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# STRUCTURAL CONNECTIVITY VIA THE TENSOR-BASED MORPHOMETRY

Seung-Goo Kim[1], Moo K. Chung[1,2,3,⋆], Jamie L. Hanson[3,4], Brian B. Avants[5], James C. Gee[5], Richard J. Davidson[3,4] and Seth D. Pollak[3,4]

[1]Department of Brain and Cognitive Sciences, Seoul National University, Korea. [2]Department of Biostatistics and Medical Informatics, [3]Waisman Laboratory for Brain Imaging and Behavior, [4]Department of Psychology, University of Wisconsin, Madison, WI, USA.
[5]Penn Image Computing and Science Laboratory, Department of Radiology, University of Pennsylvania, Philadelphia, PA, USA.
⋆mkchung@wisc.edu

## Introduction

We present a novel computational framework for investigating the white matter connectivity using tensor-based morphometry (TBM) which use only only T1-weighted magnetic resonance imaging (MRI) but no diffusion tensor imaging (DTI). To construct brain network graphs, we have developed a new data-driven approach called the $\epsilon$-neighbor method that does not need any predetermined parcellation.

The proposed pipeline is applied in detecting the topological alteration of the white matter connectivity in maltreated children who have been post-institutionalized (PI; n=32) in orphanages in East Europe and China with age and gender matching normal control subjects (NC; n=33).

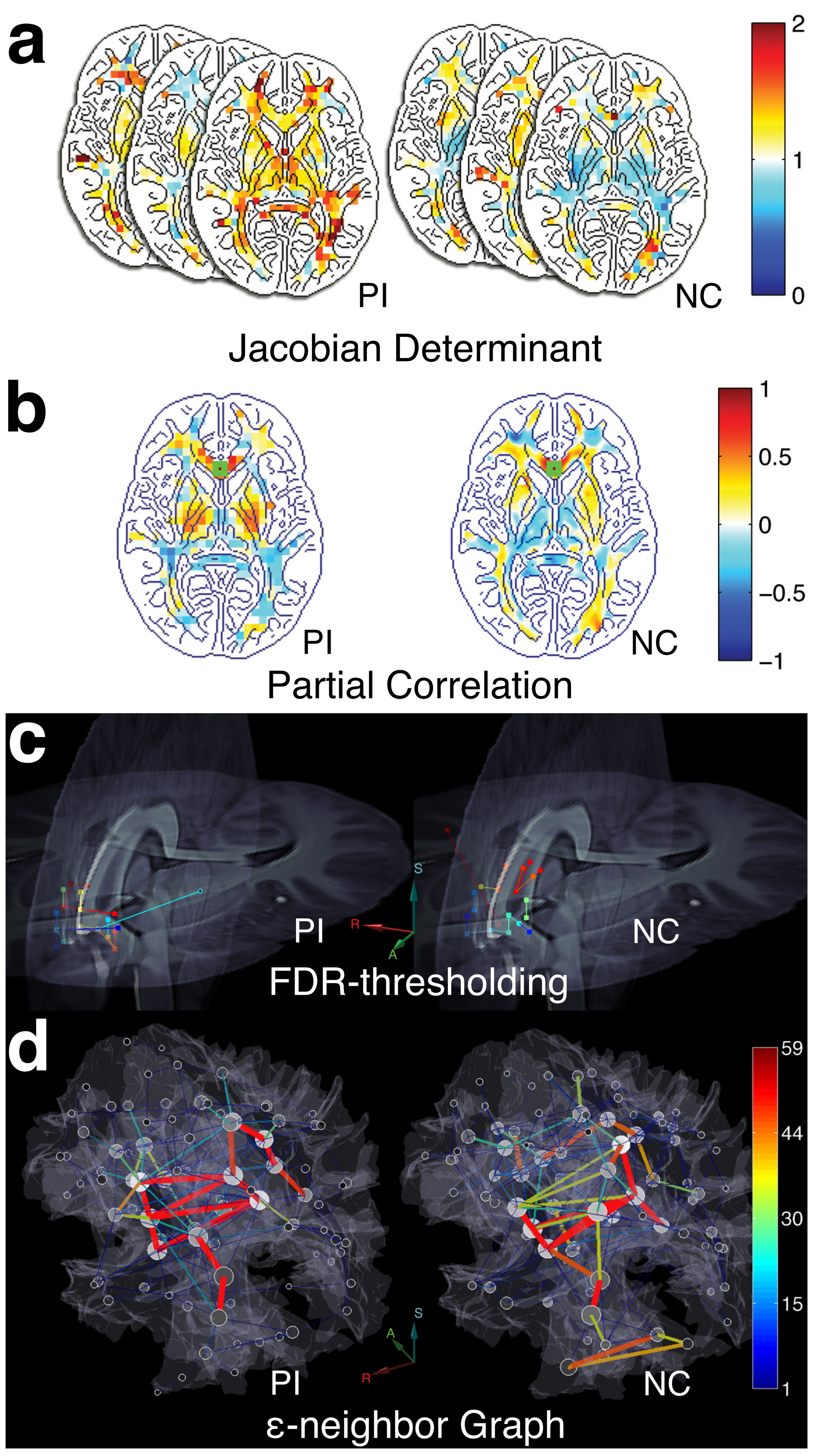



Figure 1: Framework of the proposed analysis applied to post-institutionalized (PI) children and normal control (NC). **(a)** Jacobian determinant maps of individuals projected on the template. **(b)** partial correlation maps seeded at the genu (marked with green squares) **(c)** FDR-thresholding on partial correlation is used to establish edges of the connectivity network. Only edges connecting the nodes near the genu are visualized. The different pairings are marked with different colors. **(d)** The proposed $\epsilon$-neighbor graphs of connectivity. Only positive correlations are shown here. The gray shading of nodes indicates the node degree. The size of nodes represents the number of nodes that are merged in the $\epsilon$-neighbor construction. For 3D orientation, arrows in the middle of **(c)** and **(d)** indicate Right (red), Anterior (green) and Superior (cyan) directions.

## Partial correlation on Jacobian field

Fig.1 illustrates the proposed pipeline. Between the subsampled 2692 voxels over the whole white matter, we link two nodes if the partial correlation of the Jacobian determinants is statistically significant at a certain threshold.

The Jacobian determinant is defined as $J = \det(I + \partial\mathbf{U}/\partial\mathbf{x})$ where $\mathbf{U}$ is the displacement matrix and $\mathbf{x}$ is the coordinate vector [1].

To remove the possible confounding effect of age, gender and brain size, we used the Pearson correlation of the residuals obtained from fitting general linear models (GLM) with the nuisance covariates. It is equivalent to take partial correlations.

In order to obtain the deterministic network graph, we have thresholded the partial correlations using the false discovery rate (FDR) thresholding with q=0.01 under a weak assumption of dependency. The distribution of statistics for correlations $z_{ij}$ can be trivially approximated using the Fisher transform.

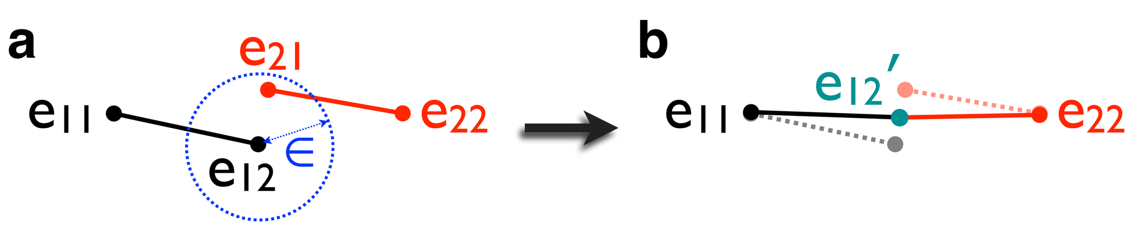
As the FDR-threshold is given by $s$ (4.86 for PIs; 4.81 for NCs), the adjacency matrix $A = (a_{ij})$ is given by $a_{ij} = 1$ if $z_{ij} \geq s$ and $a_{ij} = 0$ otherwise, with the diagonal terms $a_{ii} = 0$.

## $\epsilon$-neighbor graph simplification

Since isolated single connections are more likely false positives, we have adapted the $\epsilon$-neighbor scheme [3]. The algorithm condenses a given complex graph to a much simpler graph by iteratively merging $\epsilon$-neighbors. If the distance $\mathbf{d}(p, \mathcal{G}_k) = \min_{q \in \mathcal{V}_k} \|p - q\| \leq \epsilon$ for some radius $\epsilon$, the node $p$ is called the $\epsilon$-neighbor of $\mathcal{G}_k$. The idea is best illustrated with a toy example given in Fig.2.

To improve the stability of the original algorithm [3], we decided to update the coordinates of the pre-existing node when a merging occurs.

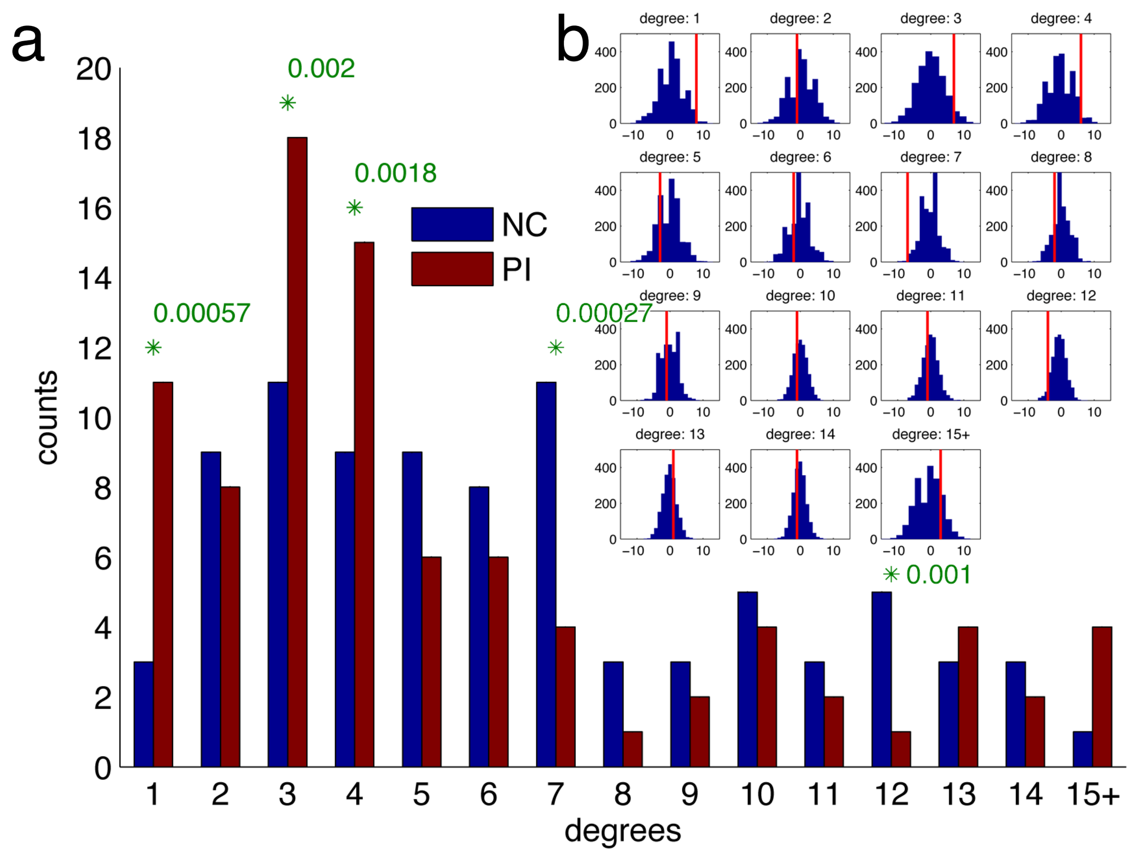
For this study, $\epsilon$ was set to be 21 mm to investigate the connectivity at macro-scale level.




Schematic illustration of the $\epsilon$-neighbor updating scheme. **(a)** Initially the graph $\mathcal{G}_1$ consists of one edge $e_{11}e_{12}$ (black). The new edge $e_{21}e_{22}$ (red) is to be considered at the next stage. The node $e_{21}$ is within the $\epsilon$ radius (blue) of the node $e_{12}$ thus it has to be merged. **(b)** The coordinates of the merged node $e_{12}$ is updated to $e_{12}{}'$ (green) and the new edge $e_{12}{}'e_{22}$ is included in $\mathcal{G}_2$.

## Results

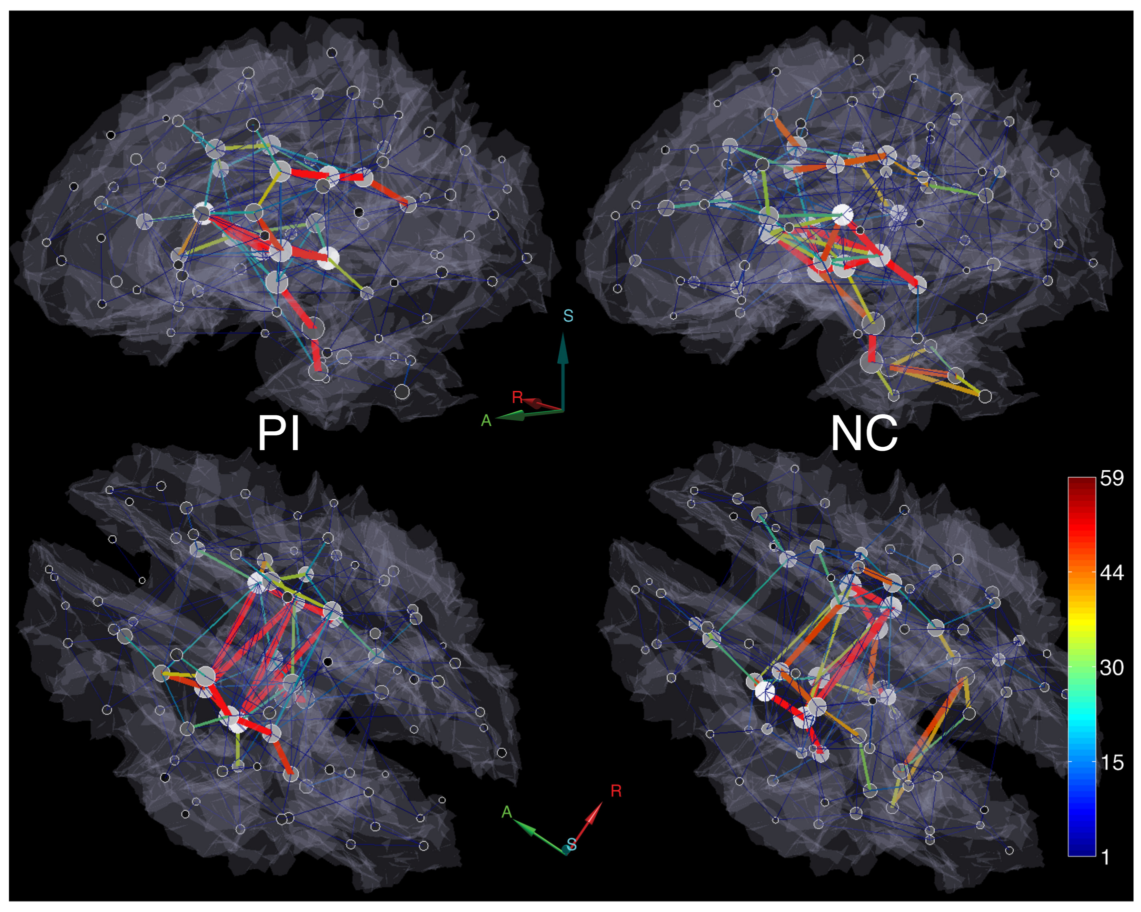
We have used the degree of nodes as a discriminating feature between the two groups (Fig.3). The significance of the degree differences is tested using permutation tests. There are significantly more nodes with the low degrees (1, 3 and 4) in the PIs than the NCs. On the other hand, there are more nodes with the high degrees (7 and 12) in the NCs than the PIs. It implicates weakened connectivity in the PIs.




Permutation tests on degree distributions. **(a)** Degree distributions. The significant differences between the PIs and the NCs marked with green asterisks with p-values (Bonferroni corrected at 0.05). **(b)** Null distribution obtained by 2000 permutations. X-axis is for the degree differences. Y-axis is for the counts of permutations. Red vertical lines note the actual differences.

## Discussions

We have presented a novel structural connectivity mapping technique that uses only T1-weighted MRI. The constructed partial correlation maps (Fig.1) look very similar to the probabilistic connectivity maps obtained from DTI. The simplified graphs showed significantly different degree distributions in PIs implying abnormal connectivity. In addition, the anatomical pattern of the white matter connectivity seems to be locally different across groups (Fig.4). However, it should be more thoroughly validated in a further study.




Local connectivity patterns of the $\epsilon$-neighbor graphs. Only positive correlations are shown. Edges are color-coded by the number of merged connections implying the strength of connections. The gray shading of nodes indicates the degree and the size of nodes represents the number of nodes that are merged.

## Reference

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