Heritability and reliability of the Human Connectome mapped using 4T HARDI in 156 young adult twins

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Introduction

The connectivity of white matter fiber pathways linking cortical regions of the brain, within and across hemispheres, is of great interest and may be altered in disorders such as Alzheimer’s disease [1] and schizophrenia [2]. Determining the underlying genetic influences behind these anatomical connections may also shed light on information processing in the cortex. Accurate assessment of genetic influence requires knowledge that the connections determined through fiber tractography are reliable and reproducible. We set out to assess the heritability of the human cortical connectivity matrix, and whether it could be computed reproducibly from 4-Tesla HARDI scans.

Methods

- **Subjects**: 156 young adult twins (43 monozygotic pairs (MZ; 30F), and 34 same-sex dizygotic pairs (DZ; 24F); and 2 individuals without their cotwin, from 79 families; mean age: 23.4 ± 2.0 SD yrs)
- **Imaging**: 4-Tesla structural MRI and HARDI
  - 94 gradient directions, 11 b0
- **T1-weighted structural image processing**:
  - N3 correction – for intensity inhomogeneities
  - Automatic skullstripping with manual editing
  - Cortical extraction with FreeSurfer
- **DWI processing**:
  - Eddy current and motion correction
  - Align to downscaled version of T1-weighted image
  - Correct gradient directions
  - Elastically register b0 images to the T1 [3]
  - Compute constant solid angle orientation distribution functions (CSA-ODFs) [4]

$$\frac{d}{dx} \ln \left( \frac{O(\Omega)}{FA(\Omega)} \right)$$

**HARDI tractography** based on Hough transform voting method [5]

- Seed voxels with probability based on FA
- Score curves based on probability of fiber existence
- One fiber with the highest score chosen per seeded voxel

Heritability assessment (Falconer’s $h^2$)

- MZ twins share 100% of their genes
- DZ twins share on average 50%
- Intra-class correlation

$$ICC = \frac{MS_g - MS_w}{MS_g + MS_w}$$

**Reliability**

- 25 individuals had repeat HARDI scans
- Intra-class correlation between repeat scans is computed for all matrix elements

White matter fiber counts connecting parcellated cortical regions, as traced using HARDI tractography, show promise for genetic analyses.

Several connections showed moderate heritability in 154 twins.

Connection measures were highly reproducible across repeated scans.

Reliability ($r$) of human connectome should be considered when its genetic determinants are studied.

References & Acknowledgements