Noninvasive Mapping of Spike Onset identifies the Epileptogenic Zone in Children with Refractory Epilepsy

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Introduction & Rationale

- For many children with **drug resistant epilepsy** (DRE) of focal onset, **resective neurosurgery** is the most efficacious treatment, but requires a biomarker that identifies the epileptogenic zone (EZ) with high precision.
- Our group has shown that **spike-onset**, identified via **intracranial electroencephalography** (iEEG), is a powerful biomarker of the EZ, but its delineation implies complications due to the **intrinsic invasiveness**. Hence, the availability of an interictal biomarker that delineates the EZ **non-invasively** is paramount.
- Here, we aim to map **spike propagations non-invasively** via high-density EEG (HD-EEG) and magnetoencephalography (MEG), assess the concordance of the non-invasively localized spike-onset with the one derived from iEEG, and examine its ability to identify the EZ.

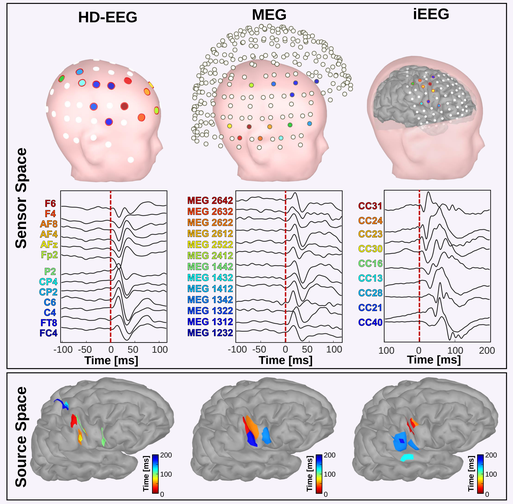

Figure 1. Spike Propagations in HD-EEG, MEG, and iEEG. For each signal, sensor locations are displayed either on the scalp (HD-EEG and MEG) or on cortex (iEEG). Spikes of selected sensors are displayed in the time domain. Events are reconstructed at the source-level and their temporal occurrence is color-coded from red (lowest time) to blue (highest time). The reconstructed propagation in the source domain is obtained using wMEM that performs source localization in the time-frequency domain using anatomical information from the geometry of gray matter surface. For each propagation, we apply a moving average within each 5 ms to regularize the sources activity and create a cortical region of activation (CRA) for each interval.

Material & Methods

- We retrospectively analyzed **interictal iEEG, HD-EEG and MEG data** from 10 children with DRE who underwent resective neurosurgery with favorable outcome (Engel 1 at one year after surgery).
- Using electromagnetic source imaging, we mapped the **spatiotemporal propagation of spikes** in the source domain with wavelet Maximum Entropy of the Mean (wMEM) (Fig. 1) and identified the **anatomical gyrus** where the spike-onset was located.
- We computed the **duration**, spatial **displacement**, and **speed** of each spike propagation.
- For each patient and modality, we defined the region that predominantly was the first to be active as **spike-onset**.
- We then estimated the **mean distance** of these noninvasive spike-onsets from **resection** and from the **spike-onset defined invasively** that served as gold standard.

Results: Concordance with iEEG and Resection

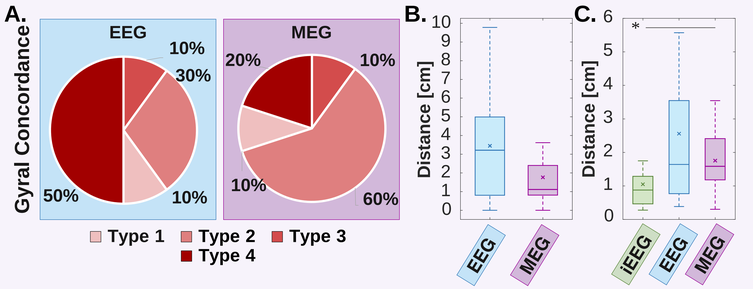

Figure 3. Comparison with iEEG gold standard and Resection. (**A**) Localization of noninvasive spike-onset compared to the invasive one. Four concordance scenarios: (i) Type 1 concordance if the noninvasive and invasive spike-onset are in the same gyrus, identified by Desikan-Killiany cortical parcellation; (ii) Type 2 and (iii) Type 3 if the noninvasive spike-onset is in the adjacent gyrus, or one gyrus above respect to the invasive spike-onset respectively; (iv) Type 4 if the two localizations are far more than two gyri. (**B**) Distance of the noninvasive spike-onset from the invasive one; and (**C**) Distance from resection for the spike-onset with the different modalities.

- The spike-onset defined via MEG and HD-EEG was **concordant with the iEEG-defined spike-onset** in 70% and 40% of patients, respectively (Fig. 3A).
- The **distance** between the non-invasively localized spike-onset from the iEEG spike-onset were 3.2 cm [0.8-5.0 cm] for the HD-EEG and 1.1 cm [0.8-2.4 cm] for the MEG (Fig. 3BE).
- Finally, the **distance from resection** was 0.9 cm (median) for the iEEG spike-onset and ~1.6 cm (median) for the spike-onsets defined via HD-EEG and MEG (Fig. 3C; p=0.15).

Results: Propagation Features

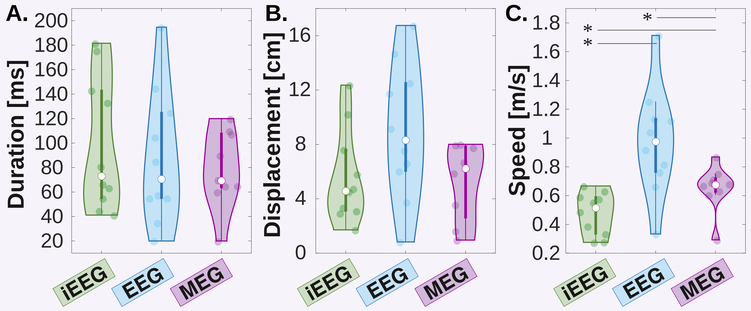

Figure 2. Comparison of spike propagation features across modalities. (**A**) Duration, i.e. time interval length where the source space activation is over threshold (**B**) spatial displacement, i.e. the sum of all distances from each CRA, and (**C**) speed of spike propagation, i.e. ratio of spatial displacement and duration, for iEEG, HD-EEG and MEG.

- We found a **higher spike propagation rate** in **iEEG than HD-EEG** (13.5 [3.8-29.4] vs. 4.3 [2.6-9.6] events/min; p=0.048).
- **No difference** in spike propagation **rate** was observed between **MEG** (6.2 [2.4-14.4] events/min) and **both HD-EEG and iEEG** (p>0.5).
- **No difference** was observed across modalities in **duration** (iEEG: 74 ms [55-143 ms]; HD-EEG: 71 ms [55-125 ms]; MEG: 70 ms [64-108 ms]; p>0.5; Fig. 2A) and spatial **displacement** (iEEG: 5 cm [3-8 cm]; HD-EEG: 8 cm [6-13 cm]; MEG: 6 cm [3-8 cm]; p>0.5; Fig. 2B).
- The lowest **propagation speed** was observed with iEEG (~0.5 m/s), followed by MEG (~0.7 m/s) and HD-EEG (~1 m/s) (Fig. 2C).

Conclusion

- Our data provide evidence that **spike propagation**, and **its onset**, can be **mapped noninvasively** with electromagnetic source imaging in children with DRE.
- The **non-invasive mapping** of such an interictal biomarker may augment the **presurgical evaluation** of children with DRE by reducing the need for invasive monitoring.

References

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