WHITE MATTER STRUCTURAL CONNECTIVITY WITHOUT DIFFUSION TENSOR IMAGING

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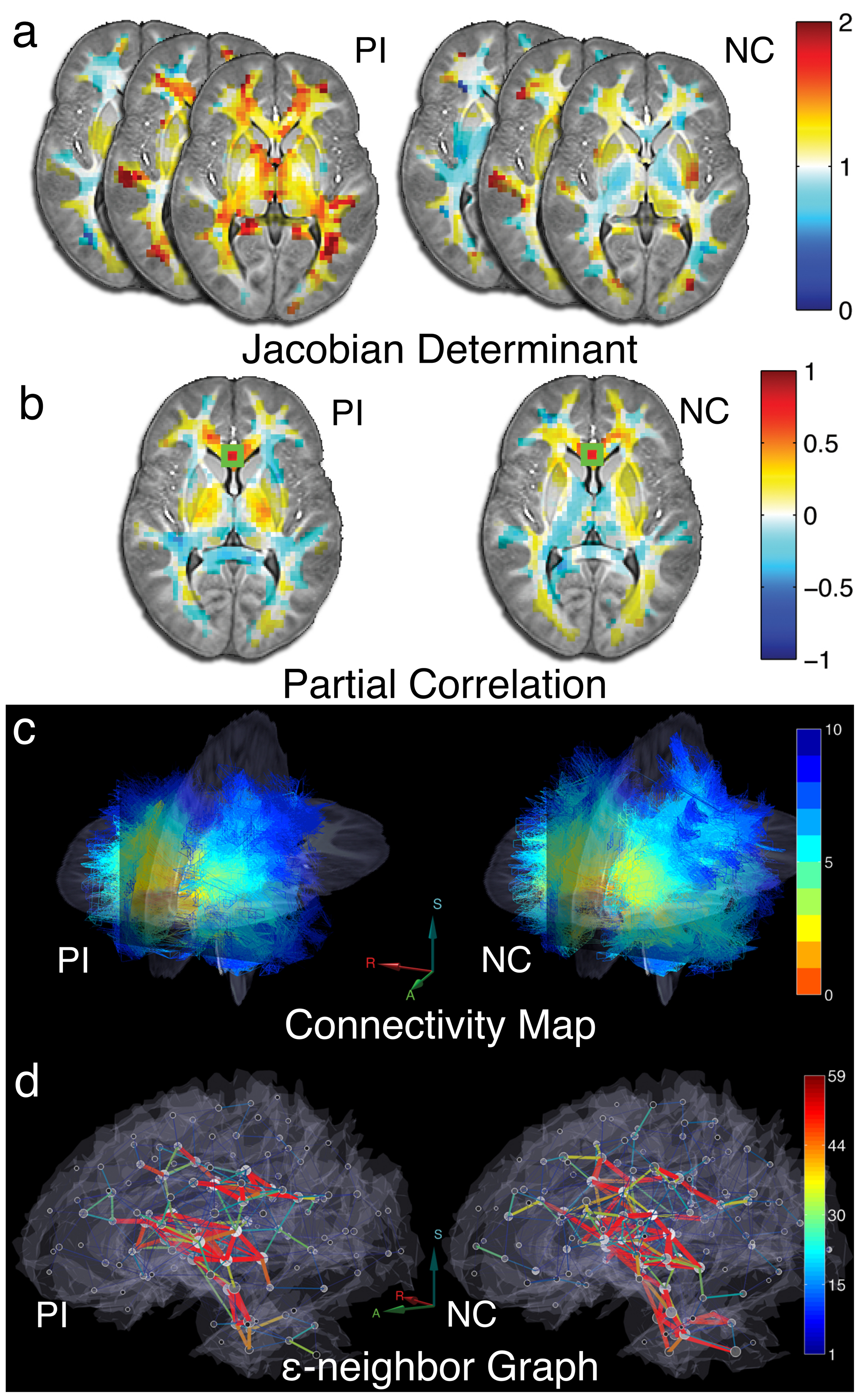
Introduction

We present a novel computational framework for characterizing white matter (WM) structural connectivity. We do not use diffusion tensor imaging (DTI) but only T1-weighted magnetic resonance imaging (MRI). Structural connectivity via MRI has been proposed using cortical thickness before [1]. We propose to use the Jacobian determinant (JD) obtained from the tensor-based morphometry (TBM) [2]. By correlating JD in TBM, we can build a connectivity matrix based on the local volume.

The primary advantage of the proposed method is that it does not require DTI. Another advantage is that it uses JD that is defined over the whole brain including WM unlike cortical thickness.

The proposed framework is applied to the brain networks of the children who experienced early maltreatment and had been post-institutionalized in orphanages (PI; n=32) and age matched normal control subjects (NC; n=33).

Framework



References

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a. Jacobian determinant map

T1-weighted MRIs were collected using a 3T GE SIGNA scanner. Symmetric diffeomorphic image normalization was performed using Advanced Normalization Tools (ANTS) [3]. JD is computed as the determinant of the gradient matrix of inverse deformation field. We uniformly sampled 12480 voxels as possible nodes at every 3mm.

b. Partial correlation

Let $\mathbf{z}$ = (1, age, gender, brain volume) be the covariate vector. We modeled JD on the i-th node as

$$J_i = \mathbf{z}\lambda_i + \varepsilon_i \tag{1}$$

where λ_i is the unknown parameter vector and ε_i is the zero-mean Gaussian noise. The residual of the fit is given by $r_i = J_i - \mathbf{z}\widehat{\lambda}_i$, where $\widehat{\lambda}_i$ are the least-squares estimation. The partial correlation ρ_{ij} between J_i and J_j is simply estimated by the Pearson correlation between the residuals r_i and r_j.

c. Connectivity map

Between 12480 nodes, we link two nodes (1) if the partial correlation of the JDs is statistically significant using false discovery rate (FDR) with q=0.01 and (2) if the distance (proximity) between the nodes is sufficiently small.

We define the adjacency matrix $\mathbf{A} = (a_{ij})$ as

$$a_{ij} = \begin{cases} 1 & \text{if } z_{ij} \geq s \text{ and } d_{ij} \leq g \\ 0 & \text{otherwise} \end{cases}, \tag{2}$$

where z_{ij} is the Fisher transform of the partial correlation between the node i and j, s is the given FDR threshold, d_{ij} is the Euclidian distance between the nodes and g is a given proximity. We fixed g=27 mm as more than 90% of the thresholded edges are shorter than that.

d. ε-neighbor simplification

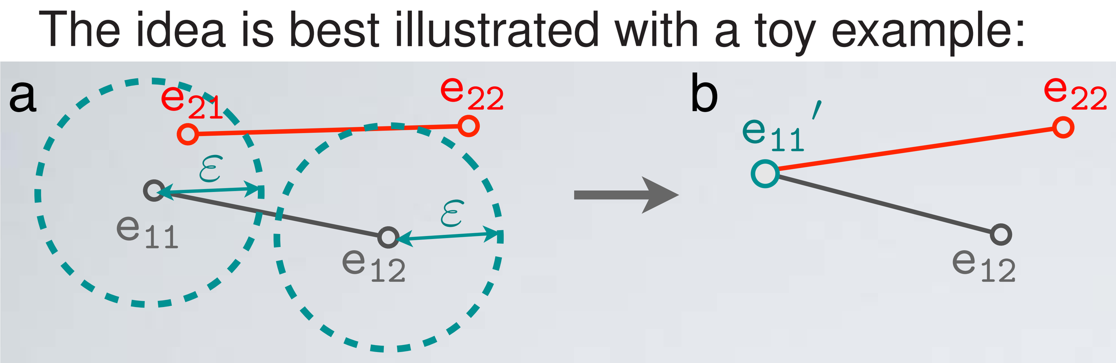
To simplify extremely complex graphs without distorting underlying topology, we adopted the ε-neighbor method [4]. Let us define the distance $\mathbf{d}(\mathrm{p}, \mathcal{G})$ of a node p to the graph $\mathcal{G}$ with the set of nodes $\mathcal{V}$ as

$$\mathbf{d}(\mathrm{p}, \mathcal{G}) = \min_{\mathrm{q} \in \mathcal{V}} \|\mathrm{p} - \mathrm{q}\|. \tag{3}$$

If $\mathbf{d}(\mathrm{p}, \mathcal{G}) \leq \epsilon$ for some radius ϵ, the node p is called the ϵ-neighbor of $\mathcal{G}$.

We start with a graph $\mathcal{G}_1$ with a single edge and two nodes. At the next iteration, we add another edge with two nodes. If any new node is the ϵ-neighbor of $\mathcal{G}_1$, then we merge it with the closest node in $\mathcal{G}_1$.

The idea is best illustrated with a toy example:

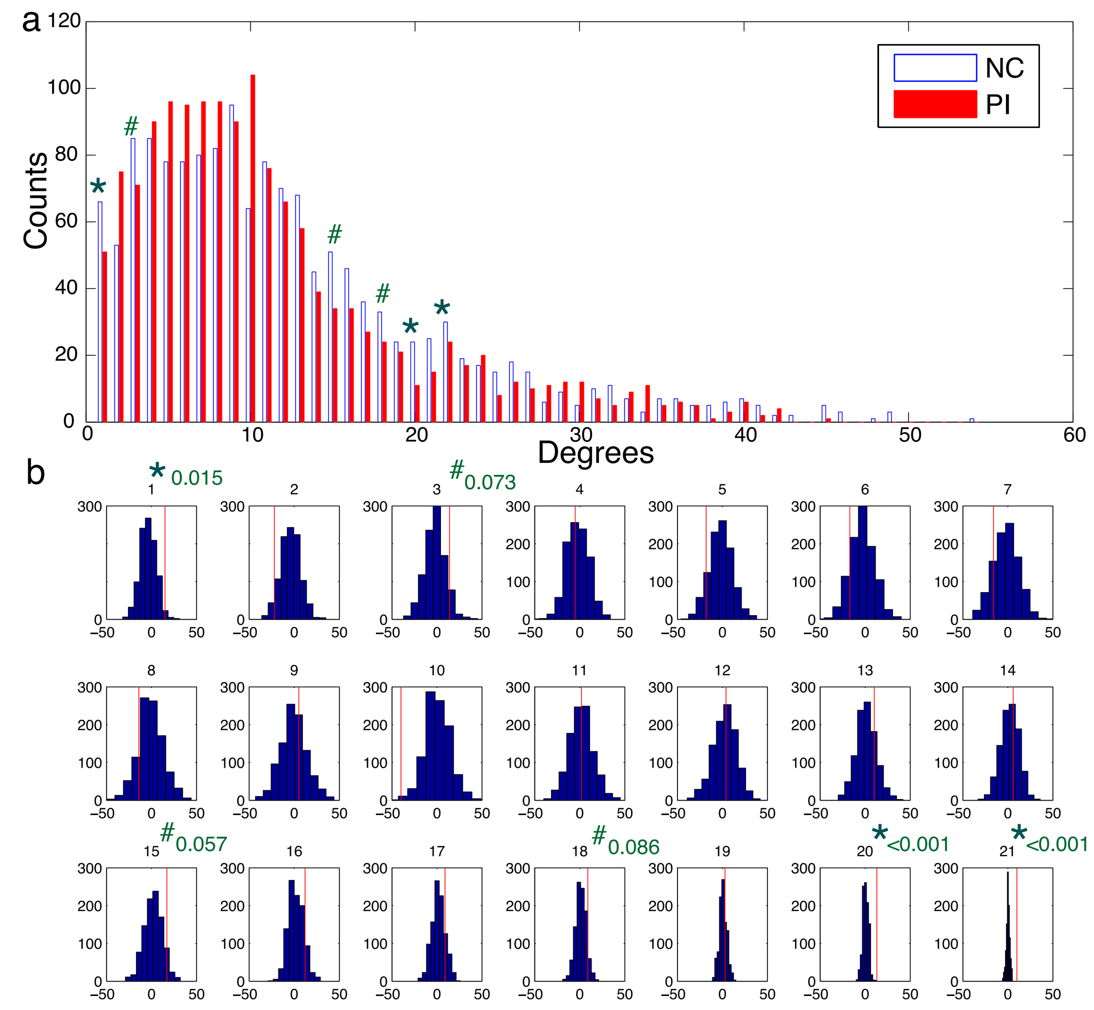


(a) Initially the graph $\mathcal{G}_1$ consists of one edge $\mathrm{e}_{11}\mathrm{e}_{12}$. At the next stage, we determine how to connect a new edge $\mathrm{e}_{21}\mathrm{e}_{22}$ to the existing graph $\mathcal{G}_1$. The node e_{21} is within the ε radius of the node e_{11}. So e_{21} is the ε-neighbor of $\mathcal{G}_1$ and has to be merged with e_{11}. (b) The coordinates of the node e_{11} is updated to e_{11}' and the new edge $\mathrm{e}_{11}'\ \mathrm{e}_{22}$ is included in $\mathcal{G}_2$. Other possibilities are explained in [4].

This merging and deletion process is iteratively performed until all edges are included into the graph.

Results

Permutation test on the degree distributions

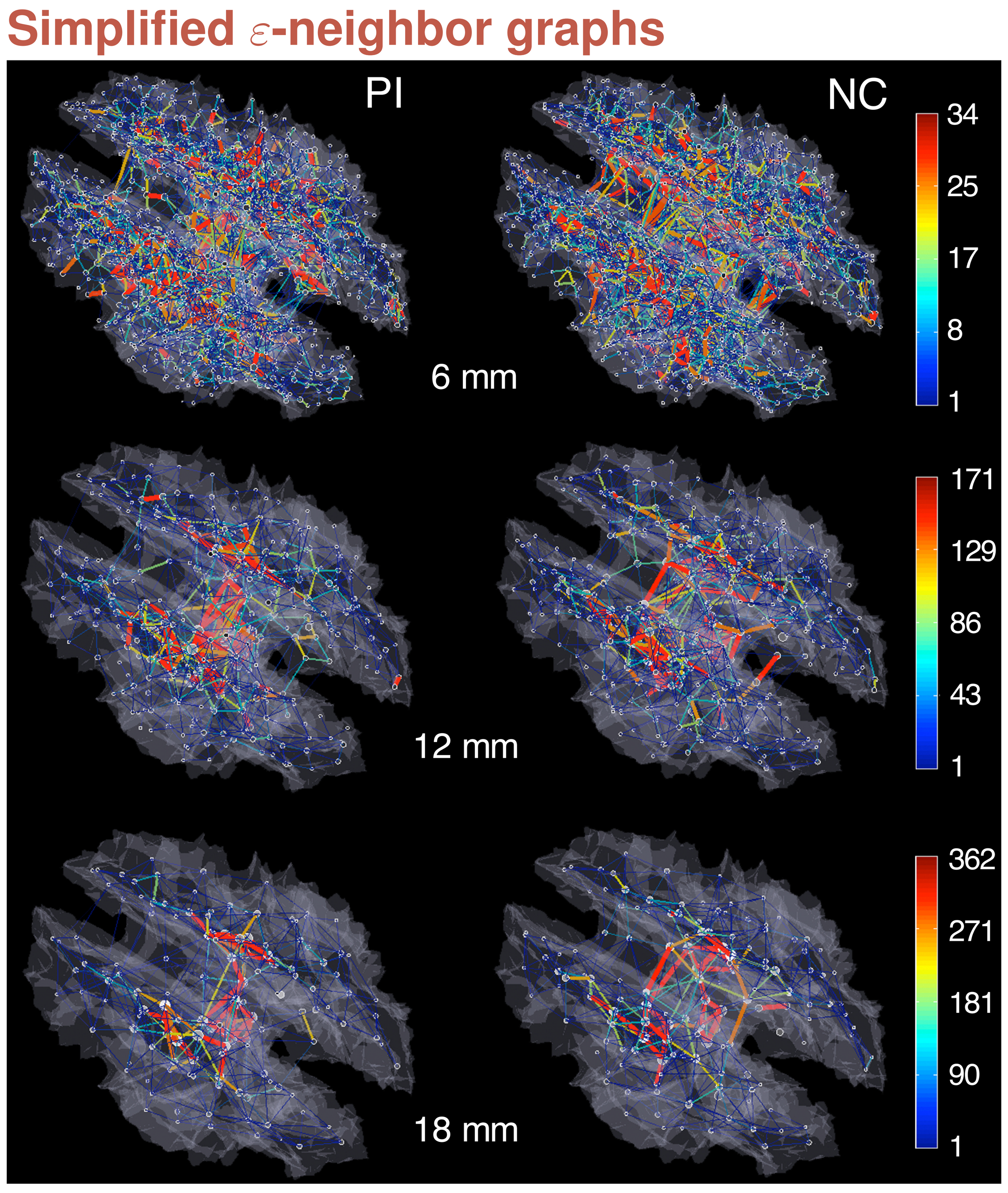


1000 permutations, Bonferroni correction, (#) p <0.10, (*) p <0.05; (a) observed differences (b) null distribution

Significant differences:

- PI > NC at low degrees (1 and 3)
- NC > PI at high degrees (15, 18, 20, 21)

Simplified ε-neighbor graphs



The thickness of edge codes the strength of connection

Connections within the corpus callosum:

- Disjointed in PI when $\varepsilon \geq$ 12 mm
- Intact in NCs even for $\varepsilon =$ 18 mm

Discussion

We have presented a novel structural connectivity mapping technique that uses only T1-weighted MRI. The global difference in degree distribution is significant. Visually, there seems to be a local network difference in the mid-body of the corpus callosum, which is known to be reduced due to the early stress [5].

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