# Impaired Small-world Efficiency in Structural Networks in Pediatric Bipolar Disorder

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## Introduction

Pediatric bipolar disorder (PBD) is a cyclical illness with episodes of mania and depression with known microstructural abnormalities in both superficial white matter (WM) as well as deep white matter tracts [1][2]. These focal WM abnormalities may contribute to mood dysregulation in PBD. In the current study, graph theoretic analyses was applied to diffusion weighted data to explore the topological efficiency of structural networks in pediatric bipolar disorder.

## Materials and Methods

This is a cross-sectional study of patients with PBD and healthy controls (HC). One hundred and seventy-five subjects participated in this study: 82 PBD patients (mean age = 13.93 ± 2.24 years, females = 44, IQ = 104.94 ± 10.48) and 93 matched HC (mean age = 14.24 ± 2.35 years, females = 41, IQ = 106.47 ± 10.29). This study was approved by the University of Illinois at Chicago's Institutional Review Board (IRB). Informed consent was obtained from at least one parent, and assent was obtained from all participants.

The participants were scanned on 3.0 Tesla GE Signa HDx scanner (General Electric Health Care, Waukesha, Wisconsin) with a quadrature head coil. Axial T1-weighted image was acquired with FSPGR BRAVO: FOV = 240x240 $mm^2$, 512x512 matrix, 120 slices, slice thickness = 1.5mm, gap = 0mm, TR = 11.58ms, TE = 4.96ms, TI = 450ms, flip angle = 13°. DTI images: TR = 5400ms, TE = 75.3ms, FOV = 200x200 mm2, matrix = 256x256, number of slices = 20 slices, slice thickness = 4mm, gap = 1mm, NEX = 2, two diffusion values of b =0 and 750 s/mm2, number of diffusion gradient directions = 27.

Diffusion weighted images were preprocessed in FSL for motion correction, eddy current correction, and b-matrix rotation. The fiber tracking based on FACT algorithm with angle threshold of 35 degree and fractional anisotropy threshold of 0.15 was performed using the Diffusion Toolkit and TrackVis software (Massachusetts General Hospital, MA, USA). Individual T1 image was parcellated into 80 cortical and subcortical regions of interest (ROI) using FreeSurfer and mapped to the DTI image space through co-registration. A connectivity matrix M(80x80) was computed for each subject, where M(i,j) represented the number of fibers that end/start at region i and j. The connectivity matrix was then threholded at different cost/density (K) to generate 80-node binarized connectivity graphs for each subject. Graph theoretic metrices including small-worldness, global efficiency were computed and compared between groups to characterize the topological changes in structural networks in PBD.

## Results and Discussion

Using this graph theory-based approach, both PBD and HC groups consistently showed a small-world architecture of structural brain networks in low-cost to medium-cost networks ($0.05<cost<0.25$).

We have also examined the group difference (PBD vs HC) in the topology of sparse structural networks at low-cost threshold K = 0.1. Significant decreased small-worldness is observed in PBD at $p < 0.03$ [small-worldness- mean (SD): HC = 2.91 (0.23) PBD = 2.83(0.23)]. Small-worldness quantitatively evaluates the effectiveness of information transfer within the complex brain networks. A small-world brain network model facilitates information processing with optimally balanced global integration and local specialization [3]. Significantly decreased small-worldness in PBD may reflect decreased efficiency in information transfer and processing, and may contribute to the affective and cognitive dysfunction in PBD.

## References

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