Disrupted modular organization of structural cortical network topology in new-onset pediatric epilepsy

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Purpose: Epilepsy is accompanied by various cognitive functional declines. Previously, we already demonstrated the disruptions in the coordination of large-scale functional brain structure network in new-onset pediatric epilepsy[1]. However, the organizational alterations in the context of ongoing active epilepsy have not been studied yet. Here, using cortical thickness, we investigated the modular organization of the cortical structural networks over the first two years after epilepsy onset among children with idiopathic generalized epilepsy (IGE), localization related epilepsy (LRE), and healthy controls.

Methods: We studied a group of 28 healthy controls (mean age 13.3 ± 3.28 years, 11 males), 21 new-onset LRE (11.6 ± 2.68 years, 12 males) and 18 new-onset IGE (15 ± 3.3 years, 7 males). Patients and controls were similar in age (p=0.92) and gender (p= 0.4). The mean age of LRE group was younger than the IGE groups (p= 0.005) but IGE and LRE groups did not significantly differ from controls (p= 0.09 and p=0.07, respectively). All subjects underwent MRI scanning utilizing the same imaging protocol yielding SPGR images (1.5 Tesla GE Signa scanner, TR = 24 ms, TE = 5 ms, Slice thickness 1.5mm). Cortical thickness data derived from FreeSurfer 'Destrieux Atlas' were utilized for the construction of group-wise adjacency matrices (controls, LRE, IGE) where each of the 148x148 entries represented the partial correlation between the thickness from each pair of regions, controlled for age, bootstrapped 1000 times. The adjacency matrices were then utilized for the evaluation of global graphical properties (Global Efficiency, Betweenness Centrality, and Clustering Coefficient) across fixed density threshold binary matrices (ranging from 0.15 to 0.50) using of the Brain Connectivity Toolbox. Bonferroni correction was made to account for multiple comparisons (0.05/[(148x148 regions) x (8 fixed density thresholds) x (1000 bootstraps) x (3 groups) x (2 time points) = 4.75e-11. Based on the previous method from Newman[2], the network modules, which refer to the groups of tightly clustered cortical regions in thickness will be identified. Finally, to determine the statistical significance of the between-group differences in all the network parameters, we applied a non-parametric permutation test method[3].

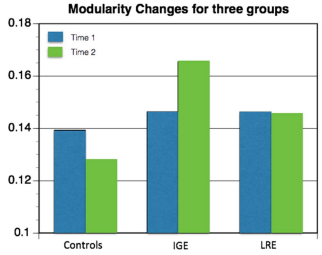

Figure 1. Modularity Change corresponding to time. The blue bar represents the modularity index in Time 1 whereas the green one is the modularity index in Time 2.

Results and discussions: All groups demonstrated prospective changes in the topology of the structural network, indicating neurodevelopmental changes over the two years. However, the modularity change from Time 1 to Time 2 varies among three groups (Figure 1). Compared with the dramatic decrease in control group, the modularity changes for patient groups almost stayed or even increased still over two years. Moreover, in Figure 2, compared with control group, Global network metrics demonstrated the decreased clustering coefficient, greater centrality, reduced efficiency and small worldness for IGE and also the increased clustering coefficient, decreased centrality, efficiency and small worldness for LRE group (Global topological properties of networks are thresholded at 15%, with bootstrapped 96% confidence interval. Differences among the three groups are significant at p<0,001, corrected for multiple comparisons).

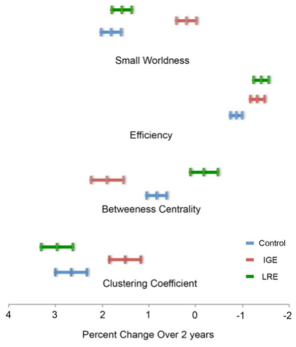

Figure 2. Percent changes in global network metrics over the prospective 2 years.

Conclusion: Children with new-onset epilepsy demonstrated an actively evolving altered large-scale neurodevelopmental trajectory over the prospective 2 years. Based on our results, new-onset pediatric epilepsy is associated with an altered modular organization in the structural brain networks. Syndromic signatures emerged with IGE showing less segregation and LRE demonstrated greater segregation over time. This leads to abnormal neurodevelopmental structural trajectories with less network efficiency and less optimal small world configuration.

Reference:

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