Graph-theoretical analysis of DTI reveals disruption in global and regional structural networks in children with localization-related epilepsy

Mojdeh Zamyadi[1], Carter Snead[1], Sam Doesburg[1], Mary Lou Smith[1], and Elysa Widjaja[2]
[1]*Neurosciences and Mental Health, The Hospital for Sick Children, Toronto, Ontario, Canada,* [2]*Diagnostic Imaging, The Hospital for Sick Children, Toronto, Ontario, Canada*

Introduction: Children with localization-related epilepsy (LRE) have abnormal resting state functional connectivity in various brain networks, and altered graph theoretical measures of functional connectivity[1]. However, less is known about structural connectivity in children with LRE other than frontal lobe epilepsy (FLE). This study aims to investigate the structural networks using graph theoretical measures in children with LRE and the subgroups with FLE and temporal lobe epilepsy (TLE), and to assess the relation between structural connectivity, IQ and other clinical parameters.

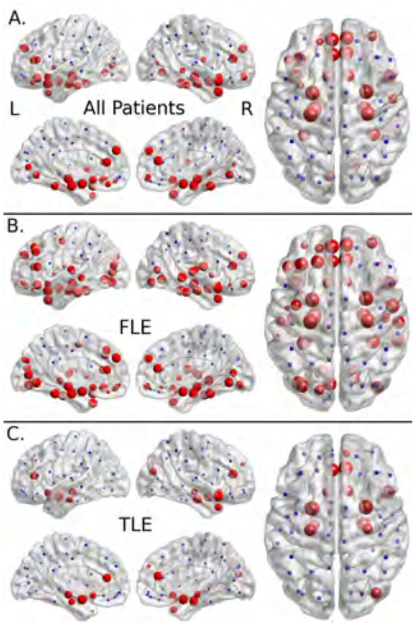

Fig 1. Reduced E_{nod} in: all LRE (A), FLE (B), TLE (C) patients relative to controls. Red: disrupted nodes with reduced E_{nod}; blue: unaffected nodes. The size of the nodes is related to the significance of between-group differences in E_{nod} between the two groups.

Methods: 45 children with non-lesional LRE including 25 with FLE and 16 with TLE, as well as 28 healthy controls were recruited. Volumetric T1 and DTI images were acquired in all subjects on Philips 3T scanner. Probabilistic fiber tracking was initiated from the grey/white matter boundary. DTI images were then parcellated into 82 cortical ROIs using the AAL template. Fiber bundles connecting each pair of ROIs were extracted, and a weighted undirected 82x82 connectivity matrix was constructed for each subject. The metrics assessed included network strength, clustering coefficient, characteristic path length, global efficiency (E_{glob}), small-world parameters, and nodal efficiency (E_{nod})[2]. Differences in network parameters of all patients as well as FLE and TLE subgroups relative to controls were assessed using *t*-tests. Network-Based-Statistics (NBS)[3] analysis was employed to identify clusters of nodes and edges (sub-networks) in a connectivity matrix which were differentially connected between patients and controls. Partial correlation analyses were done to assess the relation between network and clinical parameters (IQ, age at seizure onset, duration of epilepsy), controlling for age and gender, in LRE and FLE and TLE subgroups.

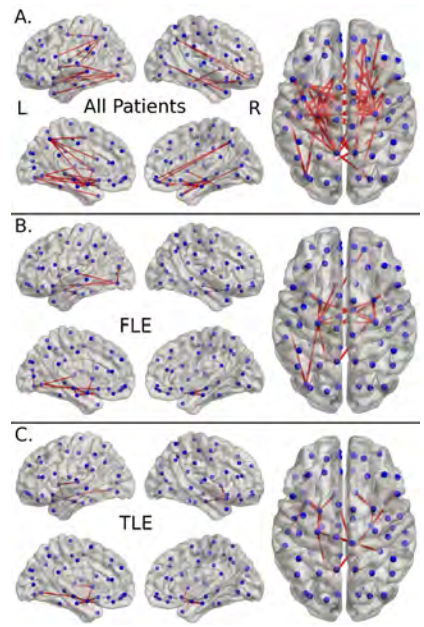

Fig 2. Results of NBS analysis in: all LRE (A), FLE (B), TLE (C) patients

Results: There were significant changes in network strength (decreased, $p < 0.001$), characteristic path length (increased, $p < 0.001$), and E_{glob} (decreased, $p < 0.001$), and no significant change in clustering coefficient in all LRE patients relative to controls. Similar findings were found in FLE patients. TLE patients showed significant increase in characteristic path length ($p = 0.01$), a trend towards reduced network strength ($p = 0.0641$) and E_{glob} ($p = 0.06$), and no significant difference in clustering coefficient compared to controls. All LRE patients, both FLE and TLE subgroups, and controls demonstrated small-world organization of the white matter networks ($\sigma > 1$). There was significant reduction in E_{nod} ($p < 0.05$) in 33 regions in LRE patients, in 51 regions in FLE patients, and in 14 regions in TLE patients compared to controls (Fig 1).

NBS analysis showed reduced connectivity ($p < 0.05$, corrected, in all groups) in 61 connections in LRE patients (involving frontal-temporal, insula-temporal, temporal-temporal, frontal-occipital and temporal-occipital lobes), 20 connections in FLE patients (involving frontal-temporal, insula-temporal, temporal-temporal, temporal-occipital, and occipital-occipital lobes), and 15 connections in TLE patients (involving frontal-temporal, insula-temporal, temporal-temporal, temporal-occipital and frontal-occipital lobes) relative to controls (Fig 2). None of the connections showed increased connectivity in LRE, FLE or TLE patients. There was no significant correlation between global network properties and IQ, age at seizure onset, or duration of epilepsy (all $p > 0.05$) in LRE, FLE and TLE subgroups.

Conclusion: We found disruption in global structural networks, reduced regional efficiency in multiple lobes and reduction in sub-network connectivity between frontal-temporal, insula-temporal, temporal-temporal, frontal-occipital and temporal-occipital networks in children with LRE, indicating widespread disruption in structural connectivity. Subgroups with FLE and TLE showed similar findings of disrupted global structural networks, but FLE patients demonstrated more areas with reduced regional efficiency than did TLE patients which may reflect more rapid spread of seizure activity from the extensive network of frontal lobe connections. There were no associations between global network properties, IQ and clinical parameters.

References: 1. Vaessen MJ, et al. Cereb Cortex. 2012; 22:2139-47. **2.** Rubinov M, Sporns O, Neuroimage. 2010; 52:1059-69. **3.** Zalesky A, et al. Neuroimage. 2010; 53:1197-1207.

Acknowledgements: This work was supported by Sickkids Foundation/Institute for Human Development, Child and Youth Health - CIHR and GE-AUR.