Connectivity levels co-segregate genetic generalized epilepsy patients and asymptomatic siblings

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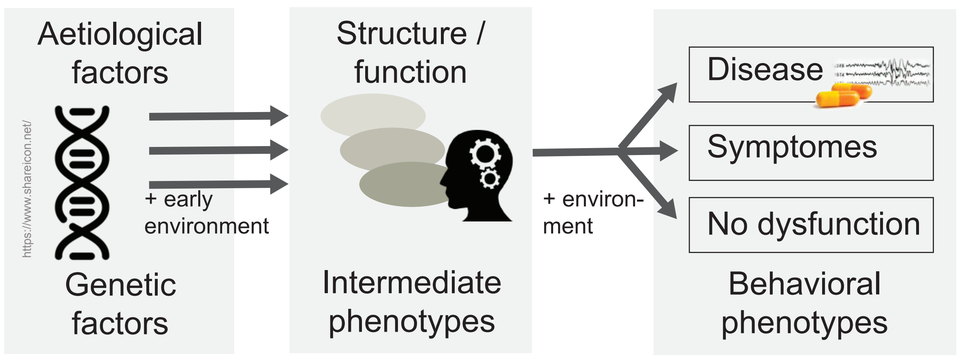
Background

Idiopathic generalized epilepsy/genetic generalized epilepsy (IGE/GGE) is a common epilepsy syndrome and the exact aetiology is unknown.

Family and twin studies revealed strong clinical evidence for a complex genetic aetiology[1]. The identification of causal genetic determinants has failed so far. Thus, it is of high interest to seek for components of the syndrome with a simpler inheritance than the full disease.



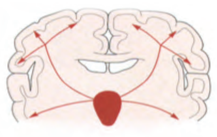
We studied MEG resting connectivity and hypothesized alterations in IGE/GGE patients and, to a lesser extent, also in their unaffected siblings.

Sample

- 25 IGE/GGE patients (64% fem, mean 30 y, SD 11 y)
- 18 unaffected siblings (55% fem, mean 31 y, SD 11 y)
- 45 controls (62% fem, 31 y, mean SD 12 y)

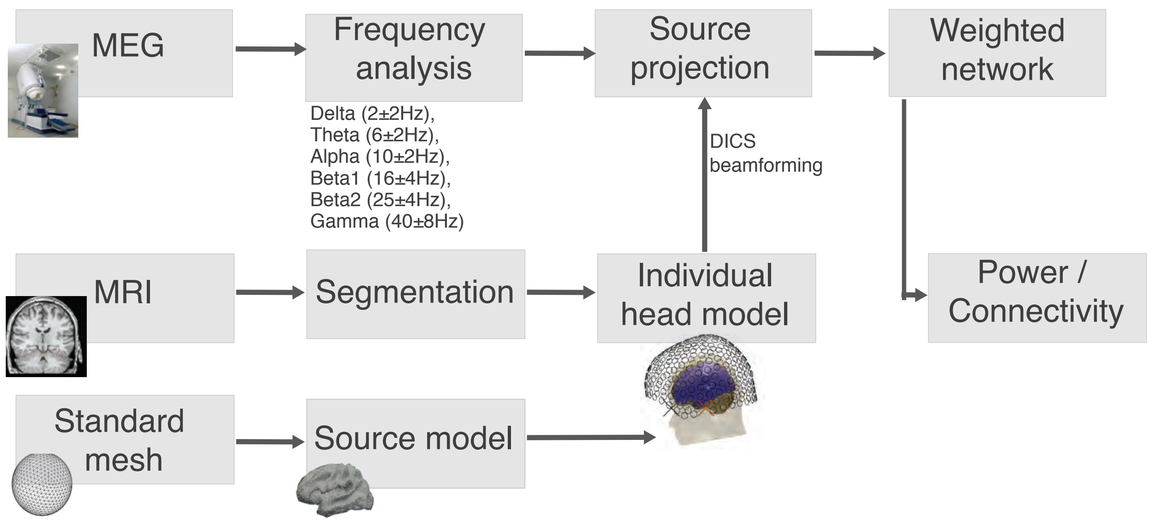
All patients received anticonvulsive treatment. 13/25 patients were seizure-free at least for 12 months at timepoint of measurements.

IGE/GGE is characterized by various seizures types (absences, myclonica, generalized tonic-clonic seizures), which are presumably generated in bilateral brain networks.



Methods

MEG network analysis



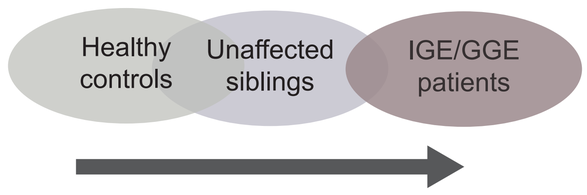
Statistical analysis

Group differences on the vertex level, i.e. on the cortical and subcortical surface, and on a global level (average across vertices) were investigated for the Imaginary part of Coherency (Nolte et al. 2014) as our connectivity measure.

Multilevel Permutation Analysis of Linear Models (PALM) was applied. (regressors: group, age; 5000 permutations, FWE correction on cluster level)

Discussion

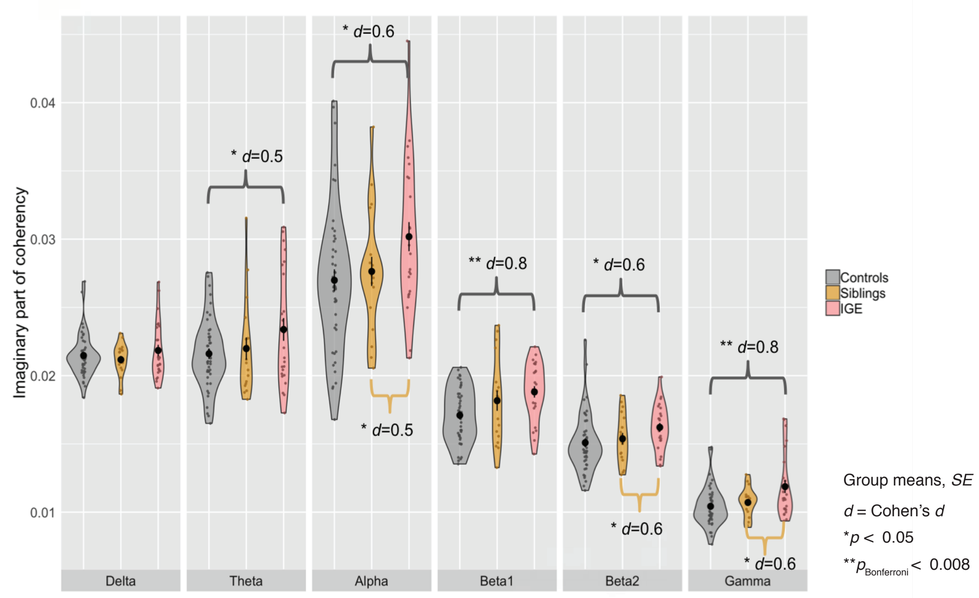
In accordance with previous studies[2], IGE/GGE patients showed elevated connectivity levels during rest. Siblings, without a history of epilepsy or seizures in the past, presented with a weaker but similar trend across the frequency spectrum. This indicates that increased connectivity could be a precursor condition of IGE/GGE, independent of disease activity and treatment.



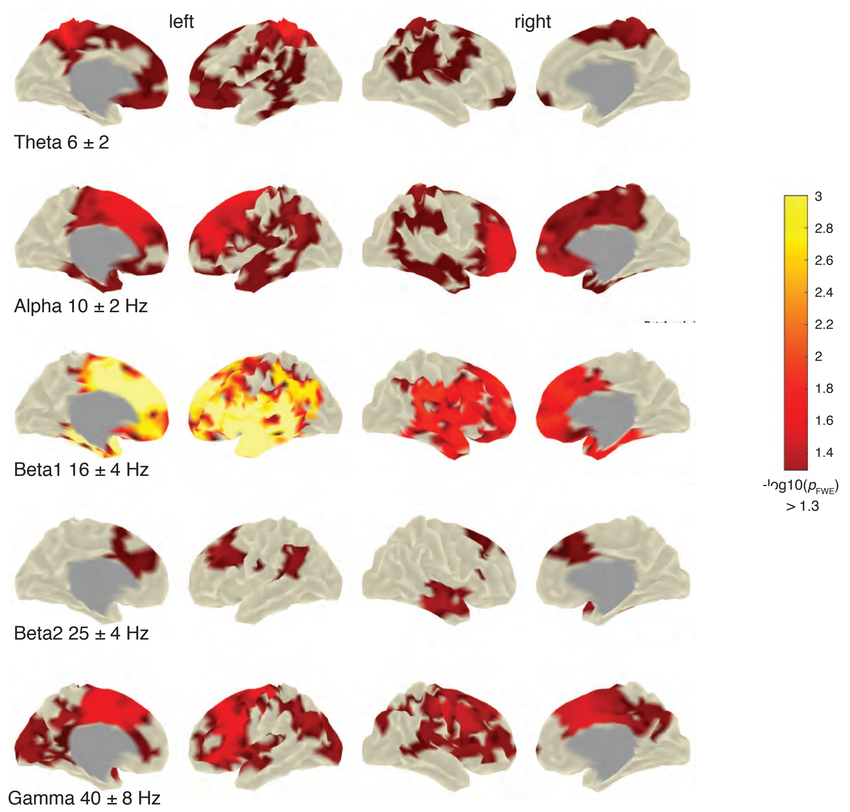
Measures of network connectivity provide means to identify diease-associated genes and elucidate neurobiological processes contributing to the disease.

Results

Increased global connectivity in patients and siblings



Vertex-based connectivity increase in patients vs. controls



Compared with controls, IGE/GGE patients showed significantly increased functional connectivity in most of the frequency bands studied and over widespread bilateral medio-frontal, temporal and parietal regions (theta to gamma, $p_{FWE} < 0.05$). Connectivity levels of siblings statistically fell between IGE/GGE patients and healthy controls (not shown).

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[1]Berkovic, S.F., et al. Epilepsies in twins: genetics of the major epilepsy syndromes. Annals of neurology 43.4 (1998)
[2]Hegner, Y., et al. Increased Functional MEG Connectivity as a Hallmark of MRI-Negative Focal and Generalized Epilepsy. Brain topography 31.5 (2018)