The Heritability of Human Connectomes: a Causal Modeling Analysis

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Summary

- Defined heritability for populations of connectomes using causal and statistical modeling.
- Associational tests show significant heritability in all genders and connectome models.
- Causal tests that control for neuroanatomy and age show significant heritability in some connectome models and some genders.
- Provide code and tools for future analysis on populations of connectomes in *graspologic* and *hyppo*.

Motivation

- Understanding how brain connectivity is influenced by genetics can improve our understanding of brain function and diseases.
- Current methods of analyzing connectomes or hertability exhibit limitations:
  - Selection Graph theoretic features
  - Multivariate normality assumptions

Do genomes cause connectomes?
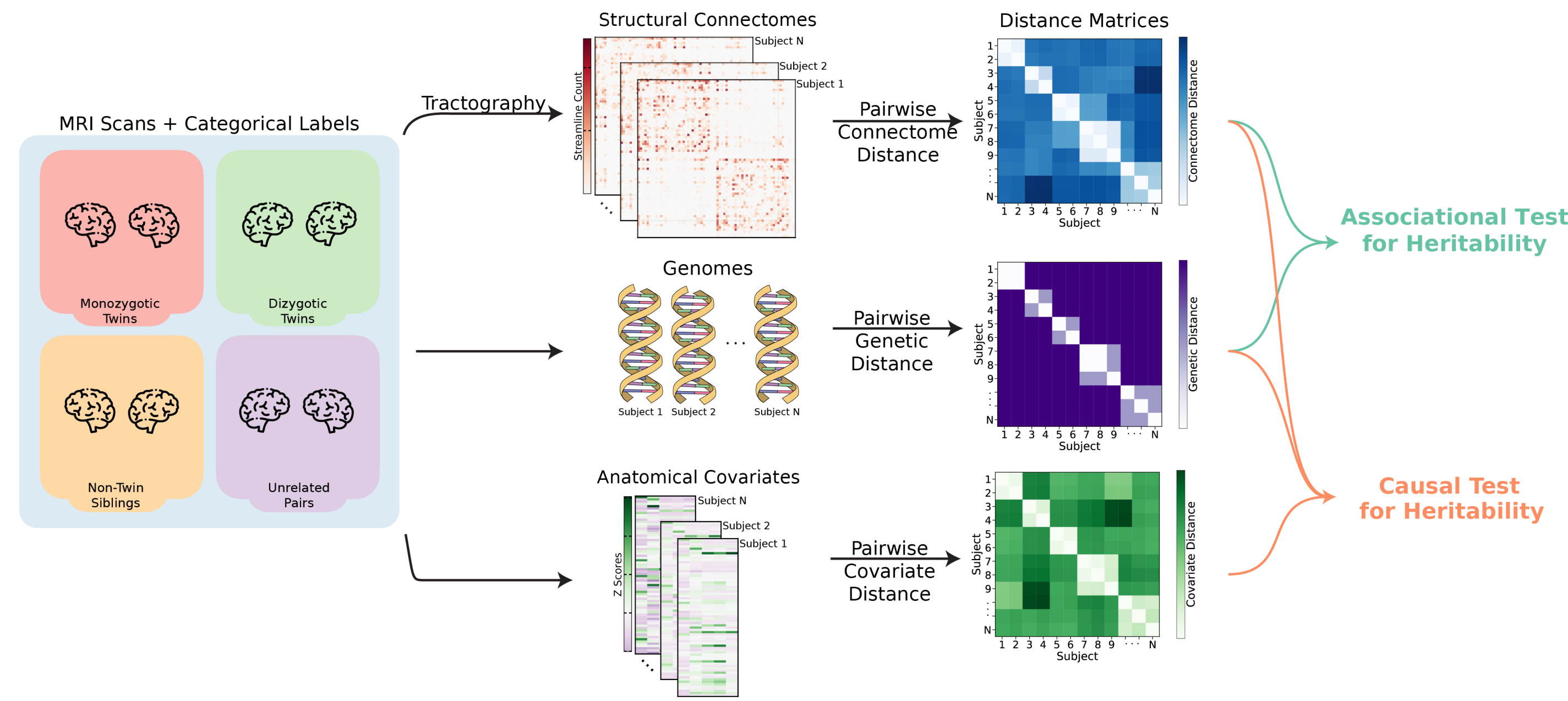
Overview of Analysis

Fig 1: Overview of the framework for detecting heritability of connectomes.

Causal Analysis of Effect of Genome on Connectomes

- Genome directly affects the structural connectome.
- Neuroanatomy (e.g. brain volume) indirectly affects the connectome.
- Participant history, such as the shared and non-shared environmental influences, and traits are potential confounders.
- The shared and non-shared environment is controlled by comparing between the same sex individuals.
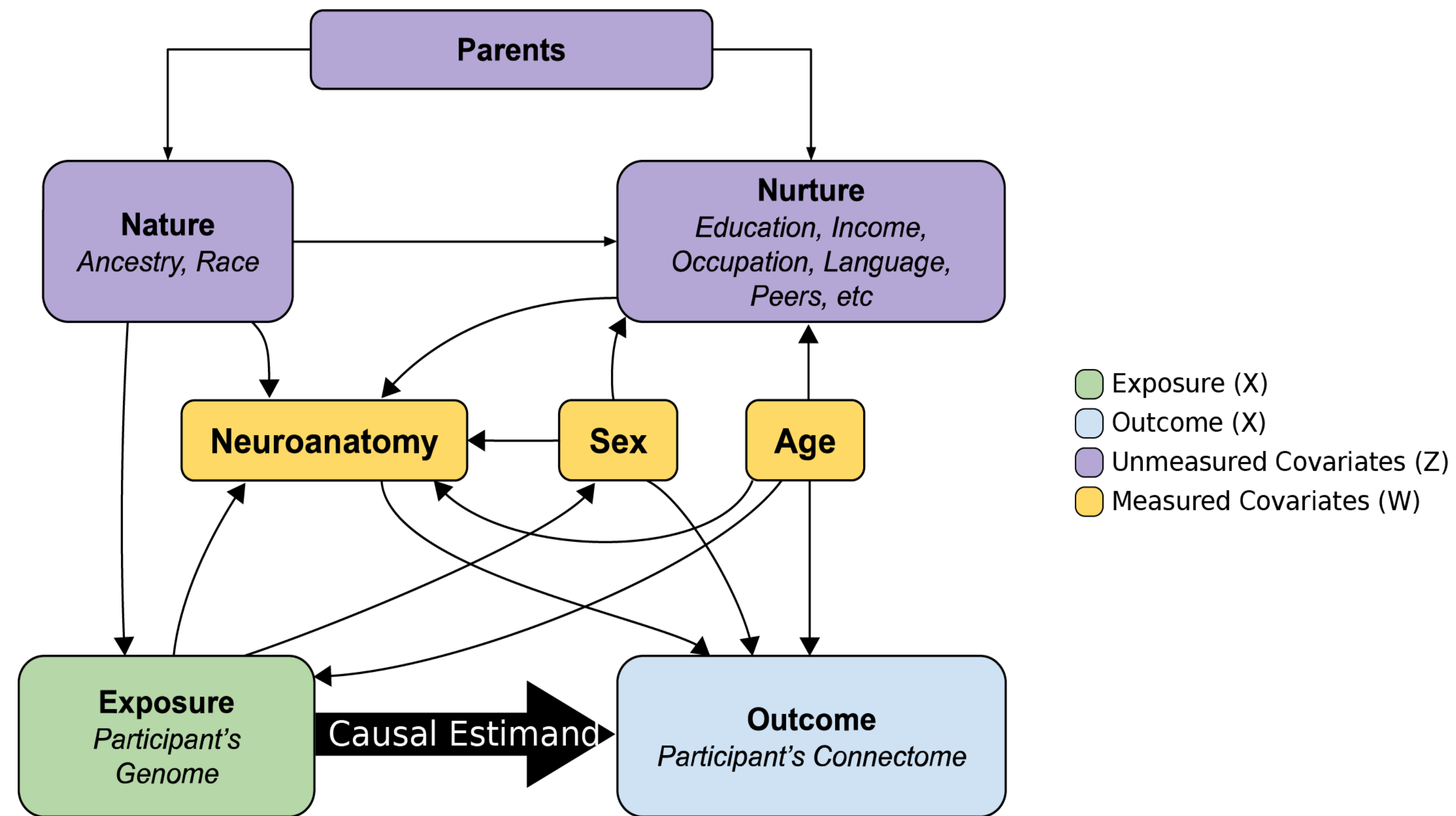

Fig 2: Directed acyclic graph (DAG) illustrating potential relationships between the genome and connectome.

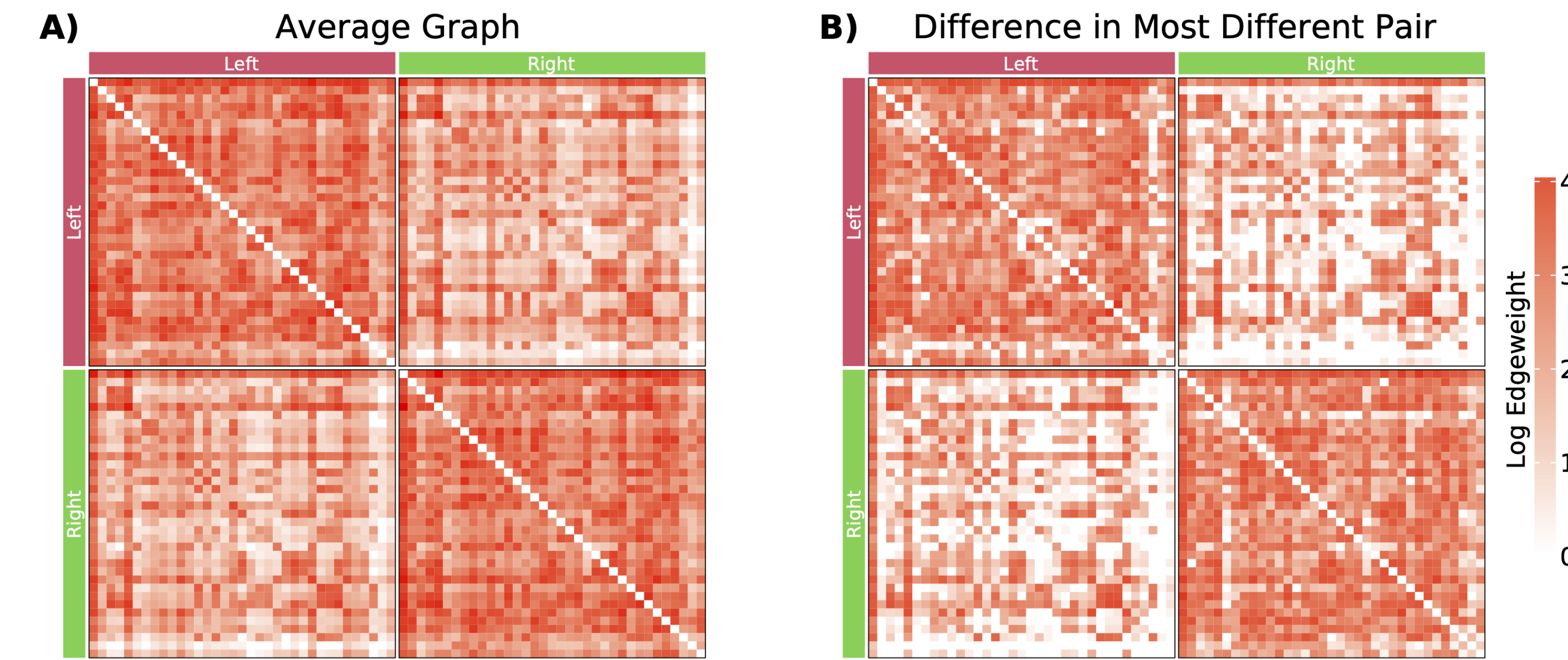## Structural Connectomes from Diffusion MRI

Fig 3: Visualization of connectomes as adjacency matrices using the projected Desikan parcellation with hemispheric labels. (A) Average connectome of all subjects with log-transformed edge weights. (B) Absolute difference of connectomes from the most different pair of subjects with log-transformed edge weights.

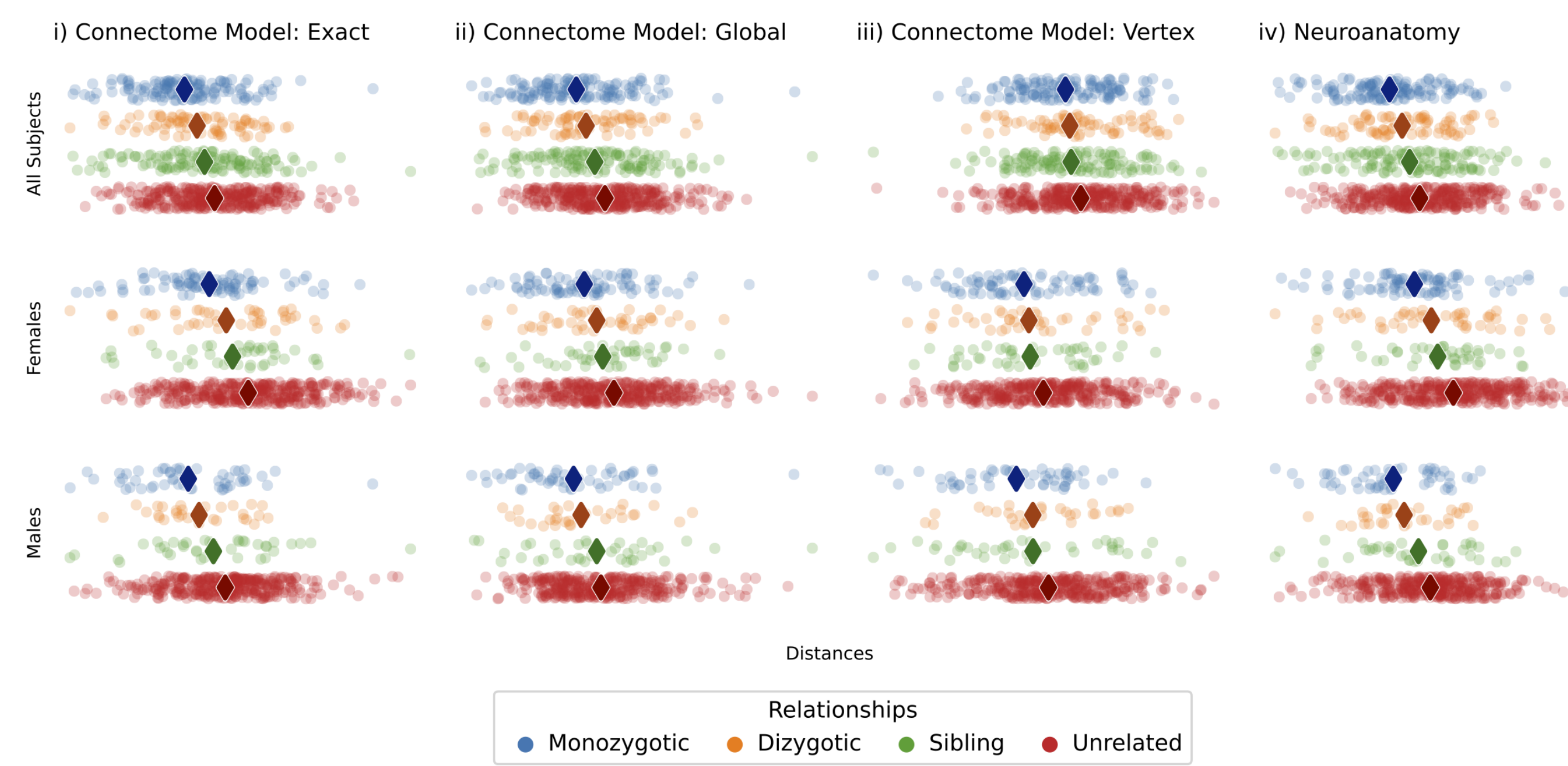## Pairwise Distances Grow as Familial Distances Grow

Fig 4: Visualization of pairwise distances of connectomes and neuroanatomy. Each point represents the pairwise distance between pairs of participants; diamond markers represent the median distance, colors are familial relationships, and rows are sex.

Associational and Causal Tests Show Significant Heritability in Some Connectome Models
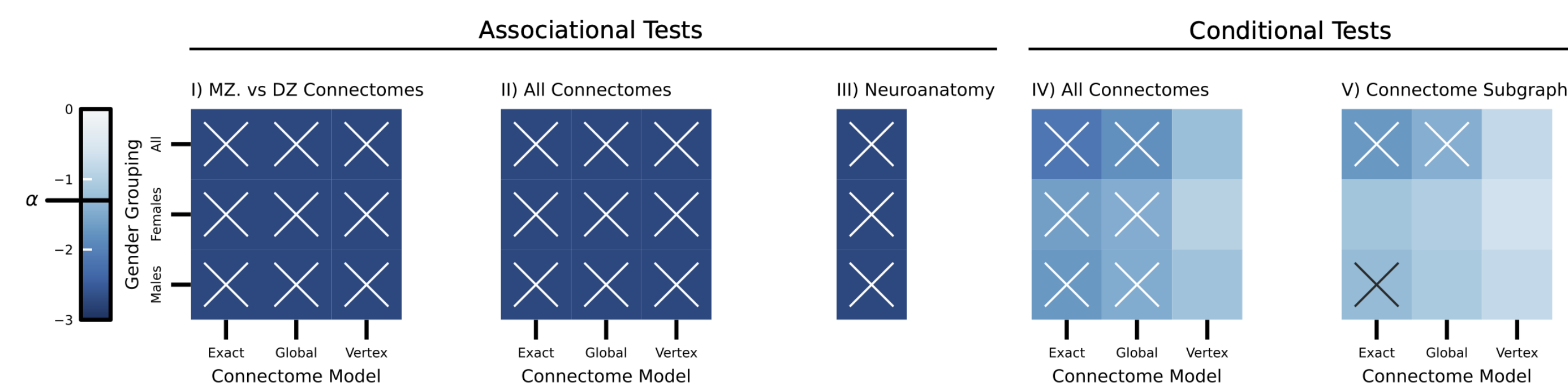

Fig 5: Testing associational and causal effect of genome on connectomes and neuroanatomy. Colors of heatmaps represent p-values, rows are gender groups, and columns are connectome models.

Human Connectome Project 1200

- Structural connectomes are estimated using structural (sMRI) and diffusion magnetic resonance imaging (dMRI).

	Monozygotic	Dizygotic	Non-twin siblings
N	322	212	490
Sex	196 F, 126 M	125 F, 87 M	237 F, 253 M
Age (mean)	29.6 (3.3)	28.9 (3.4)	28.3 (3.9)

Table 1: Participants and their demographics of HCP1200 Dataset.

Three Models for Comparing Connectomes

Exact: Are the connectome model parameters of connectomes the same?
Global scale: Are the connectome model parameters same after considering global scaling?
Vertex scale: Are the connectome model parameters same after considering vertex wise scaling?
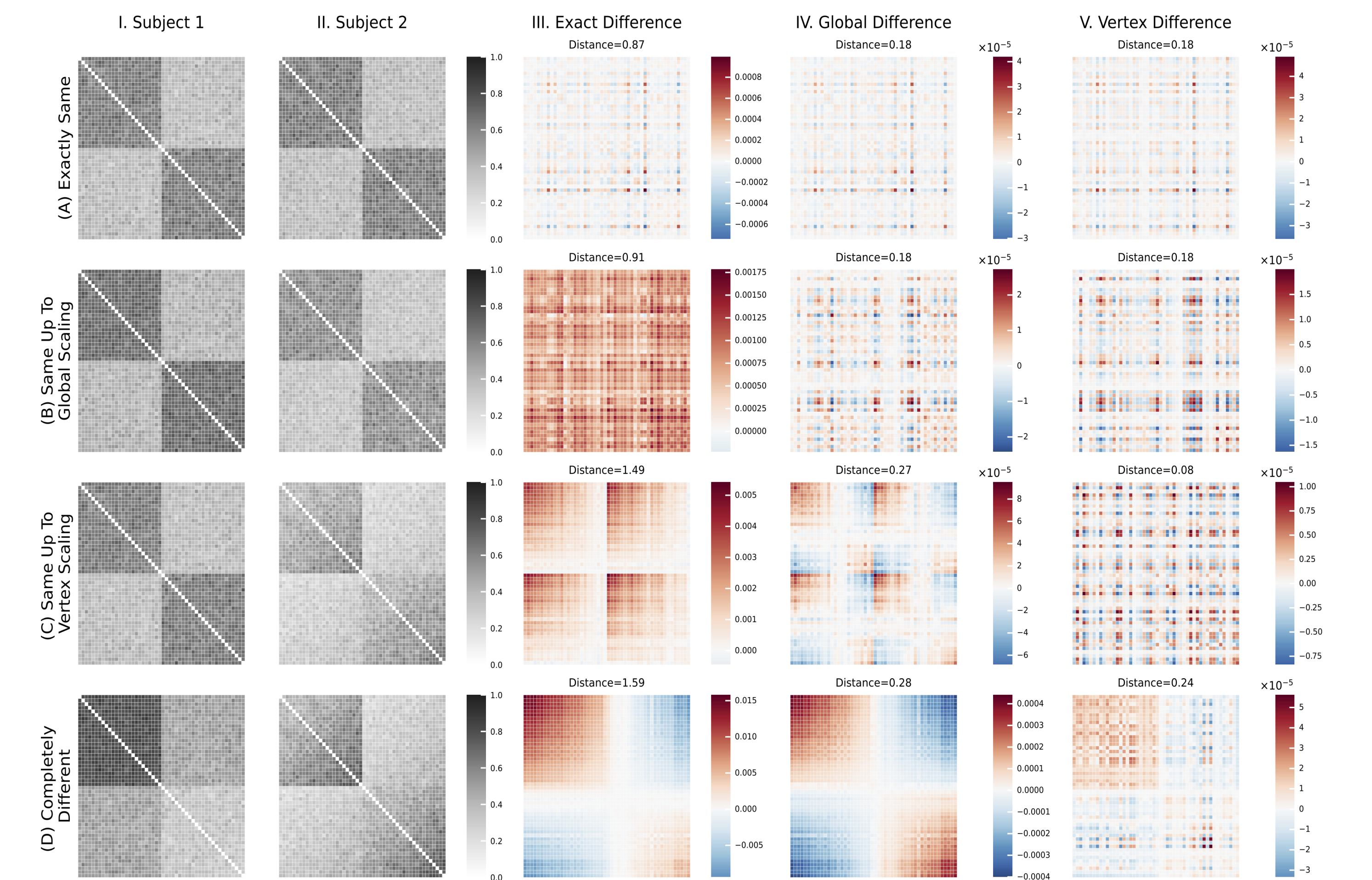

Fig 6: Examples of the three different models (exact, global scale, and vertex scale) of connectome heritability visualized as adjacency matrices. Networks are sampled from stochastic block models (SBMs) with different block probabilities.

Limitations and extensions

- Potential confounders that are not considered.
- Other staitsical models to consider (e.g. COSIE [3]).
- Repeated analysis on functional MRI or in other twin study datasets.

Code

graspologic — downloads 203k — Stars 305

hyppo — downloads 132k — Stars 173

References

[1] Chung et al. "The Heritability of Human Connectomes: a Causal Modeling Analysis," In bioRxiv (2023)
[2] Chung et al. "Statistical connectomics," Ann. Rev. Statistics and its Application (2021)
[3] Arroyo et al. "Inference for multiple heterogeneous networks with a common invariant subspace," JMLR (2021)