# DTI correlates of brain network topology in a pediatric population

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**Target Audience**

Researchers who model brain network topology by using graph theory analysis of intrinsic-connectivity fMRI data.

**Purpose**

Correlations have been shown between functional connectivity, as measured by intrinsic-connectivity fMRI (ic-fMRI), and structural connectivity, as measured by DTI or DSI [1]. However, often ic-fMRI is used to model brain network topology [2], and global measures of brain integration, segregation, and other metrics are computed. The relation between global network topology and regional DTI parameters, which reflect local differences in white matter microstructure, is currently unknown.

**Methods**

The participant population consisted of a community sample of pre-adolescent twin pairs (ages 9-13 years) born late preterm (>32 weeks) and at full term recruited from a developing region in northeast Brazil (Montes Claros, pop. ca. 410,000) as part of an ongoing longitudinal international collaborative research program investigating the genetic and environmental influences relating prematurity, long-term neurocognitive functioning and oral health outcomes.

MRI scanning was performed on a Philips 1.5 T Achieva system. Ic-fMRI was acquired with scan parameters: TR = 3000 ms, TE = 50 ms, FOV = 211.2 X 211.2 mm, imaging matrix = 80 X 80, slice thickness = 4 mm, 30 slices acquired covering the whole brain, SENSE factor = 2, 100 volumes acquired for a total scan time of 5 minutes per run. Two scan runs were acquired: one with the child asked to keep his eyes open, and one with eyes closed. After motion correction, an intensity-based cost function was used to discard frames corrupted by motion, with a threshold determined via visual inspection. Datasets were then transformed into Montreal Neurologic Institute (MNI) space using SPM8. Cerebral regions were parcellated out for each child using the 90-region AAL template [3]. Time-courses were extracted for each participant for each region and low-pass filtered with a cutoff frequency of 0.1 Hz, corrected for baseline drift, and variance-normalized. The time courses from the eyes-open and eyes-fixed runs from each subject were concatenated into a single time course. For each participant, correlations were calculated between the time courses from each set of two regions, resulting in a 90-X-90 correlation matrix. The correlation matrices were then thresholded and binarized, resulting in an undirected, unweighted graph. For each graph corresponding to each participant, global efficiency (a measure of network integration) and transitivity (a measure of network segregation) were calculated [2]. Each parameter was marginalized over all values of network cost in order to avoid threshold-specific effects.

DTI scans were acquired with the following parameters: Spin-Echo EPI, TR = 6000 ms, TE = 90 ms, slice thickness = 2 mm, matrix = 112 X 112, FOV = 22.4 X 22.4 cm, SENSE factor = 2, b value = 1000 s/mm$^2$, one scan acquired without diffusion weighting and 32 scans acquired with gradient direction according to the Philips Achieva 32-direction sequence. Pre-processing included motion and eddy current correction and slice dropout removal according to routines written in FSL. Diffusion tensor components were computed and fractional anisotropy (FA), axial diffusivity (AD), and radial diffusivity (RD) maps retained for further analysis and spatially normalized into MNI space. Only voxels with FA > 0.25 and white matter probability > 0.9 were retained for further analysis, in order to minimize the risk of spurious results obtained from imperfect spatial normalization. For the second-level analysis, a mixed-effects model was used on a voxelwise basis. For the fixed effects, efficiency/transitivity was the variable of interest and age, sex, and preterm status were covariates of no interest. The random effects were between-family variance and between-genotype (e.g. non-monozygotic twin sibling) variance. The fit was performed using restricted maximum-likelihood (ReML) estimation and an expectation-maximization (EM) algorithm using customized code written in IDL (Exelis, Boulder, CO). After the fit converged the resulting T-scores were converted into Z-scores. Results were spatially filtered (in only the white matter) with $\sigma = 3$ mm. An intensity threshold of $Z > 6.5$ and spatial extent threshold of 150 voxels was used, shown to correspond to a family-wise-error (FWE) corrected $p < 0.05$ via Monte Carlo simulation.

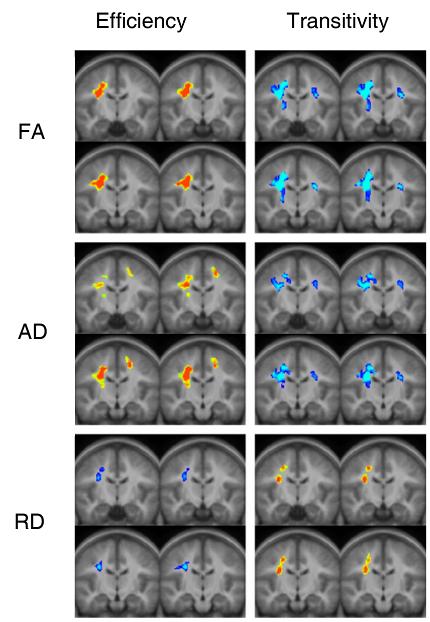


**Figure 1.** Regions with positive (hot colors) or negative (cold colors) correlations of FA (top row), AD (middle row), or RD (bottom row) with global network efficiency (left column) and network transitivity (right column). Images in radiologic orientation. Coronal slices from Y = -12 mm to Y = -18 mm (MNI coordinate space).

**Results**

FA in crossing-fiber regions involving the corona radiata, superior longitudinal fasciculus, and callosal fibers is correlated positively with global efficiency and negatively with transitivity (Figure 1, top row). The FA changes are due to increased AD/decreased RD with higher efficiency, and decreased AD/increased RD with higher transitivity (Figure 1, middle/bottom row). The effect is present bilaterally, though predominantly in the right hemisphere; some correlations in the left hemisphere did not reach statistical significance.

**Discussion**

This is the first study, to our knowledge, in which global measures of brain network topology found from ic-fMRI are related to DTI measures in specific regions. These changes are predominantly situated in a single region and its contrahemispheric homologue which contain multiple crossing fiber bundles which have mostly orthogonal directions, in inferior-superior (corona radiata), anterior-posterior (superior longitudinal fasciculus), and left-right (callosal fibers). More efficient brain function is due to decreased path length (reflected in greater efficiency) and decreased segregation (reflected in lower transitivity). Anatomically, we have shown this is due to increased fiber organization (reflected in increased AD/decreased RD) in a white matter region connecting distal regions of the brain.

**Conclusion**

Brain network topology as examined by parameters computed from ic-fMRI is highly related to brain anatomical connectivity as examined by DTI parameters, particularly in the region of right sided cortical association fibers. Future research will examine additional parameters, such as small-worldness, and connectivity as reflected by DTI or DSI tractography.

**References**

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