DeFries-Fulker regression vs. multilevel models for differential heritability and environmentality

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DeFries-Fulker regression

- Technique for estimating the
  - genetic,
  - shared environmental, and
  - non-shared environmental

  components of the variance between individuals in some trait.
- Uses data on pairs of identical (MZ) and non-identical (DZ) twins
- One twin's score is regressed on the other
- Proportion of shared environmental variation and genetic variation given by coefficients in the regression

$$\mathbf{score}_{1j} = \beta_0 + \beta_1 \mathbf{score}_{2j} + \beta_2 \mathbf{rel}_j + \beta_3 \mathbf{rel.score}_{2j} + e_j$$

DeFries & Fulker (1985)

DeFries-Fulker regression: the details

$$\textbf{score}_{1j} = \beta_0 + \beta_1 \textbf{score}_{2j} + \beta_2 \textbf{rel}_j + \beta_3 \textbf{rel.score}_{2j} + e_j$$

- i indexes twins and j twin pairs
- **rel** is the relatedness of the twins. $\textbf{rel} = \begin{cases} 1 & \text{MZ twins} \\ 0.5 & \text{DZ twins} \end{cases}$
- β_3 gives the proportion of variance in scores due to genetics
- β_1 gives the proportion due to the shared environment
- $1 - \beta_1 - \beta_3$ gives the proportion due to the non-shared environment

Assumptions

- Shared environment the same for MZ and DZ twins
- No assortative mating

DeFries & Fulker (1985)

Differential heritability and environmentality

- The amount of variation due to each component may change over some background variable
- e.g. Turkheimer et. al (2003) find genetic component of variation in IQ increases with SES while environmental components decrease
- DeFries-Fulker regression can be extended to handle this

$$\begin{aligned}\mathbf{score}_{1j} = \beta_0 + \beta_1 \mathbf{score}_{2j} + \beta_2 \mathbf{rel}_j + \beta_3 \mathbf{rel.score}_{2j} \\ + \beta_4 \mathbf{score.SES}_{2j} + \beta_5 \mathbf{rel.score.SES}_{2j} + e_j\end{aligned}$$

- $\beta_3 + \beta_5 \mathbf{SES}$ gives the proportion of variance due to genetics
- $\beta_1 + \beta_4 \mathbf{SES}$ gives the proportion due to shared environment
- $1 - (\beta_1 + \beta_3) - (\beta_4 + \beta_5)\mathbf{SES}$ gives the proportion due to the non-shared environment

LaBuda et al. (1986); Cherny et al. (1992)

Why differential heritability?

Gene-environment interactions

- Some genes have a different effect depending on the environmental context
- Genes for ability may require beneficial environments to affect development
  - Bioecological model, Bronfenbrenner & Ceci (1994)
- Genes may enable good performance despite poor environments
  - Diathesis-stress model, e.g. Gottesman (1991), Paris (1999)

Differential genetic distributions

- The distribution of genes in the population may change with the environmental variable
- e.g. if certain genes enable individuals to reach high SES, those genes will be more prevalent at high SES
- There may be more gene variants at low (or at high) SES

Why differential heritability?

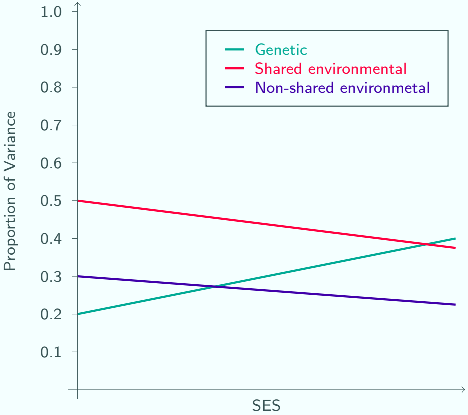
Environment-environment interactions

- Some environmental conditions may have a different effect depending on the environmental context
- They may be able to aid performance only under beneficial environments (combination of beneficial factors needed)
  - Environmental version of the bioecological model
- They may provide resilience against poor environments (combination of adverse factors needed) (Jenkins et al, 2008)
  - Diathesis-stress model

Differential environmental distributions

- The distribution of other environmental factors in the population may change with the environmental variable
- "Tolstoy hypothesis" (my name; also for differential genetic distributions)

Problem with modelling proportions



Might conclude:

- genetic variation increases: gene-environment interaction
- environmental variation thus forms smaller proportion

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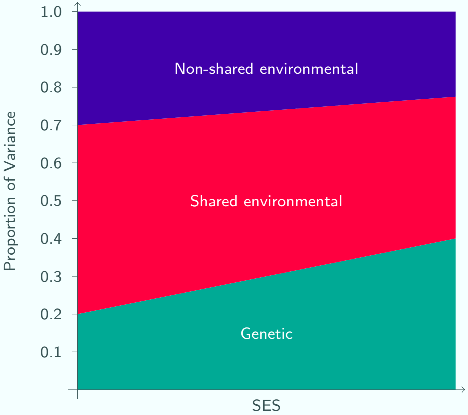

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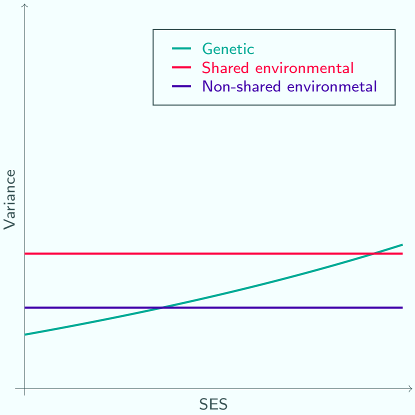

This is certainly one possibility

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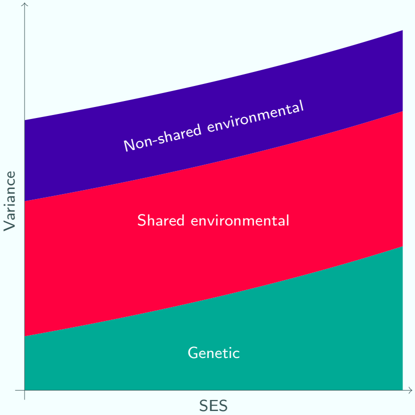

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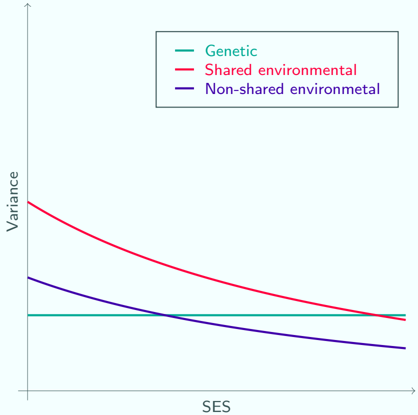

However, it could be the environmental variance decreases and the genetic variance remains constant

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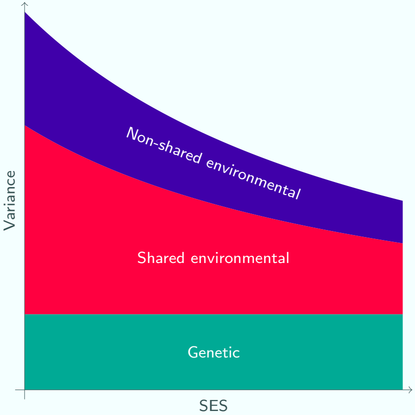

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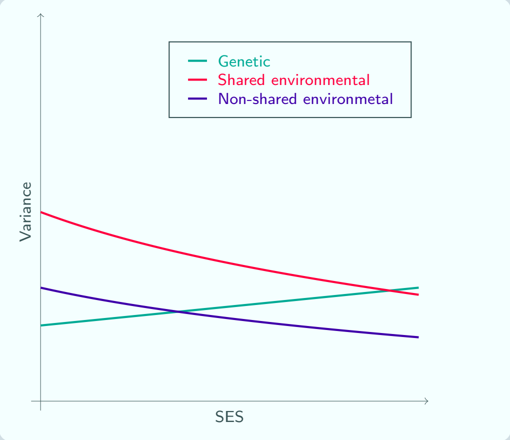

Or the genetic variance could increase and the environmental decrease

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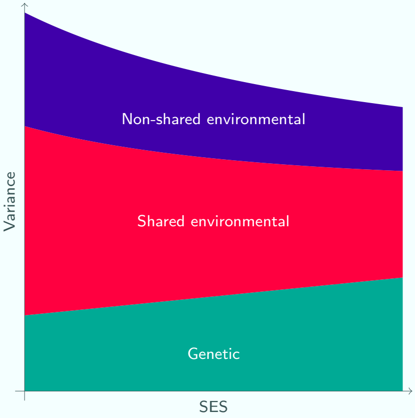

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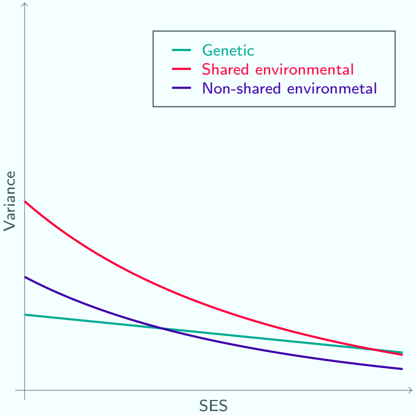
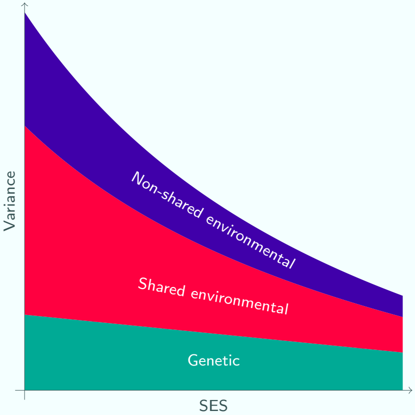


The genetic variance could even decrease

Problem with modelling proportions



The genetic variance could even decrease

Solution: multilevel modelling!

The multilevel genetic model

$$\textbf{score}_{ij} = \beta_0 + \beta_1\textbf{SES}_j + u_{0j} + u_{1j}\textbf{SES}_j + g_{0ij} + g_{1ij}\textbf{SES}_j + e_{0ij} + e_{1ij}\textbf{SES}_j$$

$$\begin{bmatrix} u_{0j} \\ u_{1j} \end{bmatrix} \sim \mathrm{N}\left(0, \begin{bmatrix} \sigma^2_{u0} & \\ \sigma_{u01} & \sigma^2_{u1} \end{bmatrix}\right)$$

$$\begin{bmatrix} g_{0ij} \\ g_{1ij} \end{bmatrix} \sim \mathrm{N}\left(0, \begin{bmatrix} \sigma^2_{g0} & \\ \sigma_{g01} & \sigma^2_{g1} \end{bmatrix}\right)$$

$$\begin{bmatrix} e_{0ij} \\ e_{1ij} \end{bmatrix} \sim \mathrm{N}\left(0, \begin{bmatrix} \sigma^2_{e0} & \\ \sigma_{e01} & \sigma^2_{e1} \end{bmatrix}\right)$$

$$\mathrm{cov}(g_{01j}, g_{02j}) = \textbf{rel}\,\sigma^2_{g0}$$

$$\mathrm{cov}(g_{11j}, g_{12j}) = \textbf{rel}\,\sigma^2_{g1}$$

$$\textbf{rel} = \begin{cases} 1 & \text{MZ twins} \\ 0.5 & \text{DZ twins} \end{cases}$$

Genetic variance:
$\sigma^2_{g0} + 2\sigma_{g01}\textbf{SES}_j + \sigma^2_{g1}\textbf{SES}^2_j$

Shared env. variance:
$\sigma^2_{u0} + 2\sigma_{u01}\textbf{SES}_j + \sigma^2_{u1}\textbf{SES}^2_j$

Non-shared env. variance:
$\sigma^2_{e0} + 2\sigma_{e01}\textbf{SES}_j + \sigma^2_{e1}\textbf{SES}^2_j$

Summary

	Genetic variation	Environmental variation
Interaction	Gene-environment interaction	Environment-environment interaction
Tolstoy hyp.	Different distributions of genes	Different distributions of environments

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Further work

Simulation

- Simulate data from scenarios similar to these examples
- Fit DeFries-Fulker and multilevel genetic models and compare results

Real data

- Find and get access to real twin data
- Fit DeFries-Fulker and multilevel genetic models and compare results

Structural Equation Modelling

- I don't have much knowledge of SEM
- Turkheimer et al. (2003) appear to have used SEM and modelled the amounts not proportions of variance so looks like SEM could be another solution
- I need to study SEM to find out

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