Heritability of cortical thickness: A Human Connectome Project study

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Introduction

Gray matter phenotypes such as area, volume and cortical thickness have been shown to be involved in several neurological disorders. Previous studies have also shown that these properties may be heritable. Using data from The Human Connectome Project, we investigated the degree of heritability of cortical thickness in sixty-six distinct areas of the brain. To do this we used the ACE mathematical model for twin studies as it provides a reliable approach for quantifying variability in human brain structure through the analysis of genetic and environmental contributions to phenotypic differences [1].

Methods

Twin Studies

The classical twin study, in which monozygotic (MZ) and dizygotic (DZ) twins are reared together in the same home is one of the most powerful designs for detecting genetic and shared environmental effects [2]. For this study we used the sixty-six cortical thickness measurements from the MZ and DZ twins pairs of 216 families of the processed Freesurfer data from the Human Connectome Project [3, 4].

Path Analysis

The common statistical technique used in twin studies is path analysis, see Fig. 1. Observed phenotypes Pi are assumed to be linear functions of the additive genetic factors (A) and environmental factors which may be divided into those that are shared in common (C) by members of a twin pair and those that are unique to each twin (E). The total variance of each factor is the square of the path coefficient: a2, c2, and e2 [5].

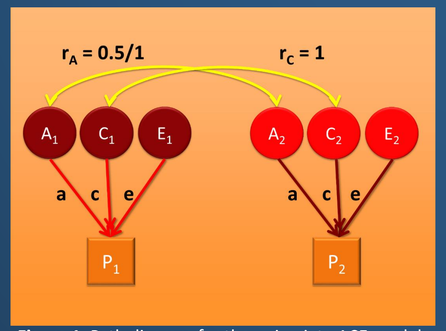

Figure 1. Path diagram for the univariate ACE model. The influence of effects A, C and E on phenotypic variability is quantified by the path coefficients a, c and e. A correlation between genetic factors as r_A = 0.5 for DZ and 1.0 for MZ is assumed in twin studies.

For each thickness we run a univariate ACE model given by $P_i = \Lambda \eta_i$, where:

$$\Lambda = \begin{bmatrix} a & c & e & 0 & 0 & 0 \\ 0 & 0 & 0 & a & c & e \end{bmatrix}, \quad P_i^t = [P_{i1}\ P_{i2}], \quad \text{and} \quad \eta_i^t = [A_1\ C_1\ E_1\ A_2\ C_2\ E_2].$$

Results

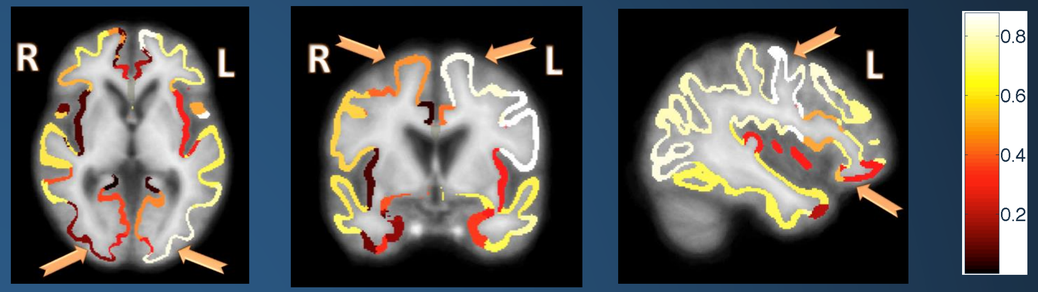

Figure 2. Horizontal (left) , coronal (middle), and sagittal (right) views of the brain. The lightest color shows the highest heritability (regions with big a^2) while the strong dark red colors shows the regions with low heritability (small a^2 value). In the horizontal and coronal slices, left and right hemisphere are flipped as indicated by R and L.

The univariate ACE models were created using the Open Mx library in the program R. Fig. 2 shows the results of ACE for modeling sixty-six thicknesses associated to different brain regions. The lightest colors show the highest heritability while the red colors shows the regions with low heritability. Arrows in the horizontal (occipital cortex) and coronal (pre-central gyrus) images indicate examples of bilateral structures showing differences across hemispheres, and arrows in the sagital image (pre-central gyrus and anterior frontal cortex) show an example of heritability differences within distinct regions of the left hemisphere.

Discussion

As seen above, a high percentage of the variability in brain structure (cortical thickness) is due to genetic contributions. Within hemisphere, distinct regions show unique values for heritability, for example as seen above left hemisphere pre-central gyrus shows very high heritability while anterior frontal regions show less. There also appears to be generally lower heritability for this data in the right hemisphere, possibly suggesting more environmental influence. Our next steps are to build a model that consider these thicknesses together, as these regions are not independent of each other, and also to look at the heritability from the other Freesurfer data available, area and volume, to see if there is unique heritability for these phenotypes.

References

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