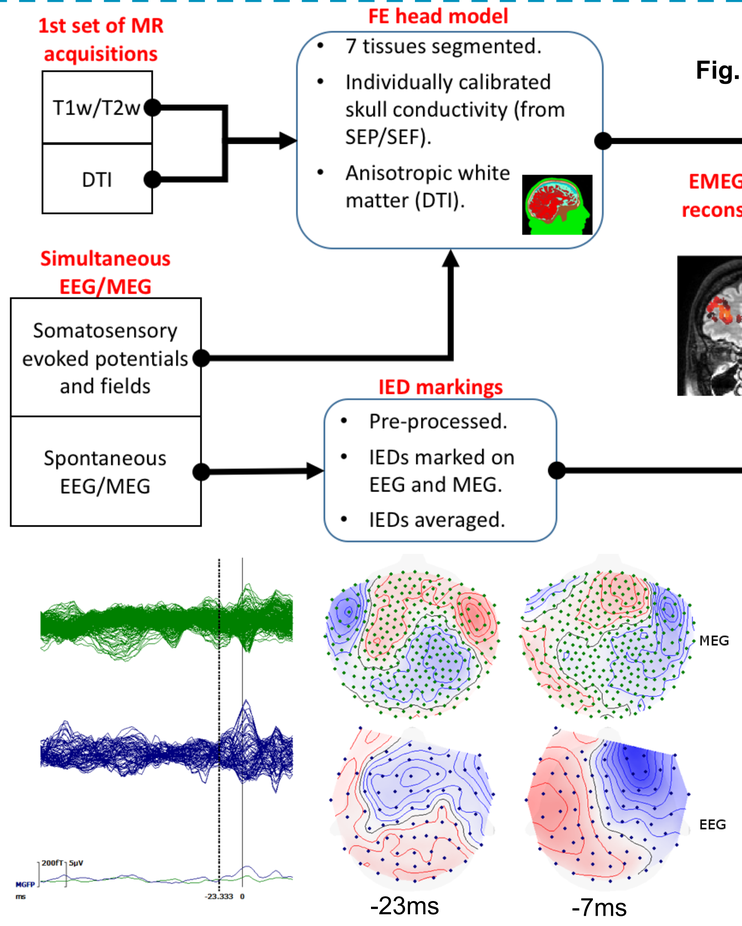

Fig. 1: Analysis scheme.

Fig. 2: Butterfly plots showing MEG (green) and EEG (blue) channels for averaged IEDs (10). MEG and EEG topographies were shown at -23ms (23 ms before the main peak) and at -7ms.

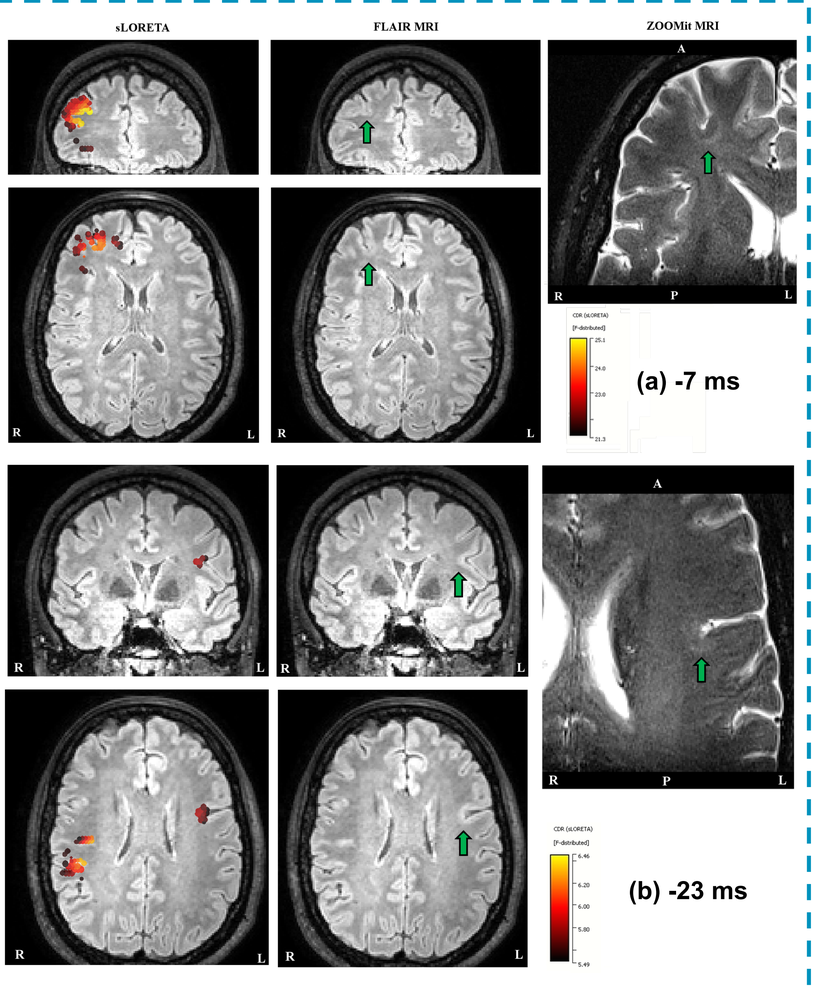

Fig. 3: EMEG source analysis at **(a)** −7 ms and **(b)** at -23ms. Left columns: the sLORETA results projected onto the FLAIR MRI (only results obtained after a threshold of 85% for the maximum F-value). Middle columns: the FLAIR image without the localizations to enable the identification of the FCDs (pointed to by green arrows). Right columns: ZOOMit MRI with the green arrow indicating the FCD. (L left, R right, A anterior, P posterior).

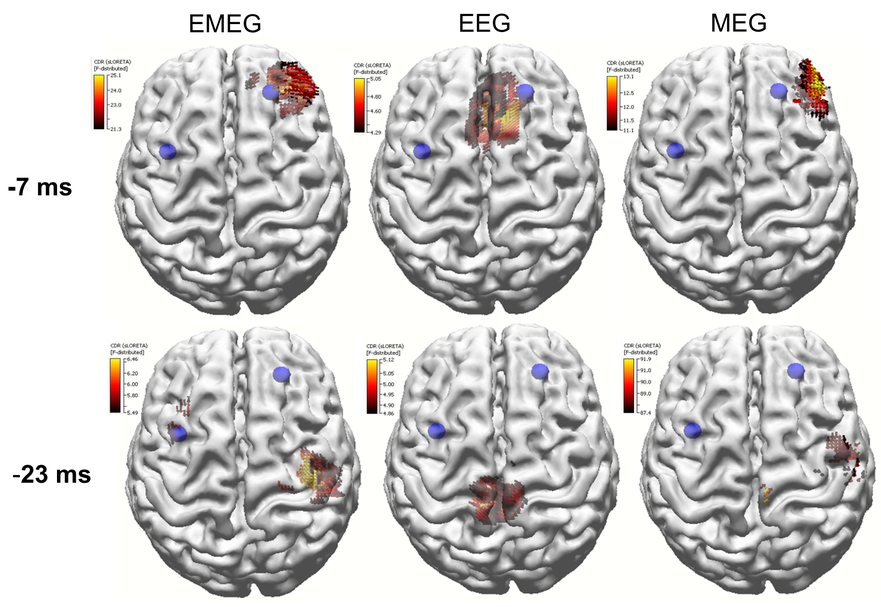

Fig. 4: EMEG, EEG only and MEG only source reconstructions at −23 ms and −7 ms . A threshold of 85% of the maximum F-value was used for the results. The FCDs detected with MRI are indicated by the blue spheres.

Results

- EMEG source analysis near the main peak of the averaged spikes pointed to the right frontal FCD (Fig. 3(a)), which was previously detected with 1 mm^3 3D-FLAIR and was not in agreement with the seizure semiology.
- Further investigation of the waveforms revealed a preceding peak occurring 23 ms before the main peak (mainly on MEG; Fig. 2).
- EMEG analysis performed at the time of the preceding peak was localized to a small region in the left fronto-central region (Fig. 3 (b)), which was in agreement with the seizure semiology.
- Acquired Zoomed MRI ($0.5 \times 0.5 \times 0.5 mm^3$) of this ROI ($160 \times 82 \times 28 mm^3$), highlighted by EMEG analysis, revealed a subtle FCD that was undetectable in lower-resolution ($1 mm^3$), even retrospectively. The role of this second FCD in seizure generation was later also verified with intracranial recordings.
- Only combined EEG/MEG source analysis was able to localize the activity at the epileptic focus (activity near the left frontocentral FCD).
- Even though single modality EEG or MEG source analysis detected activity very similar to the EMEG near the peak of the spike (localization of the right frontal FCD), their results at the preceding peak (-23 ms) were far away from the epileptic focus.

Conclusions

- We demonstrated the feasibility and possible benefits of a methodological analysis strategy combining EMEG source analysis and recent advancements in MRI parallel transmission technology in presurgical epilepsy investigation.
- The EEG/MEG source analysis was used for determining regions of interest and Zoomed-MRI was used within the ROIs to acquire high resolution data (0.5 mm edge length).
- Combined EEG/MEG source analysis significantly stabilized the accuracy and confidence of reconstructions, especially at early (noisy) time points.
- Applied to a particularly challenging case of an epilepsy patient, the real generator was only to be identified using the converging evidence from combined EMEG source analysis at the spike onset, seizure semiology, and Zoomed MRI.

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Acknowledgements

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