Structural Graph Analysis of Left and Right Temporal Lobe Epilepsy using Diffusion Spectrum Imaging

Alia Lemkaddem[1], Alessandro Daducci[1], François Lazeyras[2], Margitta Seeck[3], Jean-Philippe Thiran[1,4], and Serge Vulliemoz[3]

[1]Signal Processing Laboratory (LTS5), Ecole Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland, [2]Dpt of Radiology, University Hospital of Geneva, Switzerland, [3]EEG and Epilepsy Unit, Neurology clinic, University Hospitals and Faculty of Medicine of Geneva, Switzerland, [4]Dpt of Radiology, University Hospital Center (CHUV) and University of Lausanne (UNIL), Switzerland

PURPOSE

Patients with Temporal Lobe Epilepsy (TLE) suffer from widespread subtle white matter abnormalities and abnormal functional connectivity extending beyond the affected lobe, as revealed by volumetric and functional MRI studies. Diffusion Magnetic Resonance Imaging and fiber-tracking offer a noninvasive technique for mapping human brain connectivity and have been increasingly used to study patients with epilepsy.

In this study we investigated the effects of two types of TLE (right-sided and left-sided) on the global characteristics of brain connectivity estimated by topological measures to reduce the complexity of its interpretation. We used Diffusion Spectrum Imaging (DSI)[1], a high angular resolution diffusion technique, to address the difficulty of Diffusion Tensor Imaging (DTI) to disentangle multiple fiber orientations in a single voxel. Further, a global tractography[2] method was utilized to reconstruction the non-dominate pathways[3].

METHODS

21 healthy volunteers and 20 unilateral (11 right TLE and 9 left TLE) TLE patients underwent DSI (voxel size = 2.2x2.2x3 mm; 44 slices; 257 diffusion directions; max b-value = 6400 s/mm^2), T1-weighted MPRAGE (TR/TE = 2300/2.86 ms, voxel size = 1x1x1.2 mm, 160 slices) and T2-weighted (TR/TE = 3200/408 ms, voxel size = 1x1x1.2 mm, 160 slices) images on a 3T Trio a Tim System (Siemens, Erlangen, Germany) using a 32-channel head coil.

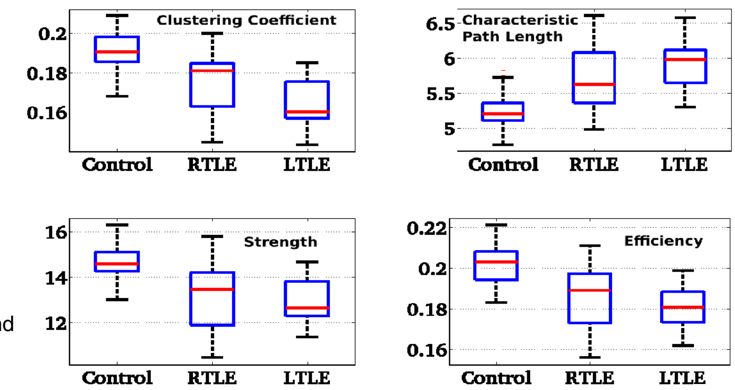
The analysis was carried out using the Connectome Mapping Toolkit (cmtk)[4]. In details, 43 regions of interest (ROI) with anatomical landmarks were mapped from individual T1 weighted images using Freesurfer 5.0 software[5] for each hemisphere. The ROIs were co-registered to the diffusion image space using a nonlinear registration between T1 to T2 , then T2 to the diffusion space[6]. A whole brain tractography was performed in the white matter areas using Gibbs tracking[2], a global tractography method based on fitting a model to the acquired data using energy functions. Next, the GFA (Generalized Fractional Anisotropy)[7] was computed from the ODFs (Orientation Distribution Function). For each subject a connectivity matrix (which represents the adjacency matrix of the corresponding network or graph) was computed to quantify the mean GFA value along all fiber-bundles connecting any pair of ROIs. Finally, we estimated the following properties[8] of these networks: *Characteristic Path Length* or *Shortest Path*, *Clustering Coefficient*, *Strength* and *Efficiency*. A Wilcoxon rank-sum test was used to assess the significant difference between the TLE patient groups and the healthy subject group.

RESULTS AND DISCUSSION

All the four global features of the connectivity networks showed a significant difference for both patient groups (RTLE and LTLE) vs the control group. As shown in the figure below, we found a higher *Characteristic Path Length* (RTLE: p=0.007 and LTLE: p=0.000493), lower *Clustering Coefficient* (RTLE: p=0.0079 and LTLE: p=0.00025), lower *Strength* (RTLE: p=0.0088 and LTLE: p=0.00081) and lower *Efficiency* (RTLE: p=0.0099 and LTLE: p=0.00042). The connectivity alterations were bilateral, although with a clear predominance for the ipsi-lateral hemisphere. Temporal as well as extra-temporal structures were affected. These results suggest that the global interaction between the nodes is decreased and that there is a lack of specialized communities, meaning that the network of the patient group is less segregated compared to the control group.

CONCLUSIONS

These global measures of the structural connectivity as estimated with DSI suggest that the network organization of unilateral TLE is less efficient compared to the control group, in relation to alteration of intra-temporal and extra-temporal connections in both hemispheres. The results of our white matter connectivity analysis are concordant with previous reports of altered functional connectivity in TLE studied with fMRI and intracranial EEG[9] as well as with altered structural networks based on grey matter thickness using T1-volumetry[10]. Further studies are needed to establish the relevance of these findings for the propagation of epileptic activity, cognitive deficits in TLE and outcome of epilepsy surgery.



REFERENCES

[1] V.J Wedeen et al, *NeuroImage,* 41 (2008),
[2] Reisert et al, *NeuroImage*, 54:955-62 (2011),
[3] C. Anastasopoulos et al, *AJNR*, (2013)
[4] Daducci et al, *PlosOne*, 7(12):e48121(2012),
[5] http://surfer.nmr.mgh.harvard.edu,
[6] http://www.fmrib.ox.ac.uk/fsl,
[7] D.S Tuch, *Magnetic Resonance in Medicine* 52 (2004),
[8] *Networks of the Brain* by Olaf Sporns (Oct 1, 2010),
[9] Bettus et al *Hum Brain Mapp* 30: 1580–1591 (2009),
[10] B.C. Bernhardt et al, *Cerebral Cortex* 21:2147-2157 (2011)

Acknowledgements: SNF No.No205321-144529, 33CM30-124089 and 320030-122073, 140332 and 141165, the Centre for Biomedical Imaging (CIBM) of Geneva and Lausanne.