Visually Evoked and Induced High Frequency Oscillations in Children with Epilepsy and Healthy Controls

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Introduction

- Epileptic seizures may arise from disrupted neural balance—either **excessive excitation** or **insufficient inhibition**. The neurophysiological hypothesis suggests a key imbalance: reduced neuronal inhibition, **altering the equilibrium** between cortical excitation and inhibition (E/I balance) in epilepsy patients (EP) .
- The cortical E/I balance is closely linked to **inhibitory GABAergic** (**γ-Aminobutyric acid**), **neurotransmission** reflected in **gamma band oscillations** (30-100 Hz). Prior studies indicate that features of gamma oscillations (i.e., peak frequency and power), assessed via non-invasive whole-head techniques such as electroencephalography (EEG) or magnetoencephalography (MEG), **correlates with GABA levels** in the human brain.
- Here, we use EEG and MEG during **visual stimulation** to **distinguish gamma oscillations in children** with epilepsy from typically developing (TD) healthy controls. Our hypothesis posits that the epilepsy group will exhibit visual-induced gamma oscillations with a **lower peak frequency** and **reduced power**.

Methods

- **Patients:** We recruited **31 TD [**Median Age: 11.61 ± 3.36 years (13 Females)] and **12 EP** [Median Age: 13.8 ± 3.68 (4 Females)].
- The participants underwent simultaneous **HD-EEG** (**256 channels**) **and MEG** (**306 channels**) recordings at ≥ 1000 Hz, while being presented with a visual stimulus (**Fig.1A**).
- EEG and MEG data were filtered from 1 to 100 Hz and notch filtered at 60 Hz. Artifact free data were segmented from -0.2 to 0.5 s after presentation of visual stimuli (**Fig.1B &C**).
- The cortical activity in the **primary visual cortex (V1)** was mapped using dynamic statistical parametric modelling (dSPM). For solving the forward problem, we used realistic **Boundary Element Method**. Virtual channels within V1 were reconstructed through electric and magnetic source imaging (**Fig.1D**).
- We estimated evoked and induced activity with the V1 in both children with EP and TD (**Fig.1E**).
- Comparisons for evoked and induced activity between the two groups were performed using Monte Carlo permutation (1,000 permutations) (corrected for multiple comparisons with FDR).

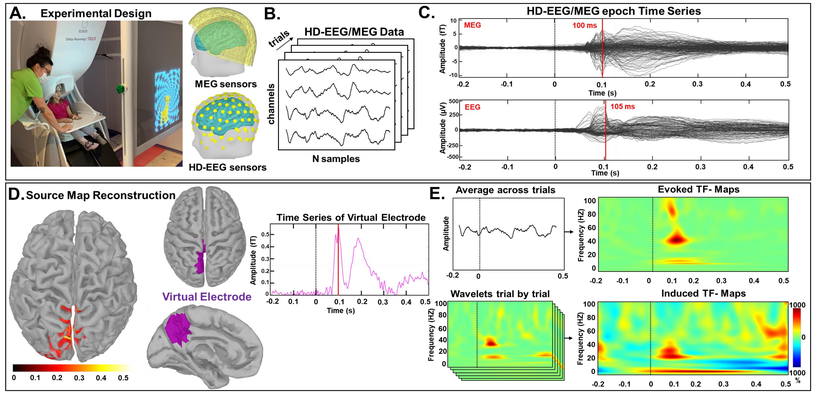

Figure 1: (**A**) Simultaneous HD-EEG and MEG recordings were conducted in a magnetically shielded room, with participants viewing a full-screen checkerboard pattern featuring a central cartoon character as a stimulus. (**B**) HD-EEG and MEG data were segmented around the visual stimuli. (**C**) Visual-evoked fields and potentials (VEFs/VEPs) for a 15-year-old female with EP child (**D**) Electric and Magnetic source imaging using the dSPM technique depicting the time series of the virtual channel with maximum activation. (**E**) Time-frequency analysis of electric and magnetic brain activity at virtual channels was performed using a complex Morlet wavelet.

Results

- Visual stimulation resulted in a **prominent cortical response** at the virtual channel within V1 for both TD and EP participants.
- Statistical analysis of TF-maps generated from VEPs showed that in the gamma frequency band, individuals with epilepsy exhibited **reduced relative power** compared to TD participants [gamma: 2470% ± 1613 vs. 4530% ± 1878; p<0.001] (**Fig. 2 & 4A**).
- The **suppression of relative power** was observed from **~30 till ~150** ms after the stimulus onset between **~40 and ~70 Hz** for the gamma band (**Fig. 2**). Similarly, we observed low gamma peak frequency for EP compared to TD participants [peak frequency: 48 Hz ± 15 vs. 36 ± 11; p<0.05] (**Fig. 4B**). No differences of relative power between the two groups were observed for induced activity (p>0.05).

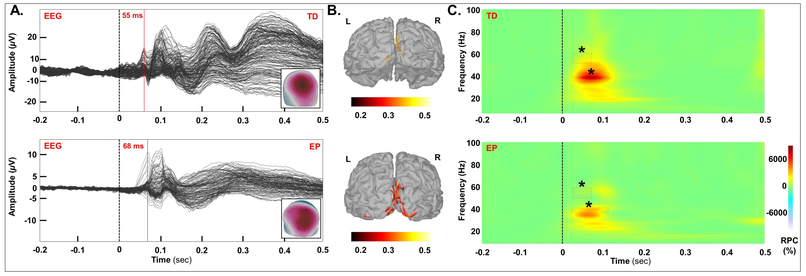

Figure 2: (**A**) Averaged visual-evoked potentials of a 13-year-old male TD (upper panel) and a 15-year-old female with EP (lower panel). Inner panels show topography field maps at the peak of the first cortical response for both groups. (**B**) Source activation maps at V1 (cuneus) using dSPM for TD and EP participants. (**c**) Grand average time-frequency maps, expressed as percentages relative to the baseline [-0.2; 0 s], displayed for TD (upper panel) and EP (lower panel) participants.

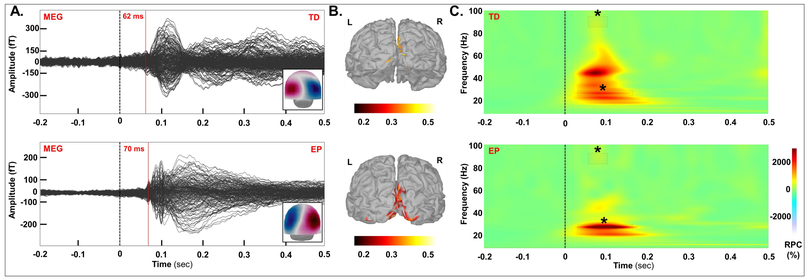

Figure 3: (**A**) Averaged visual-evoked potentials of a 13-year-old male TD (upper panel) and a 15-year-old female with EP (lower panel). Inner panels show topography field maps at the peak of the first cortical response for both groups. (**B**) Source activation maps at the primary visual cortex (cuneus) using dynamic statistical parametric mapping for TD and EP participants. (**c**) Grand average time-frequency maps, expressed as percentages relative to the baseline [-0.2; 0] sec, displayed for TD (upper panel) and EP (lower panel) participants.

- Statistical analysis of TF-maps generated from VEFs showed that in gamma frequency, individuals with epilepsy exhibited reduced relative power compared to TD. [gamma: 2837% ± 905 vs. 4716% ± 1500; p<0.001] (**Fig. 3C & 4C**).
- The **suppression of relative power** was observed from **~20 till ~180 ms** after the stimulus onset between **~30 and ~60Hz** for the low-gamma and **~85 and ~100 Hz** for the high-gamma band (**Fig. 3C**). No differences of relative power between the two groups were observed for induced activity (p>0.05).

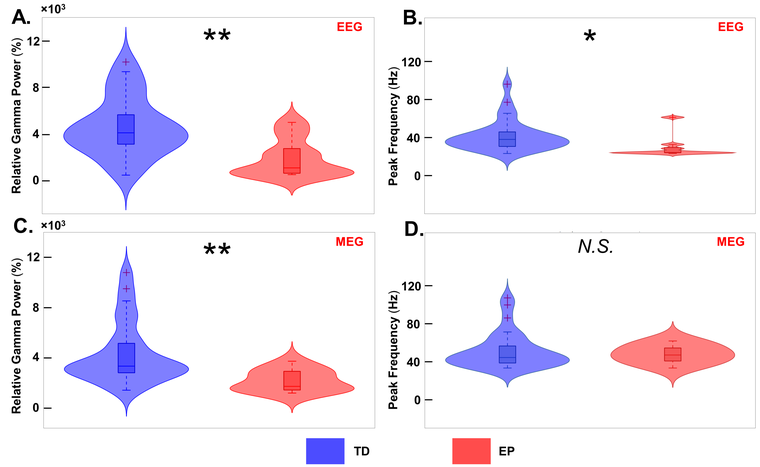

Figure 4: (**A & C**) Comparison of relative gamma power between TD (Blue) and EP (Red) participants. The top panel displays relative gamma power obtained from EEG, while the bottom panel shows gamma power from MEG. (**B & D**) Comparison of gamma peak frequency between TD and EP participants. The top panel displays gamma peak frequency obtained from EEG, while the bottom panel shows gamma peak frequency from MEG (* p value ≤ 0.05; ** p value ≤ 0.001).

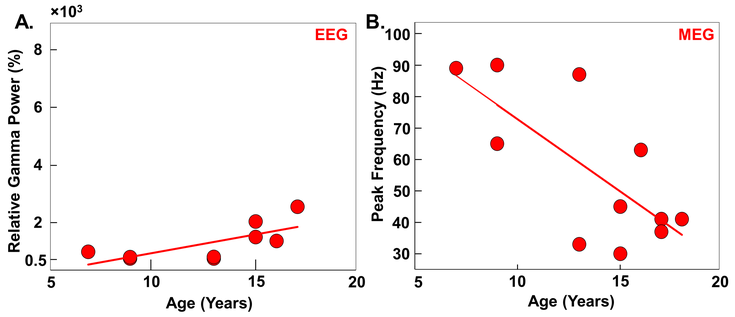

Figure 5: (**A**) Correlation of relative gamma power obtained from EEG and age of EP participants. (**B**) Comparison of gamma peak frequency obtained from MEG and age of EP participants. Red lines = best fit, linear; Pearson correlation analysis was performed to obtain correlation coefficients and p-values.

- We observed a positive correlation between gamma power measured by EEG and age of EP participants (r=0.71; p=0.031; **Fig. 5A**). No such correlation was observed for TD participants.
- Additionally, we observed a negative correlation between peak frequency measured by MEG and age of EP participants (r= -0.73; p=0.01; **Fig. 5B**). No such correlation was observed for TD participants.

Conclusions

Our study contributes to the understanding of the **pathophysiological mechanisms of evoked gamma oscillations**. Identifying **distinctive markers and patterns** in these **high-frequency oscillations** may help differentiate normal brain function from epilepsy-related pathological activity.

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