

Summary

- Defined heritability for populations of connectomes using causal and statistical modeling.
- Structural connectomes are heritable without controlling for neuroanatomy.
- Connectomes remain heritable after controlling for effects of neuroanatomy on connectomes.
- Provide tools for future analysis on populations of connectomes.
- Neuroanatomy is also highly heritable

Motivation

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

Overview of Analysis

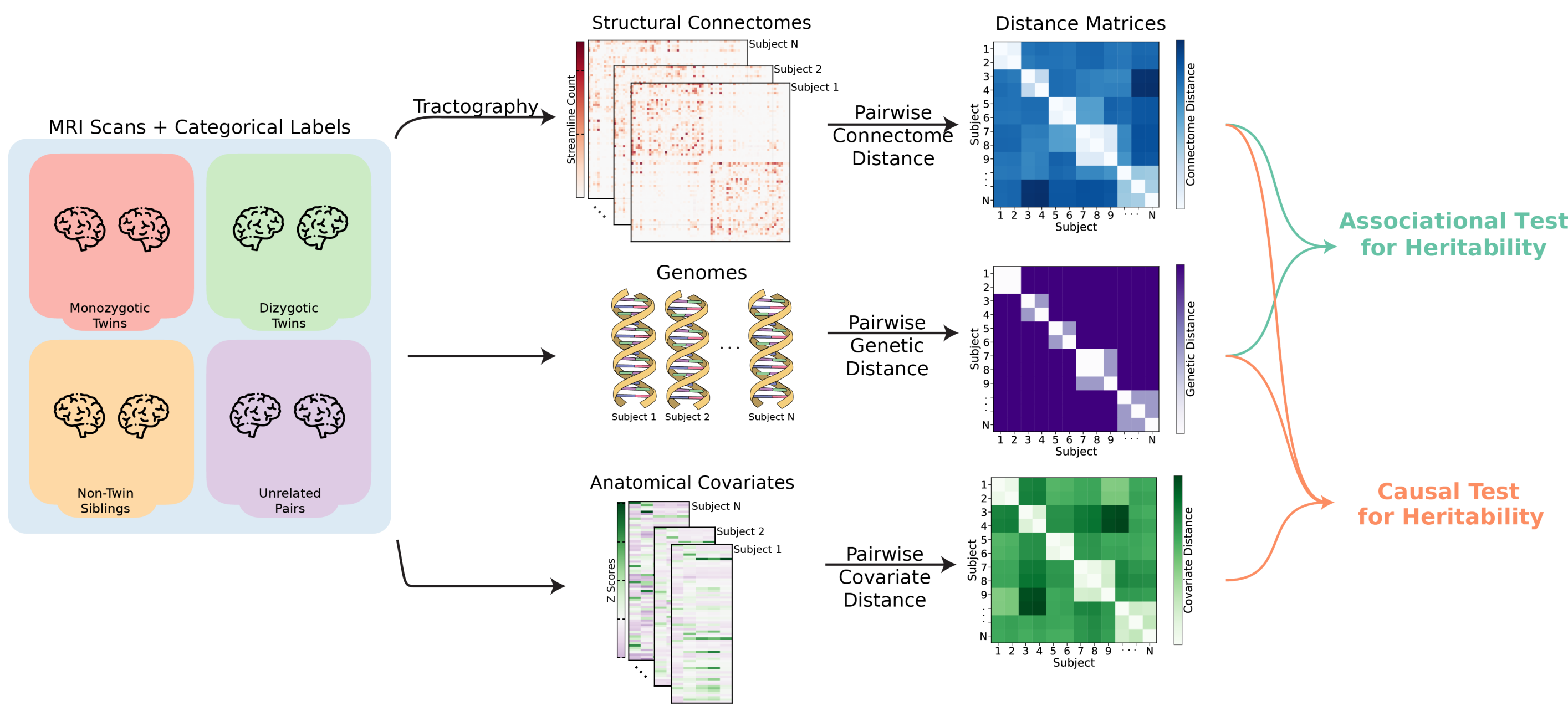


Fig 1: Overview of the framework for measuring heritability of connectomes.

Do genomes cause 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.

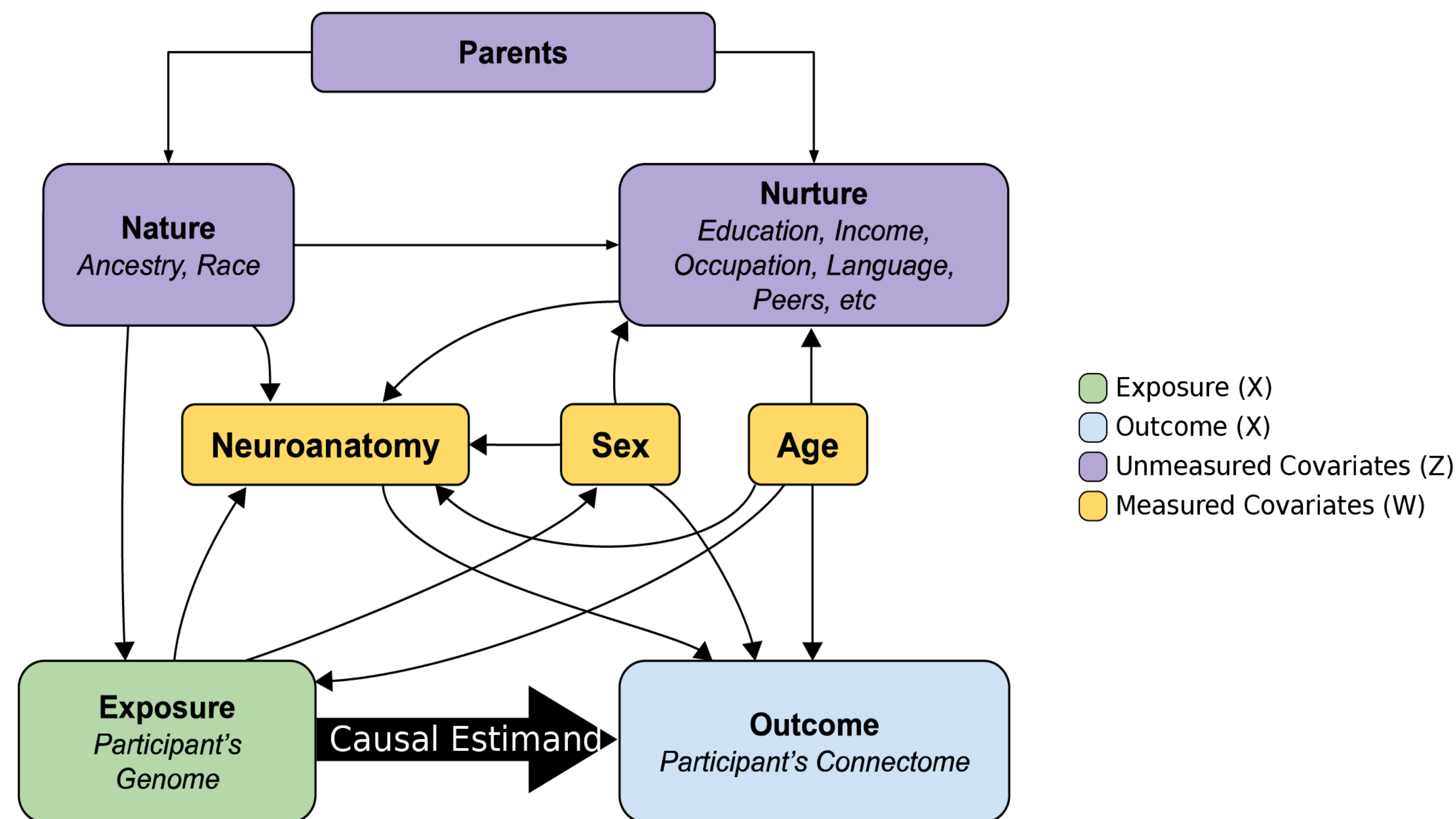


Fig 2: Directed acyclic graph (DAG) illustrating potential relationships between the genome and connectome.

Structural Connectomes from Diffusion MRI

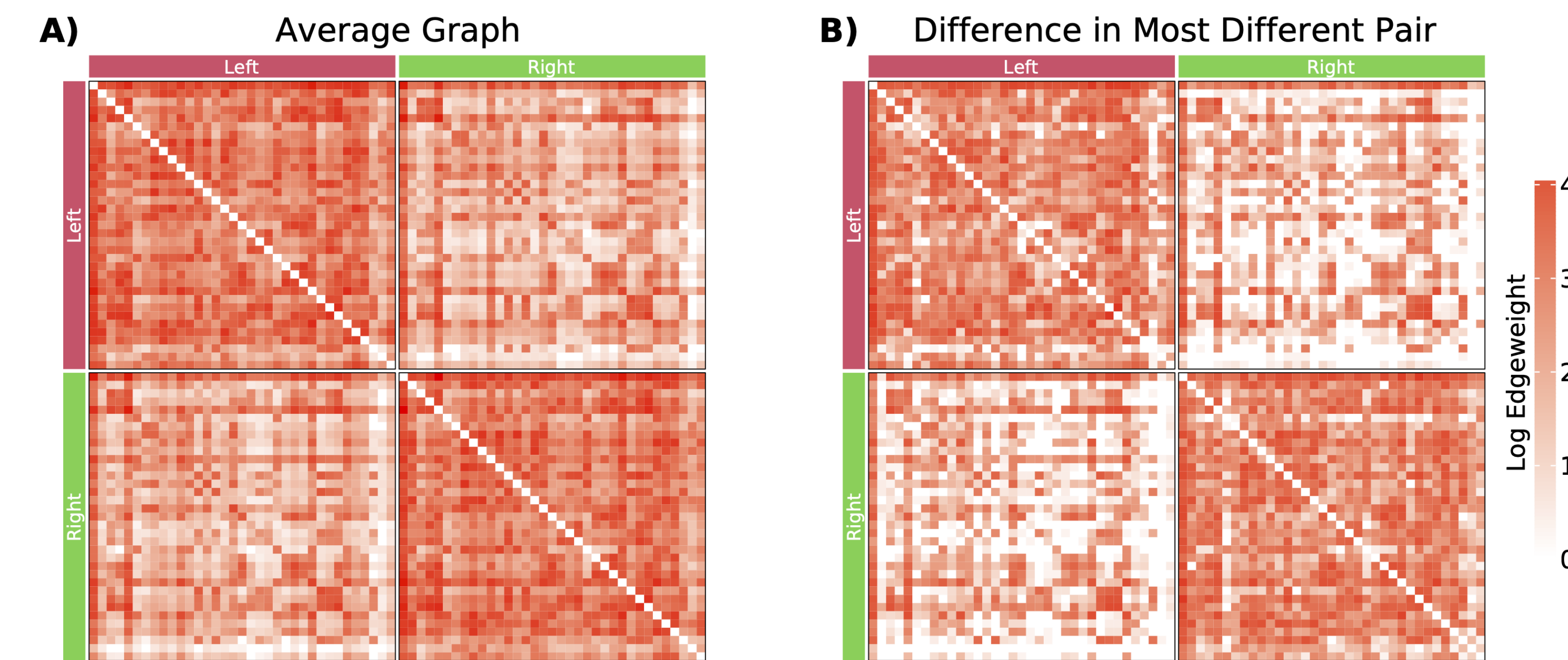


Fig 3: Visualization of connectomes as adjacency matrices using the projected Desikan parcellation with hemispheric labels. (A) Average connectome of all subjects with log-transformed edge weights. (B) Absolute difference of connectomes from the most different pair of subjects with log-transformed edge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

New title

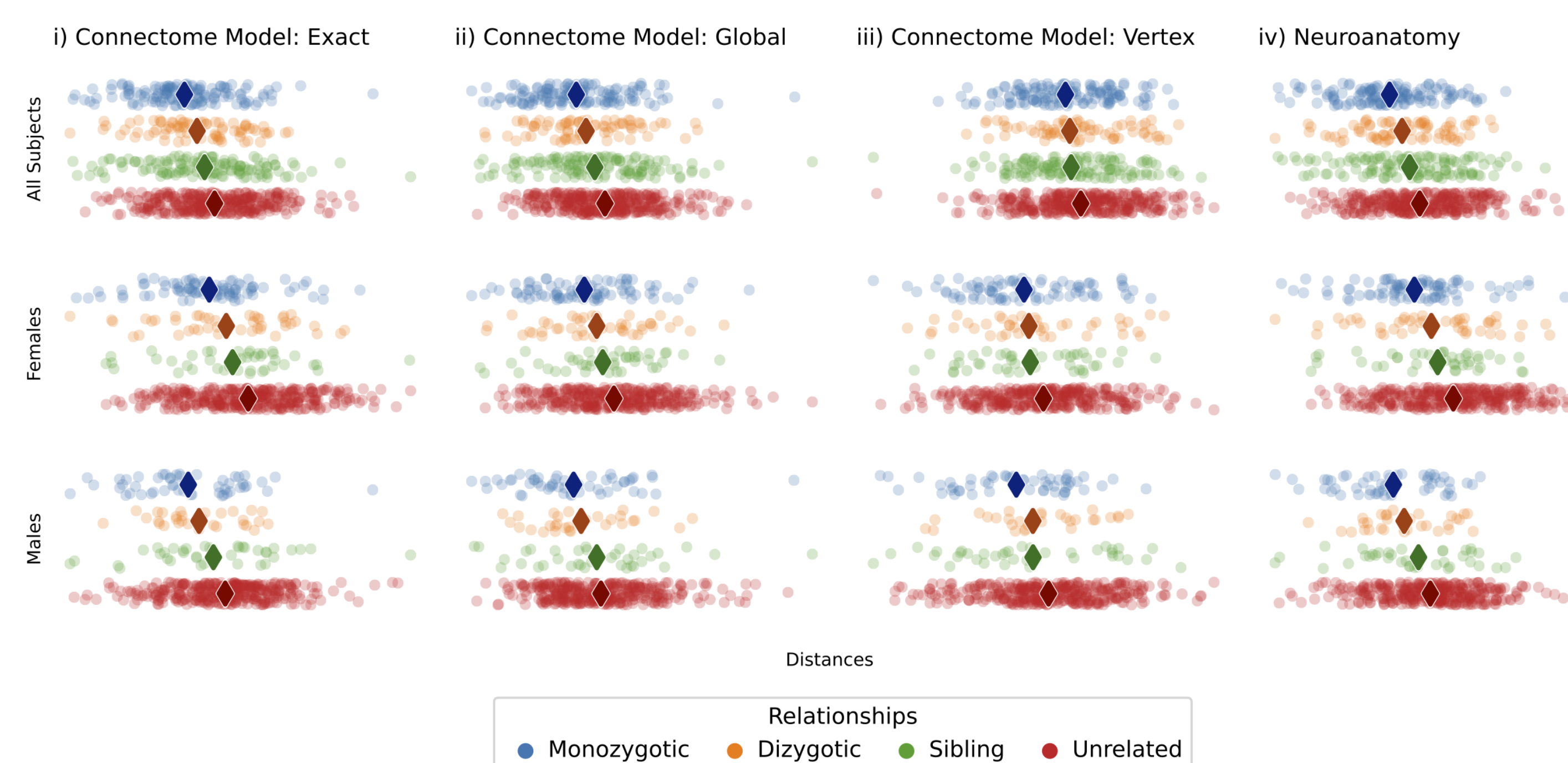


Fig 4: Visualization of pairwise distances of connectomes and neuroanatomy. Each point represents the pairwise distance between pairs of participants; diamond markers represent the median distance, colors are familial relationships, and rows are sex.

Associational and Causal Tests for Heritability

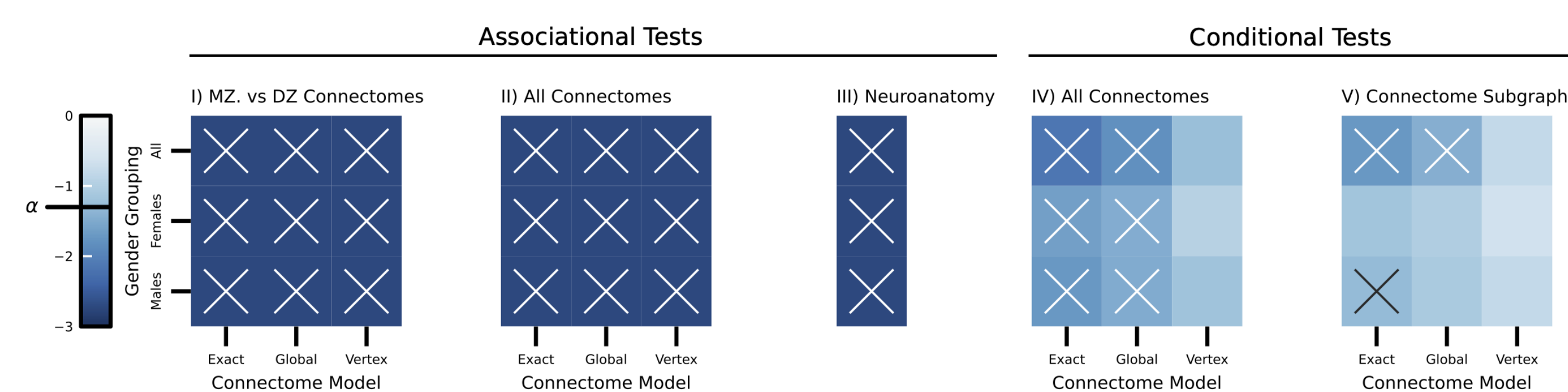


Fig 5: Testing associational and causal effect of genome on connectomes and neuroanatomy. Colors of heatmaps represent p-values, rows are gender groups, and columns are connectome models.

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 of Connectomes

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

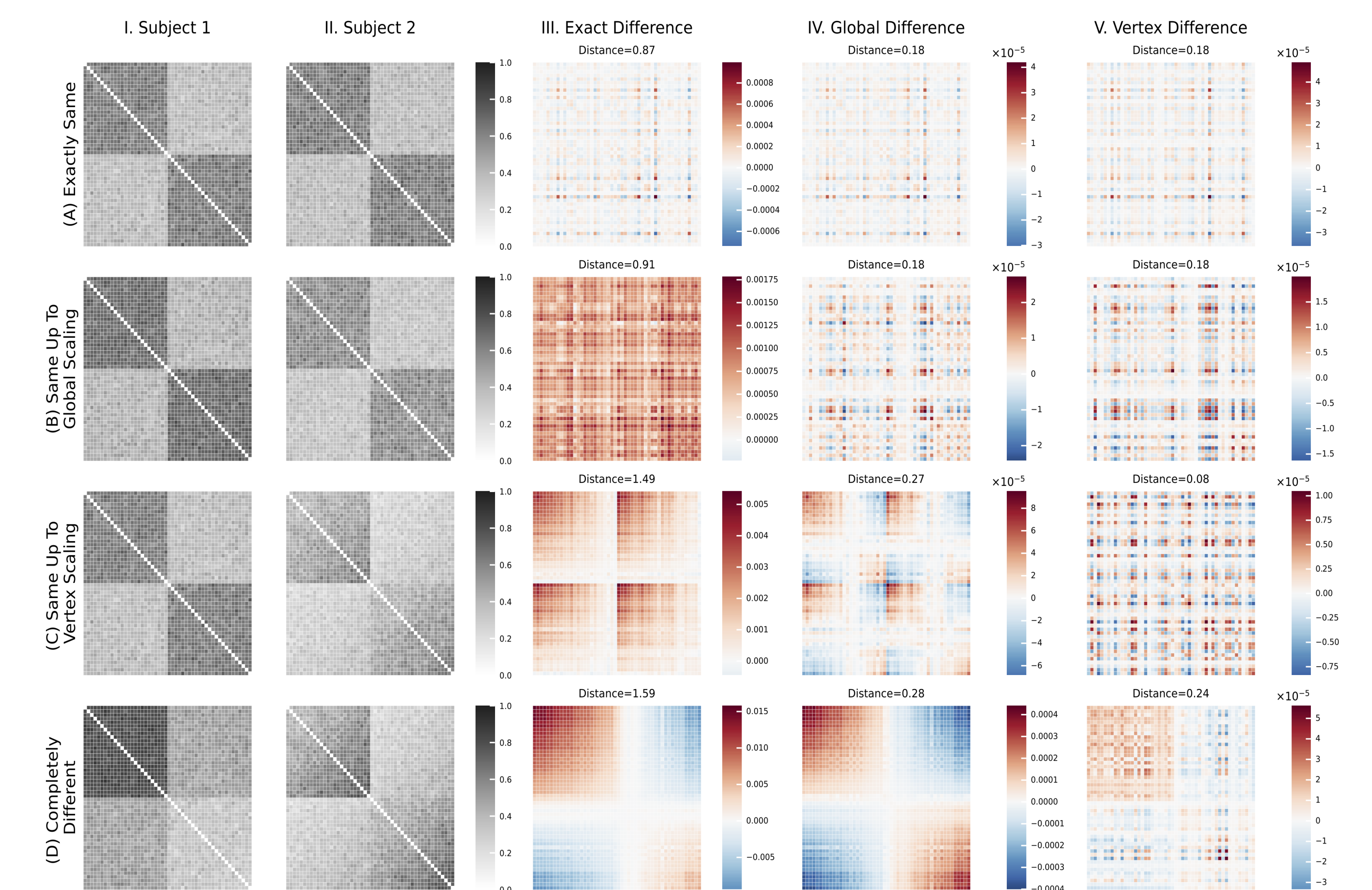
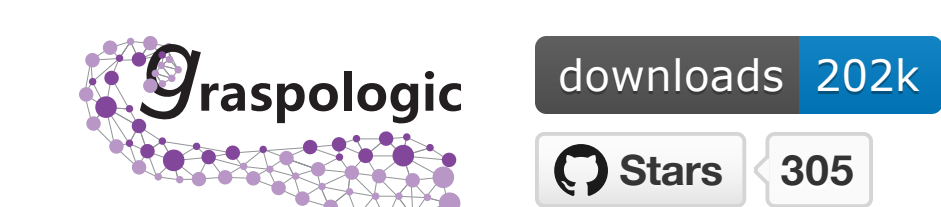


Fig 6: Examples of the three different models (exact, global scale, and vertex scale) of connectome heritability visualized as adjacency matrices. Networks are sampled from stochastic block models (SBMs) with different block probabilities.

Limitations and extensions

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

Code



hyppo



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)

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