Heritability of Human Structural Connectomes

Jaewon Chung

(he/him) - NeuroData lab

Johns Hopkins University - Biomedical Engineering

j1c@jhu.edu

@j1c (Github)

@j1c (Twitter)

Outline

- Background
  - **What is heritability?**
  - Graphs, networks, connectomes
  - Where do connectomes come from?
- Problem
  - What are we trying to estimate?
  - Causal models
  - Dcorr
  - Distance functions
- Results
  - Dataset
  - Results 1

What is heritability?

- Variations in phenotype caused by variations in genotype.
- Potentially discover relationships between diseases and genetics

Are the brain connectivity patterns heritable?

Brains connectivity as connectomes

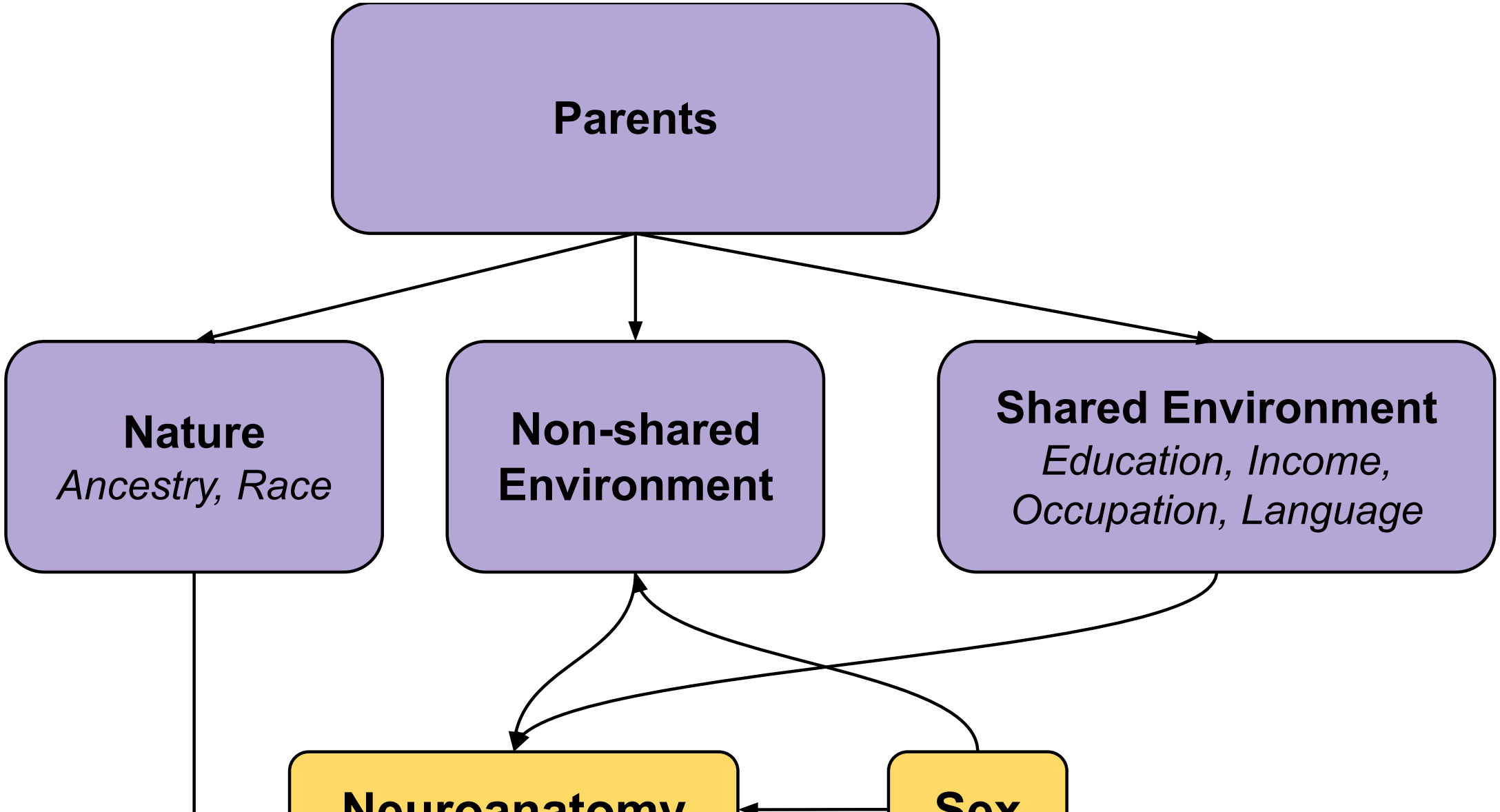
(aka networks or graphs)

- Vertex = a region of interest
- Edges = connectivity measure between a pair of vertices
- Diffusion MRI = # of estimated neuronal fibers
- Undirected = Edges have no direction

[Gu, Zijin, et al. "Heritability and interindividual variability of regional structure-function coupling." (2021)](https://www.nature.com/articles/s41467-021-25184-4)

Connectome Generation

Overall DAG


Parents
Nature
Ancestry, Race
Non-shared Environment
Shared Environment
Education, Income, Occupation, Language

Statistical problem

- Want an independence test!
- $H_0 : F(Genome, Connectome) = F(Genome)F(Connectome)$
  $H_A : F(Genome, Connectome) \neq F(Genome)F(Connectome)$
- Test statistic: Distance correlation

Statistical problem

- Want an independence test!
- $H_0 : F(Genome, Connectome|Covariates) = F(Genome|Covariates)F(Connectome|Covariates)$
  $H_A : F(Genome, Connectome|Covariates) \neq F(Genome|Covariates)F(Connectome|Covariates)$
- Test statistic: Conditional distance correlation

Distance Correlations

- Require distance functions
- Genetic distances
- Connectome distances $||X - YR||_F$

Human Connectome Project

- Demographics:

  Van Essen, David C., et al., The WU-Minn human connectome project: an overview (2013)

Monozygotic vs Dizygotic

- Assumptions:
    - Controls environment variable

Insert figure

Why compare siblings and twins?

All three groups

- Assumptions:
  - Add in environmental and genetic variance

Insert figure

Neuroanatomy (effect mediator)

Test the existence of arrow

Conditional Test as causal effect estimator

- Using conditional distance correlation

The End

Additional slides

Information on Distance Correlation

Shortcomings

- Network models
- Problems with connectome estimation.
- dominant genetic effects and epistasis.
- No interaction between environment and genetics

Environemtal effects

- Shared
  - Common experiences of siblings living in the same household.
    - household income, the family’s living situation, the dynamics between the parents, food consumed
- Non-shared
  - Everything else
  - Epigenetics
  - Luck
  - schools, peers