#1809 The Modular Organization of Heritability Across the Cortex

Nadia Blostein[1,7], Sejal Patel[1,4,5], Gabriel A. Devenyi[1,6], Raihaan Patel[1,2], M. Mallar Chakravarty[1,2,3,6]

[1]Cerebral Imaging Centre, Douglas Mental Health University Institute, Verdun, Canada [2]Department of Biological and Biomedical Engineering, McGill University, Montreal, Canada [3]Integrated Program in Neuroscience, McGill University, Montreal, Canada [4]Campbell Family Mental Health Research Institute, Centre for Addiction and Mental Health, Toronto, Canada [5]Institute of Medical Science, University of Toronto, Toronto, Canada [6]Department of Psychiatry, McGill University, Montreal, Canada [7]Faculty of Arts & Science, McGill University, Montreal, Canada

CoBrA Lab
Computational Brain
Anatomy Laboratory

## INTRODUCTION

Heritability estimates are a straightforward gauge of the specificity of additive genetic effects and can be extended to a bivariate model in order to examine the genetic relationship between two phenotypes. The current project extends previous work from our group[3,4] to examine the shared heritability and genetic cross-correlation of cortical thickness (CT) and surface area (SA) across the human cortex, using a twin and non-twin sibling heritability design.
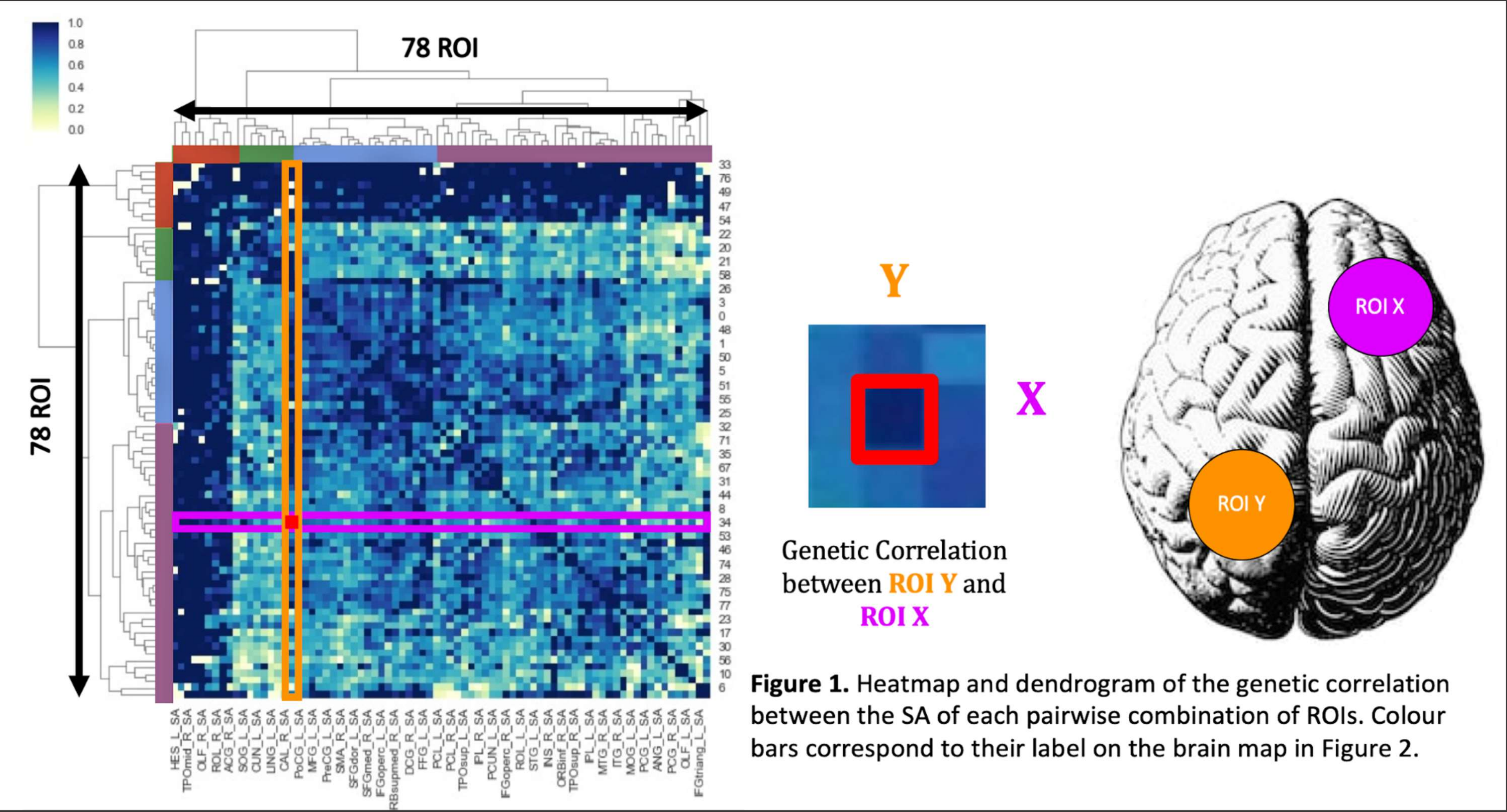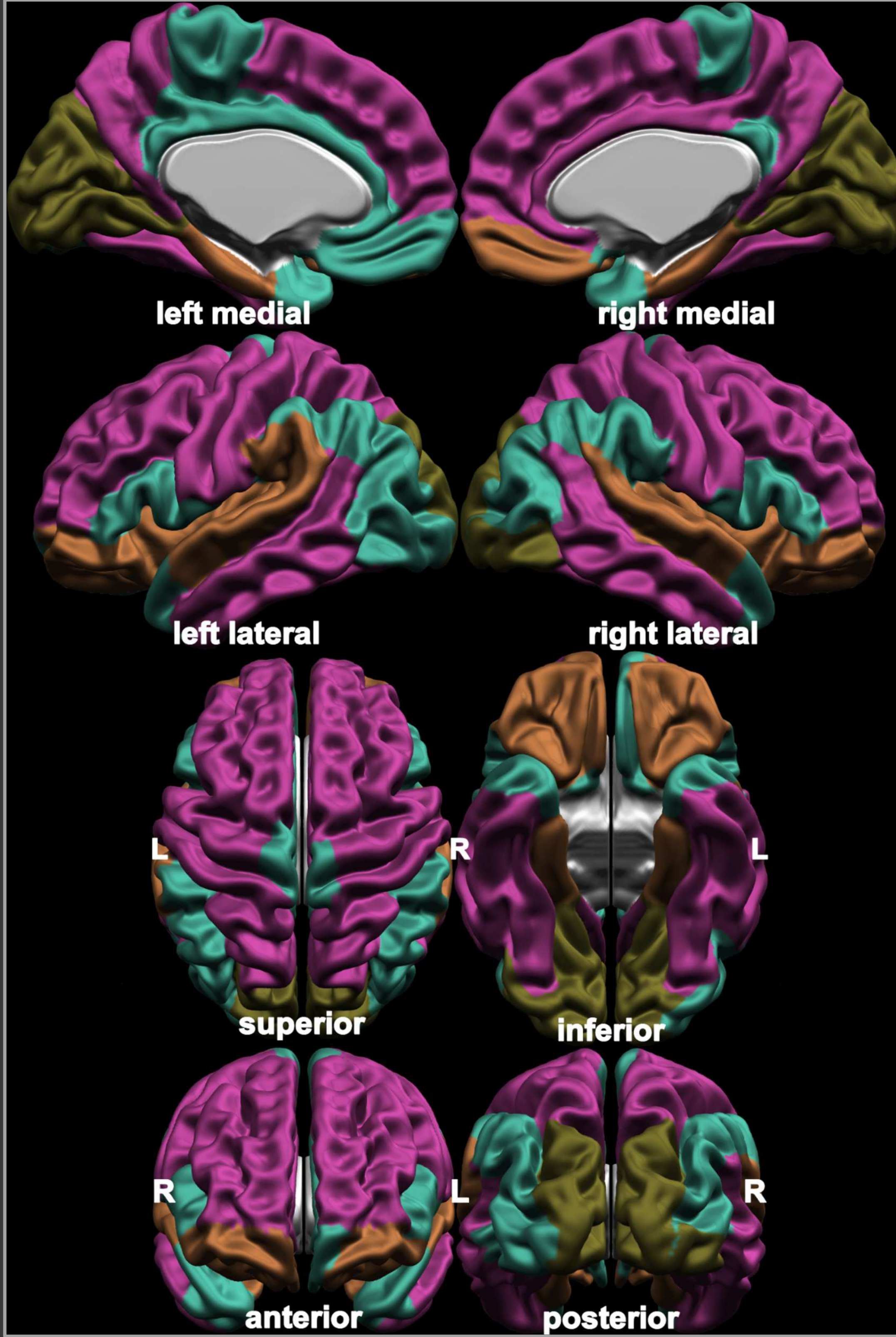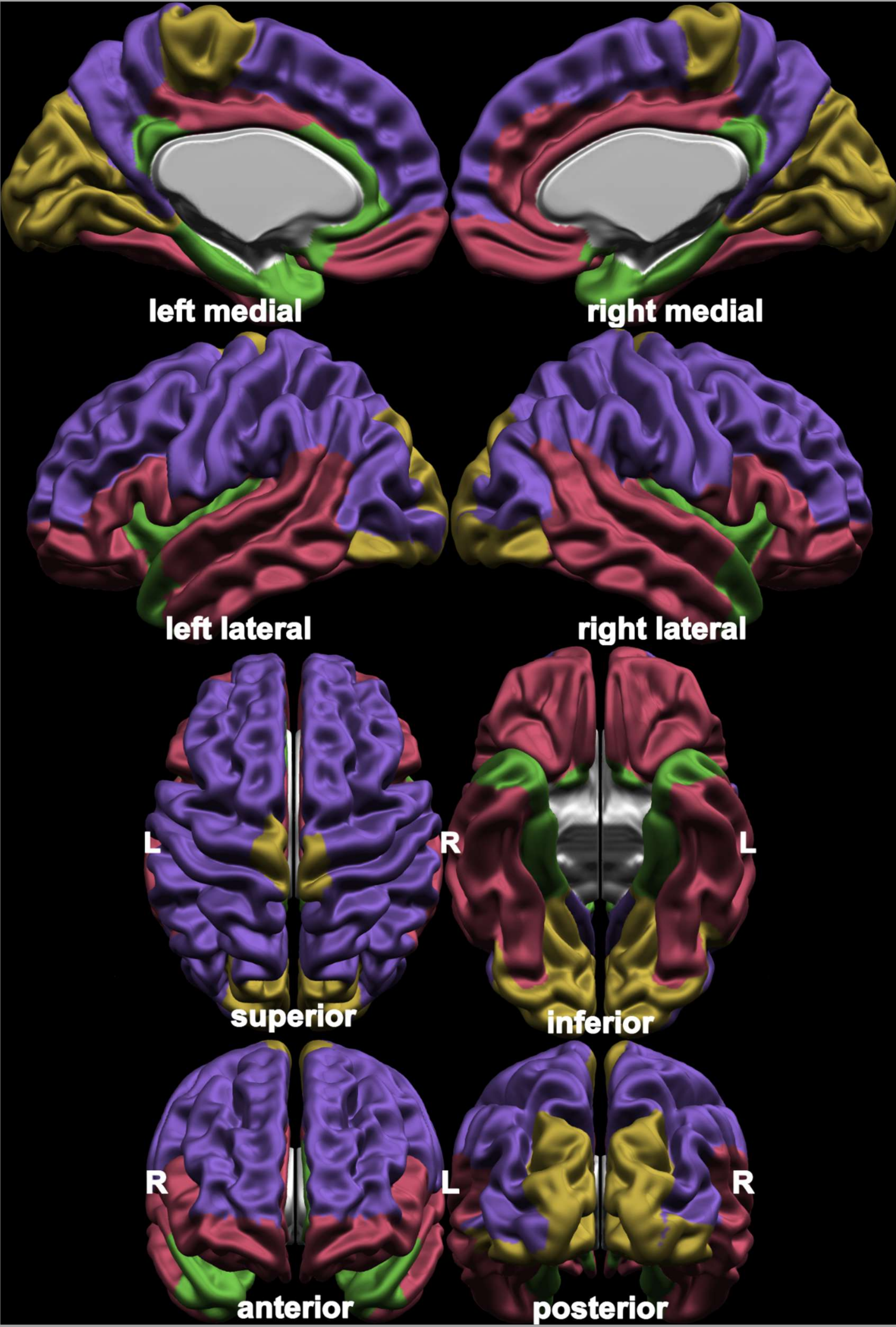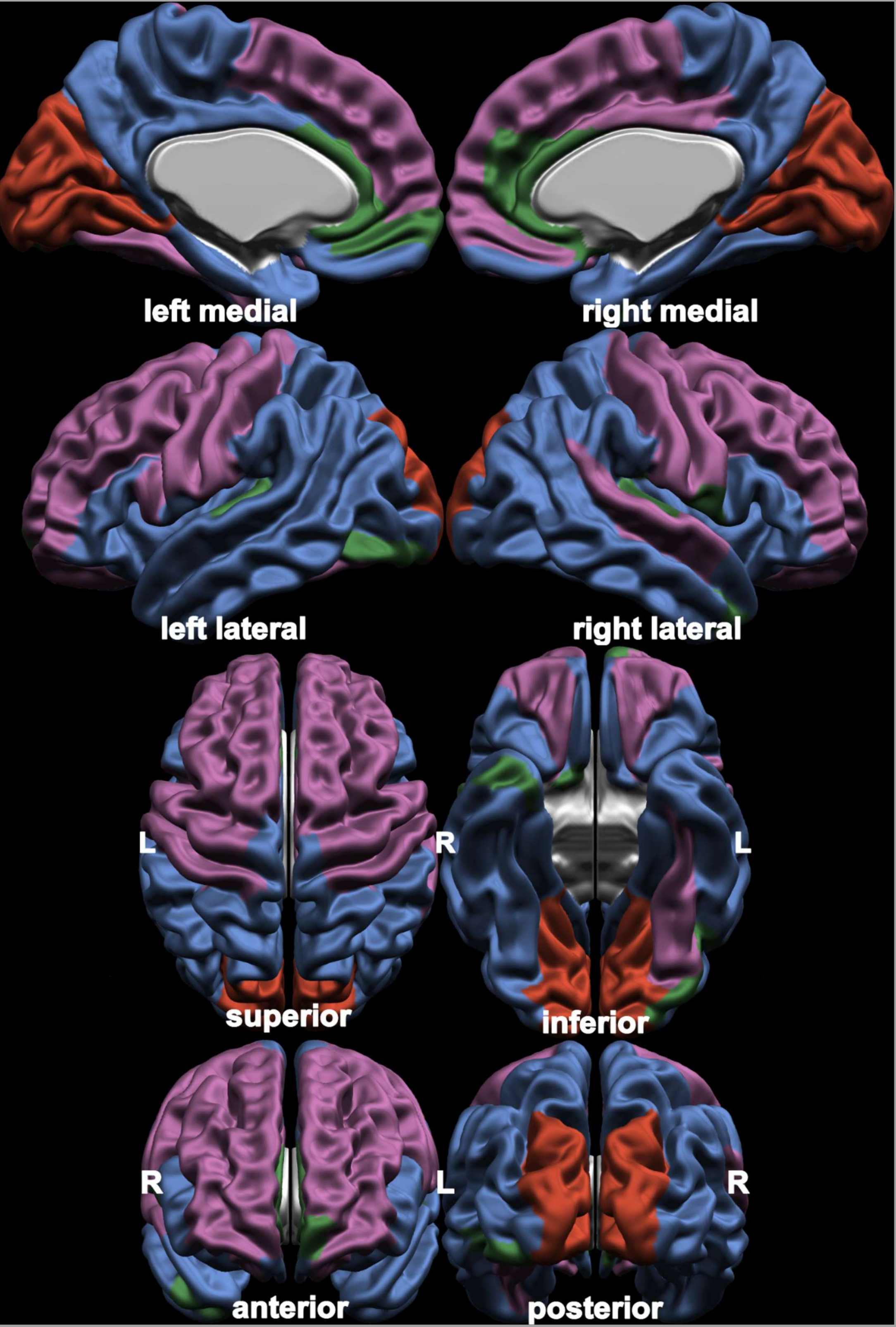
METHODS

Data Acquisition: The WU-Minn Human Connectome Project[6]. S900 Release of structural MRI data on healthy young adult twin and non-twin siblings (N = 875)[3,4]

Image Processing. The CIVET/2.1.0 pipeline[1] CT and cortical SA maps within 78 cortical regions of interest (ROIs), predefined by the AAL atlas[5]

Heritability Estimates. The OpenMx package (2.12.2) in R (3.5.1) was used to compute the **shared heritability** (h^2, proportion of covariance between two traits explained by additive genetic effects) and **genetic cross-correlation** (r_g, degree of genetic overlap between two traits) of the CT and SA between each possible pair of cortical ROIs, using a twin and non-twin sibling design.

Structural Correlation Matrices. **Structural correlation** matrices (Pearson r correlation between two neuroanatomical measures) of the CT and SA between each pairwise combination of ROIs were computed in R (3.5.1).

Matrix Clustering. The matrices generated by these pairwise combinations of cortical ROIs were hierarchically clustered using Ward's method in Python 3.

Figure 1. Heatmap and dendrogram of the genetic correlation between the SA of each pairwise combination of ROIs. Colour bars correspond to their label on the brain map in Figure 2.

Genetic Correlation between ROI Y and ROI X

Figure 2. Four modules of genetically correlated SA across ROIs.

Figure 3. Four modules of structurally correlated mean CT across ROIs

Figure 4. Four modules of structurally correlated total SA across ROIs

RESULTS: Main Finding

- The **genetic cross-correlation** of the SA between pairwise combinations of cortical ROIs is significant ($p < 0.05$) and forms four modules (fig. 1, fig. 2):
  1. One clusters the frontal lobe together (fig. 1, fig. 2 purple);
  2. A second clusters portions of the temporal and parietal lobes together with the associative cortex (fig 1, fig 2, blue);
  3. A third pulls together the medial occipital lobe (fig 2, red);
  4. A fourth forms an emotion regulation cluster as it groups the anterior cingulate and orbitofrontal cortex (fig 1, fig 2, green).

RESULTS: Supplementary

CONCLUSION

- There are four cortical SA modules that are mediated by the same genetic factors and they are not driven by structural correlation.

- Given the spatially heterogeneous laminar structure of the cortex, gene expression plays a significant in corticogenesis.

- These cortical modules could inform future studies aiming to parse the relationship between neurodevelopment and human-specific cortical expansion.

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