Structural Connectome Abnormalities in Non-Lesional Frontal Lobe Epilepsy

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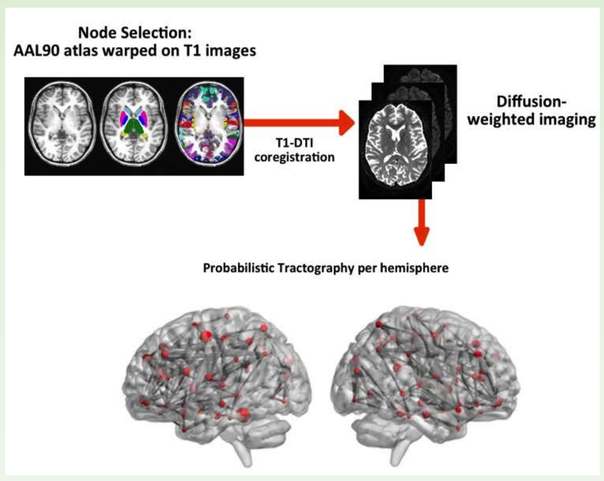
INTRODUCTION

Frontal lobe epilepsy (FLE) is a common form of epilepsy (1) in which seizure onset is usually caused by a lesion or by a cortical dysplasia. This leads to great variability in the brain characteristics of patients, raising issues in identifying homogeneous samples for neuroimaging studies. However, some patients with FLE can be defined non lesional (nlFLE), i.e., seizures start in the frontal lobe, but there is no clearly identifiable abnormality on magnetic resonance imaging (MRI). For this reason, nlFLE patients represent an ideal sample for the study of the epileptic syndrome itself, regardless of the nature and location of the epileptogenic focus.

In this study, we applied graph-analysis analysis to diffusion MRI data of nlFLE patients and healthy controls, in order to analyze network, rather than local, properties that may be altered due to the disease.

MATERIALS AND METHODS

Patients & MRI acquisition: Twenty-two patients with nlFLE (7 female, mean age (standard deviation) 37.0 (15.5)) and 22 age- and sex-matched healthy controls underwent the same 3 Tesla MRI protocol including whole-brain, 3D T1-weighted, spoiled gradient recall echo (TE/TR = 3.7/ 9.2 ms, flip angle 12° , voxel size= $1 \times 1 \times 1$ mm^3) and diffusion-weighted MRI (b=1000 s/mm2; diffusion-weighting along 27 non-collinear gradient directions; matrix size 128 × 128; 80 axial slice; number of b0 images = 4; NEX = 2; voxel size = $2 \times 2 \times 2$ mm^3).



Connectome reconstruction: The structural connectome (2) was computed as follows. The AAL90 atlas was used to identify cortical and subcortical regions to be used as nodes of the network. Probabilistic tractography in network-mode was used to obtain connectivity matrices, in which each entry represented the number of probabilistic fibers connecting regions i and j.

Graph analysis: Entries of the matrices were normalized by the total number of generated fibers, and the following graph-based measures were computed at different network densities [ten values from 0.001 to 0.01]: clustering coefficient, measuring how strongly inter-connected neighboring nodes are; shortest path length and global efficiency, related to the global integration of the network; the nodal efficiencies, related to the importance of a node in the network. All measures were compared through analysis of covariance, with age, sex and intracranial volume as covariates.

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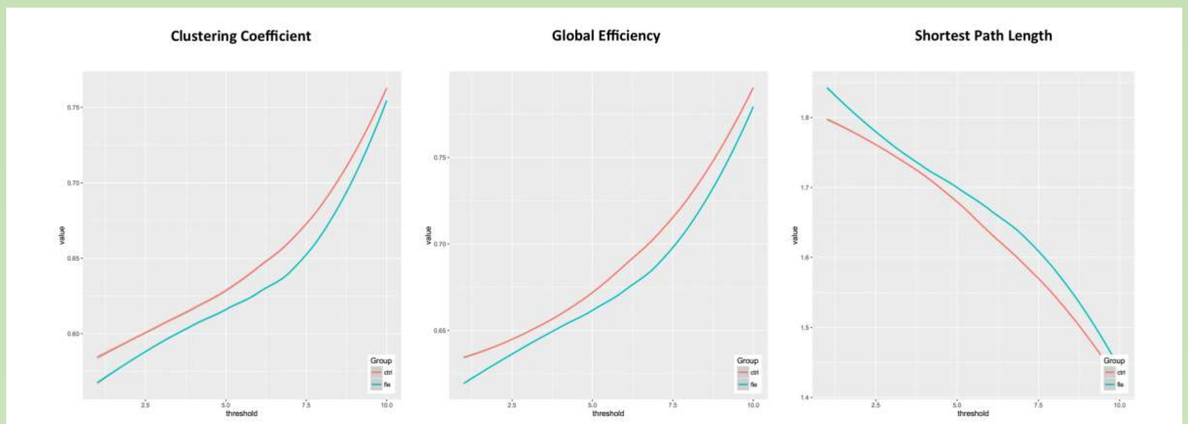
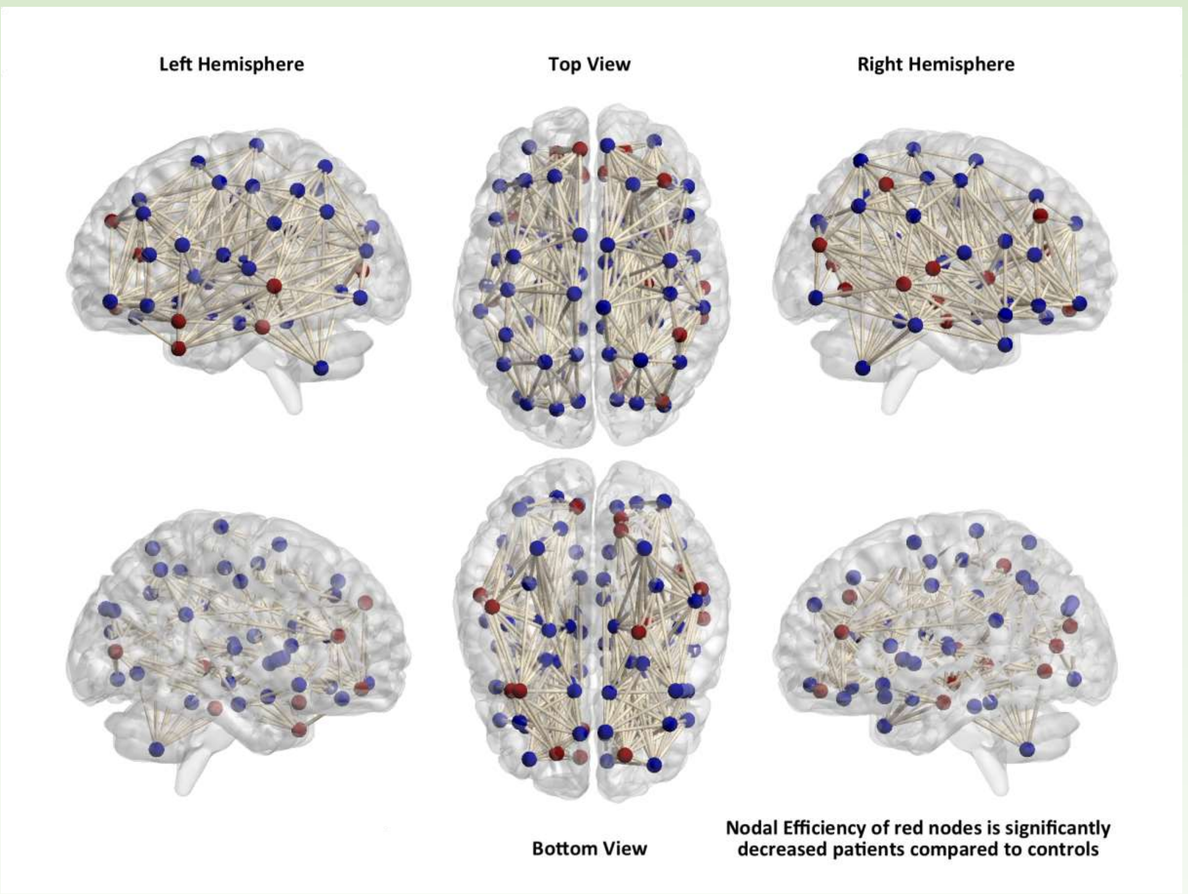
RESULTS

Figure 1: Clustering coefficient, global efficiency and shortest path length in nlFLE patients and healthy controls.



Patients with nlFLE showed abnormalities in network properties at both global and nodal level. In particular, across all network densities, patients showed significantly lower values of global efficiency (p=0.003) and clustering coefficient (p=0.001), whereas the shortest path length was lower in the control group (Figure 1). At the nodal level, we observed that several regions, not limited to the frontal lobe (Figure 2), had decreased nodal efficiency in patients compared to healthy controls (p<0.05 corrected).

Figure 2: Nodal efficiency in the structural connectome of non lesional frontal lobe epilepsy and healthy controls. Red nodes have significantly reduced efficiency in patients.



CONCLUSIONS

The absence of focal lesions allowed us to explore the characteristics of a uniform sample, and thus to observe that nlFLE involves the brain as a network that goes beyond the frontal lobe, rather than affecting a specific region.

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