Multi-Site Genetic Analysis of 1151 Diffusion MRI Scans from the ENIGMA–DTI Working Group

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http://enigma.loni.ucla.edu/ongoing/dti-working-group/

Background

Human brain structure is genetically influenced, and many brain imaging measures are heritable, i.e., a proportion of their variance is due to differences in the human genome. Recently, the Enhancing Neuroimaging Genetics through Meta-Analysis (ENIGMA) Consortium created a Diffusion Tensor Imaging (DTI) Working Group to study genetic influences on white matter micro-architecture and integrity. To make it feasible to analyze DTI on a large scale from many cohorts, we first set out to define reliable, and heritable, measures from DTI scans of cohorts of different ages and ethnicities, scanned with various acquisition protocols. We aimed to prioritize the most promising brain measures for genetic analysis, based on their consistently high heritability in different cohorts.

Methods

Making the target and Standardizing Protocols

From each of four independently collected datasets, we randomly selected 100 subjects (50 male, 50 female) to create a common template (i.e., 400 subjects total). FA images from all subjects were aligned, using FSL’s ‘flirt’ (Jenkinson et al., 2002), to the Johns Hopkins University (JHU) DTI atlas in ICBM space (ICBM-DTI-81 white matter labels atlas) (Mori et al., 2008).

A target was created as previously described (Kochunov et al., 2001; Kochunov et al., 2003) from these aligned images.

The target was then skeletonized with FSL’s TBSS (Smith et al., 2005). The mean FA in various ROIs were extracted.

Calculating Heritability

Two ethnically different family-based datasets, QTIM and GOBS (the Queensland Twin Imaging and the Genetics of Brain Structure and Function Studies) with different imaging protocols were used to estimate heritability on a voxelwise and ROI level.

To calculate heritability across images, we used a variance components method, as implemented in the SOLAR software package (http://www.nitrc.org/projects/solar/) (Almas and Blangero, 1998). Methods used to calculate heritability in SOLAR are detailed elsewhere (Kochunov et al., 2010, Winkler et al., 2010).

Meta analysis

To obtain meta-analyzed heritability ($h^2$), we used two alternative methods:

1) Weight the heritability from each study by its sample size (n) (Sutton, 2000) as:

\[
\hat{h}^2 = \frac{\hat{h}^2_1 n_1 + \hat{h}^2_2 n_2}{n_1 + n_2}
\]

for n=1 to N, - the total number of voxels along the skeleton, or the total number of ROIs; subscripts 1 and 2 refer to the two datasets used.

Results

Publically available processing and QC protocols: enigma.loni.ucla.edu/ongoing/dti-working-group/