Structural Connectivity Abnormalities in Adult Patients with Frontal Lobe Epilepsy: A Pilot Study

Ezequiel Gleichgerrcht[1], Heath Pardoe[2], Ruben Kuzniecky[3], Leonardo Bonilha[1]

1. Department of Neurology, Medical University of South Carolina, Charleston, SC, USA
2. Department of Neurology, New York University School of Medicine, NYC, NY
3. Department of Neurology, Hofstra Northwell School of Medicine, NY

@e_gleich
@bonilha_lab

Background

- With the advancement of computational models and neuroimaging techniques to map the structure and function of the human brain, it has now become evident that epilepsy, both focal and generalized, is a disorder of abnormal brain networks.
- Several studies have sought to understand whether patients with frontal lobe epilepsy (FLE) demonstrate macro- and/or microscopic changes in their brain networks.
- The majority of studies have focused on functional connectivity, most commonly by means of resting state fMRI.
- A smaller number of studies have focused on structural connectivity, that is, the physical white matter pathways that link different regions of the brain, although these were conducted mostly among pediatric populations, or concentrated on specific sub-regions (e.g. supplementary motor area), or analyzed specific DTI features (e.g. functional anisotropy).
- The goal of this pilot study was, rather, to compare the structural connectome of adult patients with FLE and healthy controls using a "whole brain" approach.
- By doing so, we sought to identify potentially anomalous white matter tracts among patients with FLE in terms of fiber density (i.e., significantly stronger or weaker than paired controls) without *a priori* anatomical assumptions and to protray the potential utility of structural connectome analysis in epilepsy

Methods & Results

- Eight adult patients with diagnosis of FLE (50% male, aged 35.1 ± 12.0) and twenty age- ($t_{26} = 0.86$, $p = .40$) and gender- ($\chi^2 = 0.54$, $p = .46$) matched controls (35% male, aged 31.1 ± 10.8) underwent MRI diffusion tensor imaging
- Their structural connectomes were constructed using probabilistic tractography based on a cortical atlas (AICHA) of 384 distinct regions of interest (ROI).
- We then conducted whole brain link-by-link t-test comparisons between patients and controls.

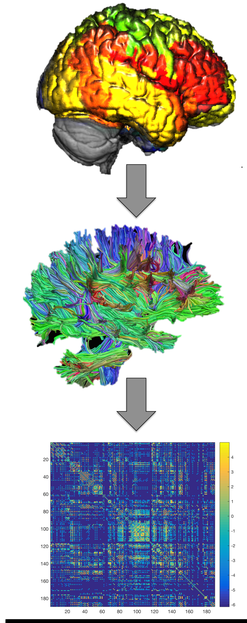
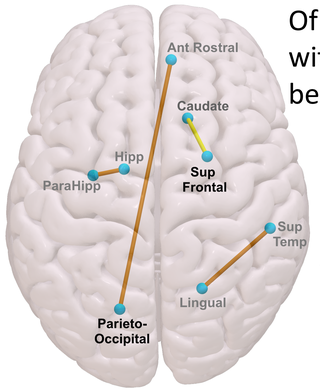


Figure 1. Building the structural connectome. A high resolution gray matter image (e.g. T1) in normalized space is segmented into regions of interest (ROIs) based on a predefined neuroanatomical atlas.

Probabilistic or deterministic tractography is then applied to compute the probability or strength of all possible connections between all ROIs.

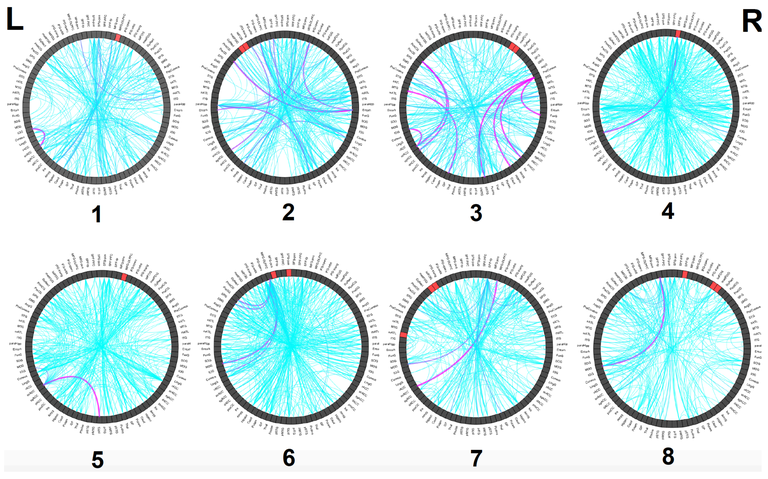
The structural connectome can then be represented as a two-dimensional matrix where each row and each column represents a ROI, with each cell of the matrix representing the weight of each link. This matrix can be subjected to pairwise comparisons as well as to the computation of graph theory measures.



Of all possible 147,072 connections (based on the AICHA atlas with 384 ROIs), **four** were significantly different ($p < .001$) between patients and controls.

Figure 2. Two connections involved a ROI in the frontal lobes: R sup frontal gyrus to R caudate was significantly stronger among controls ($t = 4.29$, $p = .0002$), and R anterior rostral region to L parieto-occipital area was significantly stronger among patients ($t = -4.05$, $p = .0004$). Two connections were extra-frontal and both were stronger among patients with FLE: R lingual gyrus to R sup temporal region ($t = -4.49$, $p = .0001$), and L hippocampal and parahippocampal areas ($t = -4.15$, $p = .0003$).

Figure 3. Each patient's individual structural connectome is represented by means of a circular diagram where each box represents ROI. Red ROIs represent the most approximately equivalent epileptogenic focus as identified clinically. Only links with Z > 2 relative to the control group are shown. Thicker lines with more purple tint represent higher Z values.



Conclusions

This pilot study employed a whole brain comparison of the structural connectome between patients with FLE and healthy controls to identify abnormal brain links. We showed that a small number of connections involving both frontal and extra-frontal regions are abnormally strong or weaker among patients. The varied nature of these abnormal links likely reflects the heterogeneous small sample of patients analyzed here, but these results shed light on the potential clinical and theoretical utility of studying the structural connectome in epilepsy.