NeuroImage: Clinical 8 (2015) 322–328

Contents lists available at ScienceDirect

NeuroImage: Clinical

journal homepage: www.elsevier.com/locate/ynicl

Structural connectivity changes in temporal lobe epilepsy: Spatial features contribute more than topological measures

Peter N. Taylor [a,1], Cheol E. Han [b,c,1], Jan-Christoph Schoene-Bake [d,e], Bernd Weber [e,f], Marcus Kaiser [a,g,*]

[a] Interdisciplinary Computing and Complex BioSystems (ICOS) Research Group, School of Computing Science, Newcastle University, United Kingdom
[b] Dept. of Biomedical Engineering, Korea University, Seoul, Republic of Korea
[c] Dept. of Brain and Cognitive Sciences, Seoul National University, Republic of Korea
[d] Center for Pediatric and Adolescent Medicine, Freiburg University, Freiburg, Germany
[e] Dept. of Epileptology, University of Bonn, Bonn, Germany
[f] Center for Economics and Neuroscience, University of Bonn, Bonn, Germany
[g] Institute of Neuroscience, Newcastle University, United Kingdom

ARTICLE INFO

Article history:
Received 28 October 2014
Received in revised form 23 January 2015
Accepted 14 February 2015
Available online 20 February 2015

Keywords:
Epilepsy
Diffusion MRI
Brain network
Temporal lobe
Connectome

ABSTRACT

Background: Previous studies reported reduced volumes of many brain regions for temporal lobe epilepsy (TLE). It has also been suggested that there may be widespread changes in network features of TLE patients. It is not fully understood, however, how these two observations are related.
Methods: Using magnetic resonance imaging data, we perform parcellation of the brains of 22 patients with left TLE and 39 non-epileptic controls. In each parcellated region of interest (ROI) we computed the surface area and, using diffusion tensor imaging and deterministic tractography, infer the number of streamlines and their average length between each pair of connected ROIs. For comparison to previous studies, we use a connectivity 'weight' and investigate how ROI surface area, number of streamlines & mean streamline length contribute to such weight.
Results: We find that although there are widespread significant changes in surface area and position of ROIs in patients compared to controls, the changes in connectivity are much more subtle. Significant changes in connectivity weight can be accounted for by decreased surface area and increased streamline count.
Conclusion: Changes in the surface area of ROIs can be a reliable biomarker for TLE with a large influence on connectivity. However, changes in structural connectivity via white matter streamlines are more subtle with a relatively lower influence on connection weights.

1. Introduction

Epilepsy is a neurological disease characterised by abnormal electrophysiological events, leading to recurring seizures in the brain. Epileptic seizures can be broadly grouped into two categories. Generalised seizures involve widespread distributed bilateral networks, whilst focal seizures are limited to one hemisphere and involve a more localised area (Berg et al., 2010). The most common form of epilepsy is medial temporal lobe epilepsy (TLE) which most frequently occurs in the left hemisphere. Despite the traditional view of focal and generalised seizures being different in terms of their extent, recent evidence suggests involvement of brain areas far beyond the temporal lobe in TLE patients (Richardson, 2012).

Changes in grey matter volume and concentration have been shown in many brain regions in patients with TLE. Specifically, volumetric decreases have been shown in the amygdala, thalamus, entorhinal cortex, caudate nucleus, putamen and globus pallidus amongst others (DeCarli et al., 1998; Pitkänen et al., 1998; Bernasconi et al., 2004; Keller and Roberts, 2008; Meade et al., 2008). These changes are clearly wide-ranging and, although technically categorised as focal epilepsy, do involve several brain areas.

An alternative in considering brain regions on an individual basis is to consider a network of brain regions interconnected via the white matter. At the macroscopic scale, diffusion weighted magnetic resonance imaging (DW-MRI) has emerged in recent years as a valuable tool for inferring anatomical brain connectivity between brain regions (Le Bihan and Johansen-Berg, 2012; De Reus and Van den Heuvel, 2013). Some studies have found differences in TLE patient connectivity. Bonilha et al. (2012) showed a decrease in connectivity between bilateral posterior cingulate regions. Further decreases in connectivity to several other areas were also reported in the limbic network, though they were not significant after correction for false discovery rate (FDR) (Genovese et al., 2002). In a separate study by the same group patients had reduced connectivity between thalamic and precentral areas in

* Corresponding author.
E-mail address: m.kaiser@ncl.ac.uk (M. Kaiser).
[1] Both authors contributed equally.

http://dx.doi.org/10.1016/j.nicl.2015.02.004

addition to increased connectivity between parietal and supramarginal areas (Bonilha et al., 2013). In both studies the connectivity was determined as the number of streamlines between two areas, normalised by the total volume of the two areas. Another recent analysis of DW-MRI inferred connectivity in patients with left TLE also showed differences in the anatomical network of patients when compared to controls (Liu et al., 2014). That study also normalised connections between two ROIs by their average volumes. De Salvo et al. (2014) showed in patients with TLE decreases in connectivity from the cingulate, precuneus and orbitofrontal regions to other areas within the same module. In that study the connectivity weight was defined as a combination of the surface area, number of connecting streamlines and the average streamline length.

Thus, many of the previous studies of anatomical connectivity in TLE between two regions of interest (ROI) have combined (a) the number of streamlines with (b) measures influenced by the size of those ROIs (either volume or surface area) into a single value: a connection weight. Since widespread variation has been shown in the volume and surface size of many ROIs, it is unclear how each of the two measures contributes to connectivity. In this study, we systematically elucidated the changes in surface area, the changes in connectivity between areas, and their contribution to connections weights.

2. Methods

2.1. Subjects and MRI acquisition

We collected 22 left temporal lobe epilepsy subjects and 39 age-matched controls. All patients have medial temporal lobe epilepsy with unilateral hippocampal sclerosis according to MRI criteria with ipsilateral seizure onset during non-invasive/invasive EEG monitoring and underwent epilepsy surgery (selective amygdalohippocampectomy) afterwards. Further details on the subject population can be found in Table S1. For all subjects, we obtained T1-weighted MR images and diffusion-weighted MR images with a 3 Tesla scanner (Siemens MAGNETOM Trio Tim syngo, Erlangen, Germany). T1-weighted MRI data were recorded with 1 mm isovoxel, FoV 256 mm, TR = 2500 ms, and TE = 3.5 ms. DTI data were recorded with 2 mm isovoxel, FoV = 256 mm, TR = 100,000 ms, TE = 91 ms, and 64 diffusion directions with *b*-factor of 1000 s mm^{-2} and 12 *b*0 images.

2.2. Network construction

We used FreeSurfer to obtain surface meshes of the boundary between grey matter and white matter from T1 anatomical brain images (http://surfer.nmr.mgh.harvard.edu, cf. Fig. 1; Image processing on the Left Side). After registering surface meshes into the diffusion space, we generated volume regions of interest (ROIs), which are voxels in the grey matter. FreeSurfer provides parcellation of anatomical regions of cortices (34 for each hemisphere) based on the Desikan atlas (Fischl et al., 2004; Desikan et al., 2006) and subcortical regions (Fischl et al., 2004, 2002) of which seven for each hemisphere (nucleus accumbens, amygdala, caudate, hippocampus, pallidum, putamen, and thalamus) were included (see Fig. 2a for names of ROIs). Thus, our structural brain networks, observing both hemispheres, consisted of 82 cortical and subcortical regions in total. Parcellation and registration were manually checked for errors by visual inspection.

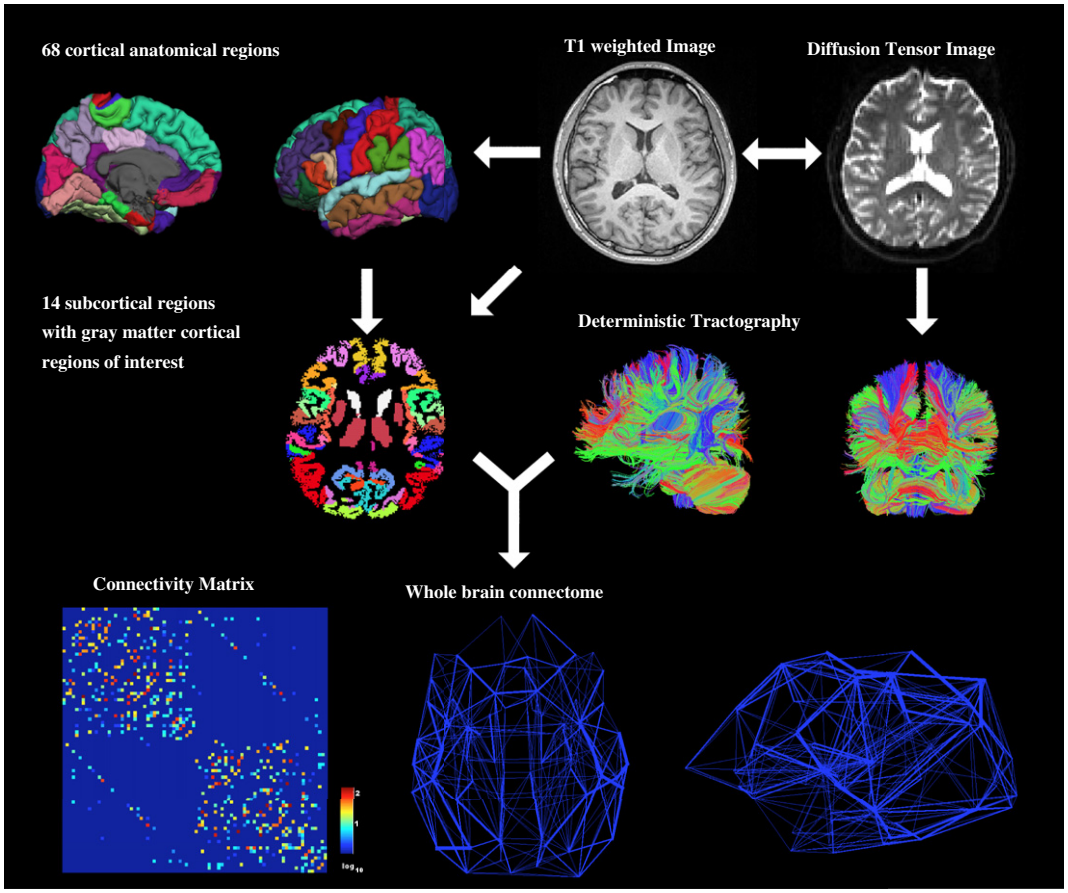

Fig. 1. Overall procedure. From T1-weighted images, we generated 82 regions of interest (ROIs, 34 cortical areas and 7 subcortical areas a hemisphere, on the left). From diffusion weighted images, we reconstructed streamlines using deterministic tracking (on the right). Combining these two pre-processing steps, we constructed a weighted network where weights are determined by the number of streamlines connecting two ROIs.