Statistical Modeling of Structural Connectomes Reveal High Genetic Influence on Connectivity

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Summary

- Aimed to define heritability for populations of connectomes using statistical modelling.
- Structural connectomes are heritable without controlling for neuroanatomy.
- Neuroanatomy is also highly heritable
- Connectomes remain heritable after controlling for effects of neuroanatomy on connectomes.
- Provide tools for future analysis on populations of connectomes.

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
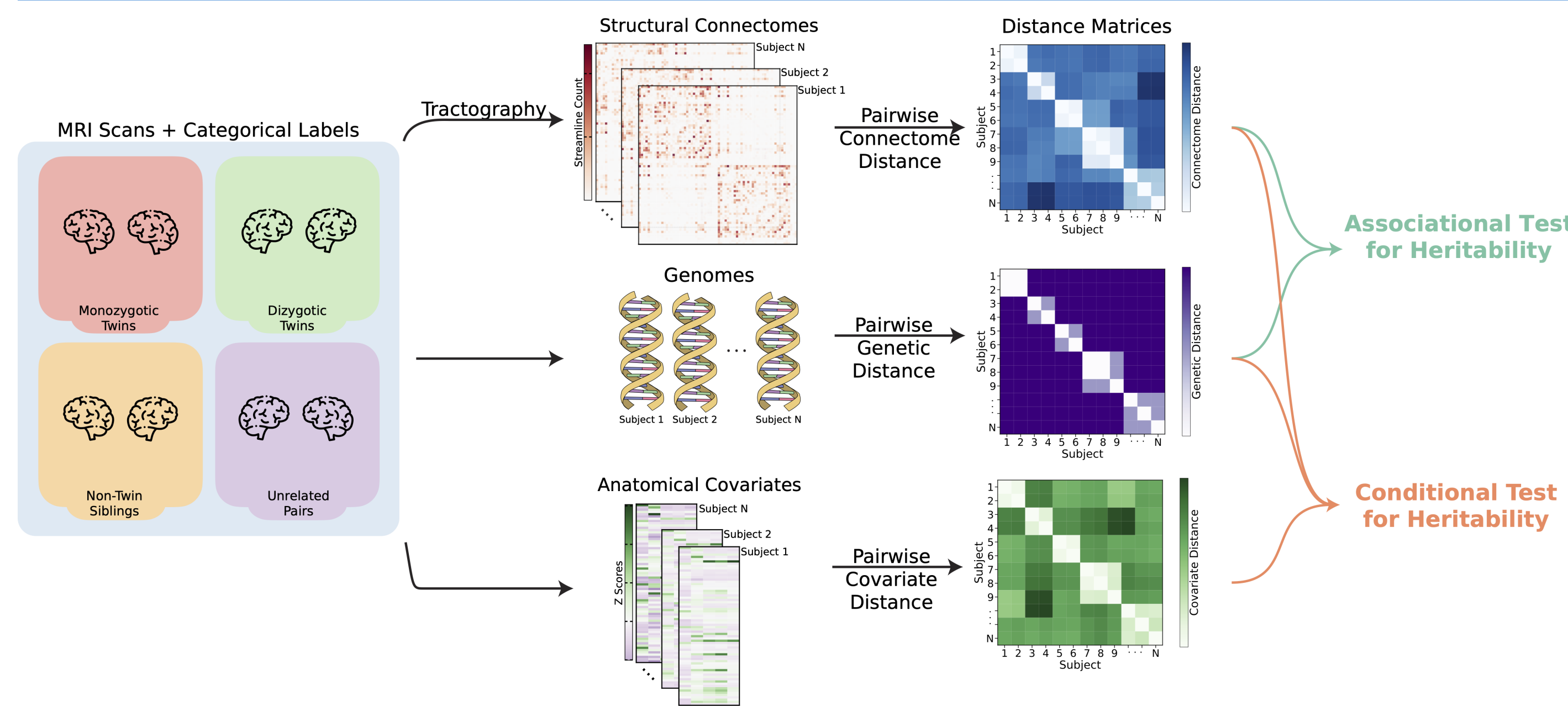 - Multivariate normality assumptions

Overview of Analysis

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

Do genomes cause in 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.
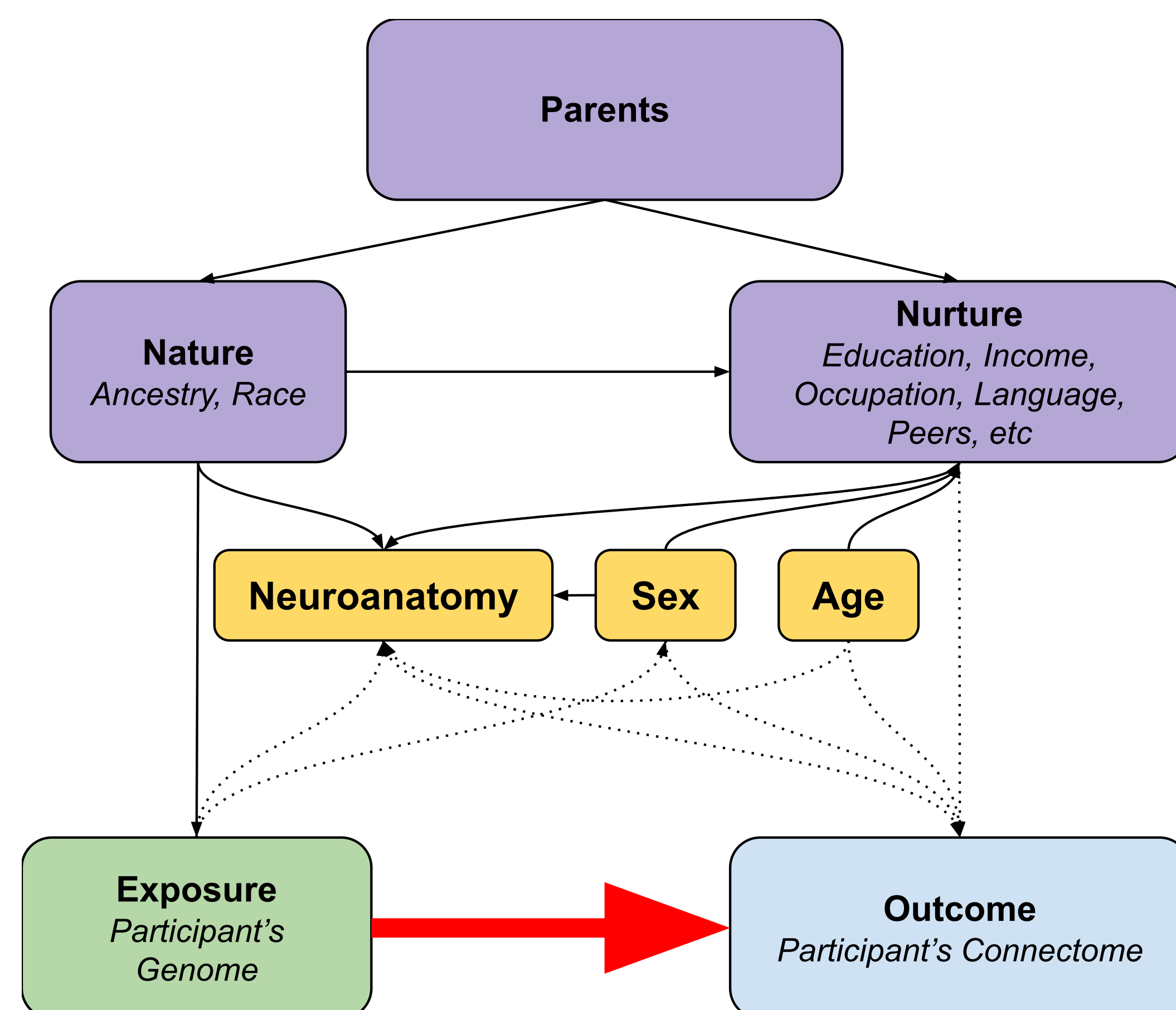
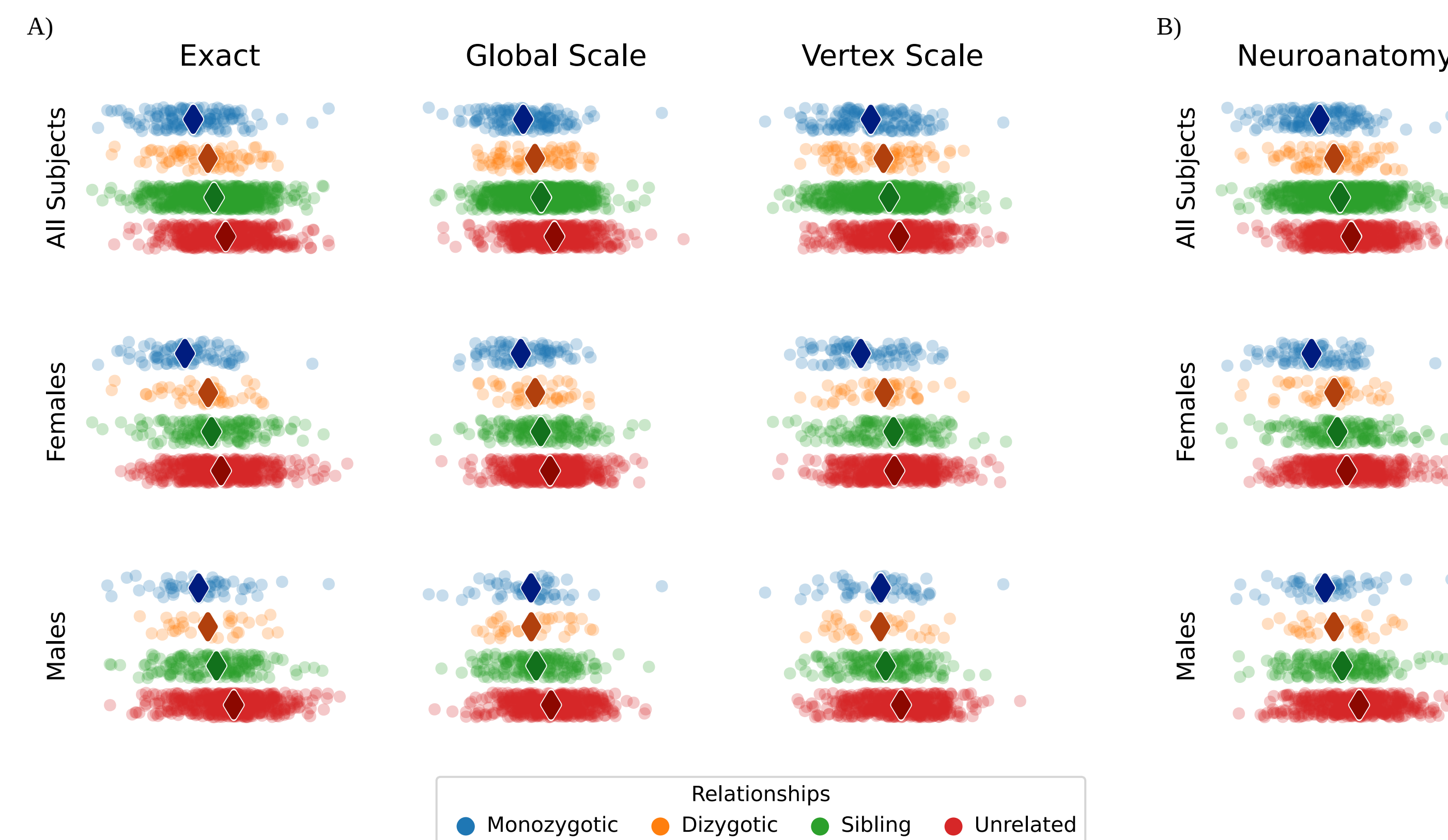## Associational Heritability for Connectomes and Neuroanatomy

Fig 3: Visualization of pairwise distances of connectomes and neuroanatomy. Diamonds represent the median. Median distances grow as genetic distances increase.
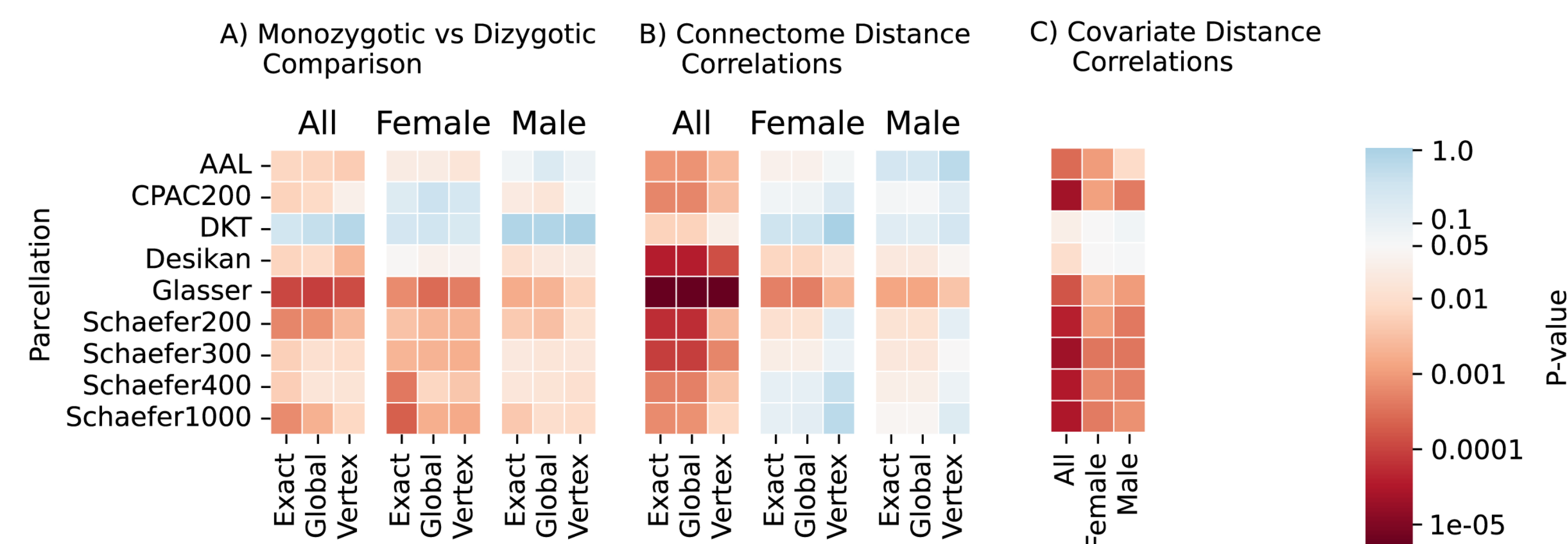

Fig 4: Testing for associational heritability of connectomes and neuroanatomy. Red squares indicate significant tests; blue indicate non-significant tests.
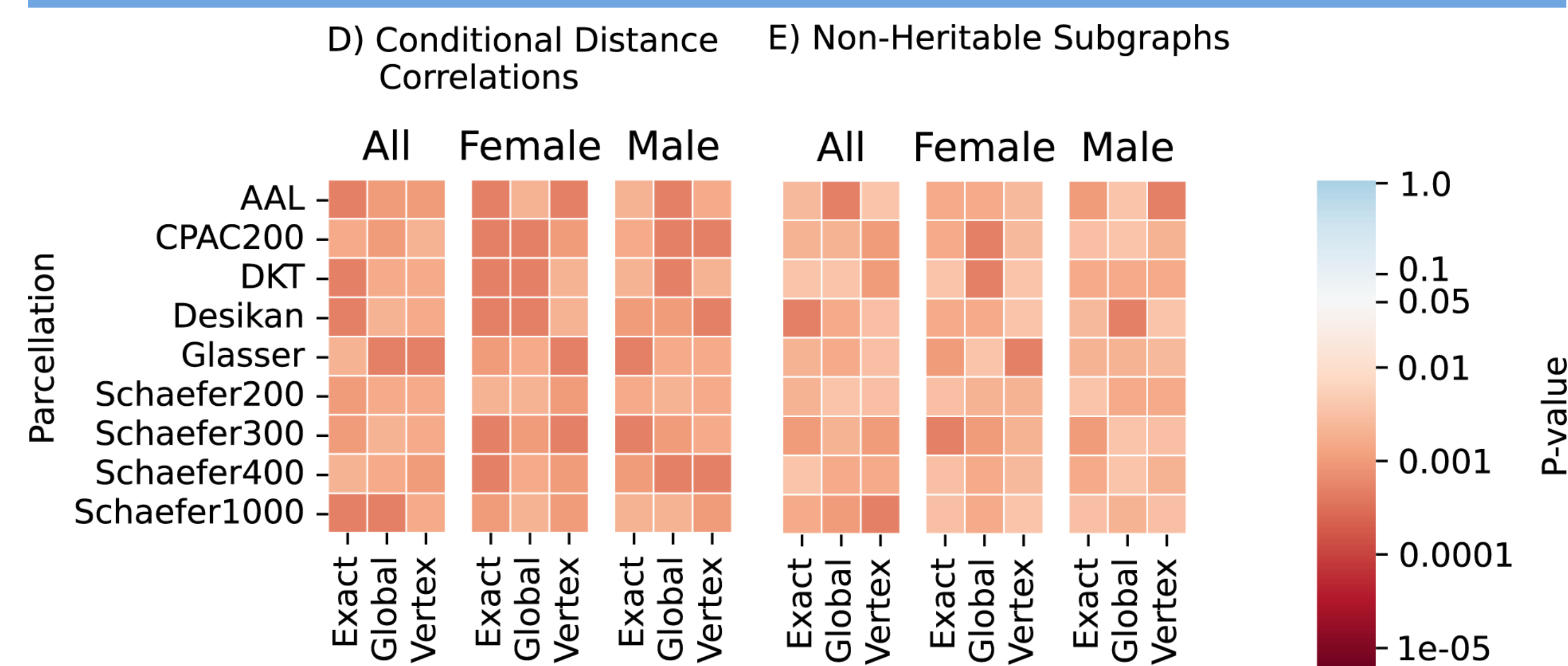
Conditional Heritability of Connectomes

Fig 5: Testing for conditional heritability of connectomes. Red squares indicate significant tests; blue indicate non-significant tests.

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 of Connectomes

- **Exact:** Are the generative models of connectomes the same?
- **Global scale:** Are the generative models same after considering global scaling?
- **Vertex scale:** Are the generative models same after considering vertex wise scaling?
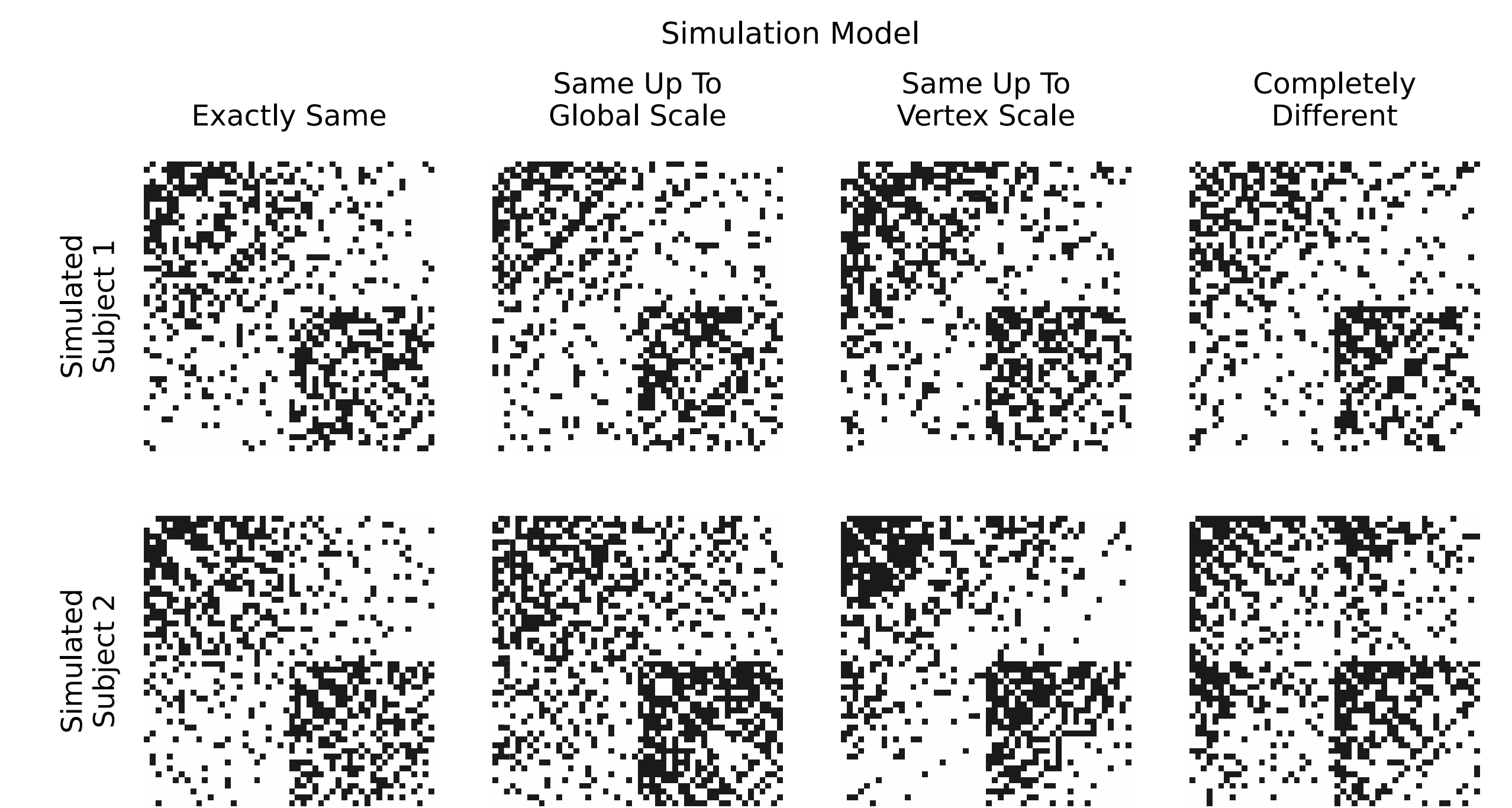

Fig 3: Examples of the three different models (exact, global scale, and vertex scale) of connectome heritability visualized as adjacency matrices. Networks are sampled from stochastic block models (SBMs) with different block probabilities.

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 162k
⬤ Stars 268

hyppo
downloads 108k
⬤ Stars 133

References

[1] Chung et al. "Connectomic Heritability," In preparation (2022)
[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)