Aberrant Global Functional Connectivity in Children with Epilepsy estimated through Electromagnetic Source Imaging

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Background & Rationale

- Epilepsy is considered as a **disorder of brain networks**, with interictal and ictal activity generated and spread across networks that involve one or both hemispheres.
- Brain networks can be studied with resting-state **functional connectivity** (FC) metrics that describes how different brain areas are functionally connected.
- Whole-brain FC measures via **electric and magnetic source imaging** (ESI/MSI) are powerful tools for noninvasively mapping the neural activity of functionally connected brain regions.
- Our **aim** is to examine global FC in the brain of children with drug resistant epilepsy (DRE).
- We **hypothesize** that increased FC is mostly observed in the pathological hemisphere of children with DRE compared to their contralateral hemisphere, and both hemispheres of typically developing (TD) children.

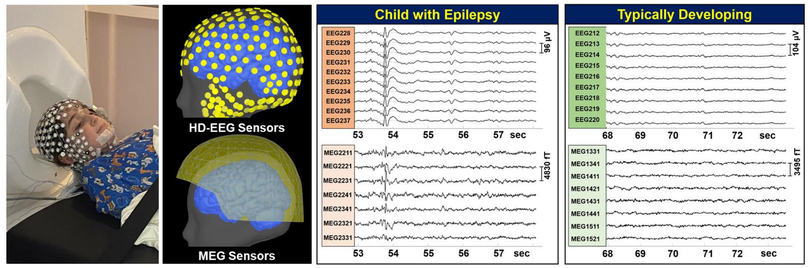

Fig. 1 Simultaneous HD-EEG and MEG recordings. *Top:* HD-EEG and MEG systems were used to acquire simultaneous HD-EEG and MEG recordings. The brain activity of each child was recorded in a supine position and each child was instructed to sleep.

Methods

- We prospectively analyzed simultaneous high-density electroencephalography (HD-EEG) and magnetoencephalography (MEG) data from **9 children with DRE** (4 females, age: 12.9 years, median: 14 years) and **9 TD children** (6 females, age: 10.2 years, median: 10 years) (**Fig.1**).
- We constructed a realistic head model from each child's MRI, and defined regions of interest (ROIs) through volume parcellation based on the automated anatomical labelling atlas (AAL) (**Fig. 2**).
- We performed **combined ESI/MSI** to reconstruct each ROI's neuronal activity in the whole-brain, as well as separately for the left and right hemispheres (**Fig. 2**).
- From each signal, we identified 3-minute duration of artifact-free segments for both children with DRE and TD.
- For each ROI, we estimated the Amplitude Envelope Correlation (**AEC**) and corrected imaginary Phase Locking Value (**ciPLV**) for physiologically relevant frequency bands: delta, theta, alpha, beta, gamma, and broadband (**Fig. 3**).
- From each FC matrix, we generated a brain network using the Minimum Spanning Tree (**MST**) (**Fig. 2**).
- To define the importance of each ROI, we used FC matrices to compute **betweenness** and **closeness** centrality metrics of the MST to define the importance of each ROI (**Fig. 2**).
- For each child, we finally estimated a unique mean **whole-brain FC** value and a two **unique mean FC** values separately for each **hemisphere**.
- We compared global FC measures between children with DRE and TD children (*Wilcoxon rank-sum* test). We also compared FC in the pathological (vs. the contralateral) hemisphere for children with DRE (*Wilcoxon signed-rank* test).

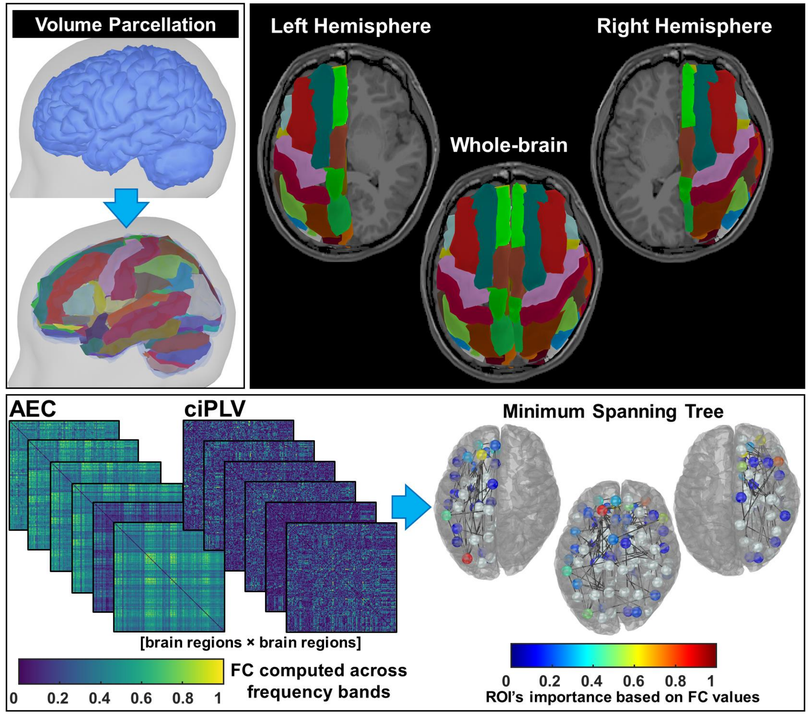

Fig. 2 FC Analysis on source reconstructed ROIs. *Top left:* Defined brain regions of interest (ROIs) obtained through a volume parcellation of cortical surfaces based on the automated anatomical labelling (AAL3) atlas; *Top right*: Each ROI's neuronal activity was reconstructed in the whole-brain, as well as separately for the left and right hemispheres, using combined ESI/MSI. *Bottom left*: For each ROI, undirected AEC and ciPLV computed for delta (1-4 Hz), theta (4-8 Hz), alpha (8-12 Hz), beta (12-30 Hz), gamma (30-70 Hz), and broadband (1-70 Hz). *Bottom right*: Brain networks generated from each averaged FC matrix using the MST

Results

- We found higher global FC in patients with DRE compared to TD for the ciPLV in (gamma band) and AEC closeness centrality (gamma and broad bands) (**Fig. 3A**).
- For patients with DRE, we found higher ciPLV (beta band) inside the pathological hemisphere, as well as higher ciPLV betweenness centrality (beta band) (**Fig. 3B**).

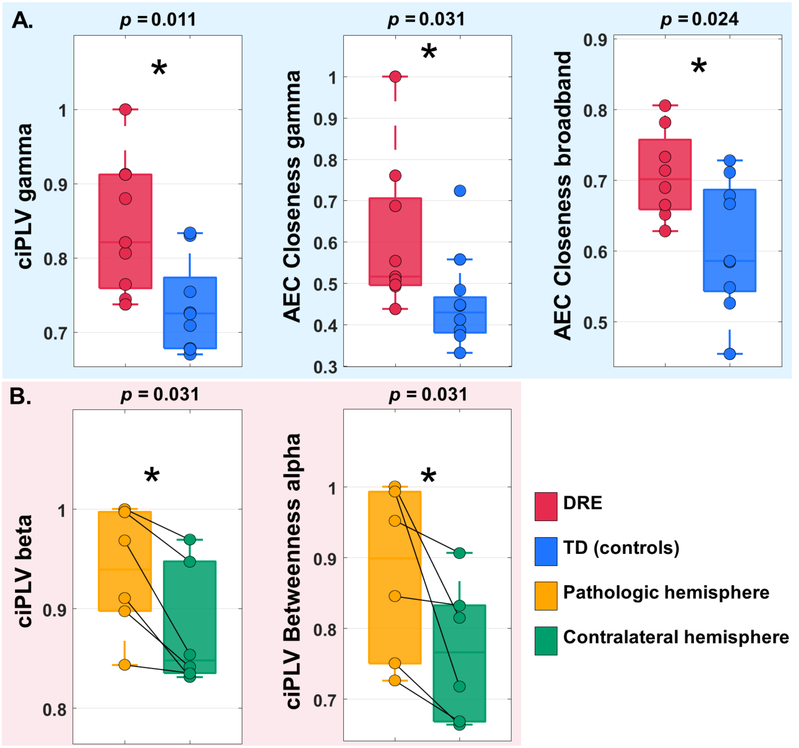

Fig. 3 Source FC results at the global and inter-hemispheric levels. (**A**) ciPLV and AEC closeness showed significant increases of whole-brain FC values for children with DRE vs. TD children in gamma and broad bands. (**B**) For children with DRE, ciPLV beta and ciPLV betweenness alpha showed significant differences between the pathological and contralateral hemispheres.

Conclusions

- Building on recent advances of neuroimaging and signal processing, we present here evidence of **aberrant FC in children with DRE** that are more prominent in the hemisphere of epileptogenic focus compared to the control one.
- Our findings may provide a better understanding of brain networks and potentially help guide surgical planning in patients with DRE.

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