

From ACE to MACE: Genetic Correlation and Multivariate Models 1

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Plan

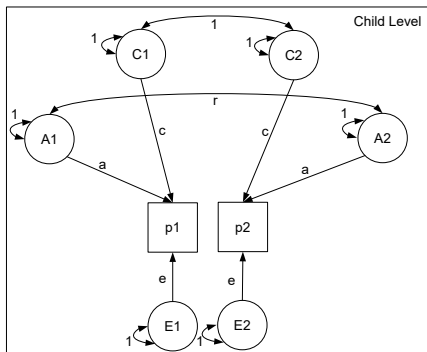
- ▶ ACE Model as Factor Model
- ▶ ACE Model as Variance Component Model
- ▶ ACE Model for Two Phenotypes
- ▶ “Genetic Correlation”
- ▶ Modeling Genetic Correlation Matrices

Basic Idea of ACE

- ▶ Use monozygotic (MZ) and dizygotic (DZ) twin pairs
- ▶ Decompose between-person phenotypic variation
 - ▶ A = Additive genetics
 - ▶ C = Common environments (e.g., nuclear family environment)
 - ▶ E = unique Environments
- ▶ Confirmatory factor model with known factor covariances

ACE

Single Level Diagram: multilevel versions in Hunter (2021); Tamimy et al. (2021)



ACE Equations 1: Factor Model

$$\begin{aligned}
 Cov \begin{pmatrix} p1 \\ p2 \end{pmatrix} &= \begin{pmatrix} a & 0 \\ 0 & a \end{pmatrix} \begin{pmatrix} 1 & r \\ r & 1 \end{pmatrix} \begin{pmatrix} a & 0 \\ 0 & a \end{pmatrix}^T \\
 &+ \begin{pmatrix} c & 0 \\ 0 & c \end{pmatrix} \begin{pmatrix} 1 & 1 \\ 1 & 1 \end{pmatrix} \begin{pmatrix} c & 0 \\ 0 & c \end{pmatrix}^T \\
 &+ \begin{pmatrix} e & 0 \\ 0 & e \end{pmatrix} \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} \begin{pmatrix} e & 0 \\ 0 & e \end{pmatrix}^T \quad (1)
 \end{aligned}$$

$$\begin{pmatrix} Var(p1) & Cov(p1, p2) \\ Cov(p1, p2) & Var(p2) \end{pmatrix} = \begin{pmatrix} a^2 + c^2 + e^2 & ra^2 + c^2 \\ ra^2 + c^2 & a^2 + c^2 + e^2 \end{pmatrix}$$



ACE Equations 2: Variance Component Model

$$\begin{aligned}
 \Sigma(\boldsymbol{\theta}) &= \begin{pmatrix} \Sigma_{MZ}(\boldsymbol{\theta}) & 0 \\ 0 & \Sigma_{DZ}(\boldsymbol{\theta}) \end{pmatrix} \\
 &= \underbrace{\begin{pmatrix} 1 & 1 & 0 & 0 \\ 1 & 1 & 0 & 0 \\ 0 & 0 & 1 & .5 \\ 0 & 0 & .5 & 1 \end{pmatrix}}_{R_A} a^2 \\
 &+ \underbrace{\begin{pmatrix} 1 & 1 & 0 & 0 \\ 1 & 1 & 0 & 0 \\ 0 & 0 & 1 & 1 \\ 0 & 0 & 1 & 1 \end{pmatrix}}_{R_C} c^2 + \underbrace{\begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix}}_{R_E} e^2 \quad (3)
 \end{aligned}$$

ACE Equations 2: Variance Component Model

$$\Sigma_r(\boldsymbol{\theta}) = \begin{pmatrix} 1 & r \\ r & 1 \end{pmatrix} a^2 + \begin{pmatrix} 1 & 1 \\ 1 & 1 \end{pmatrix} c^2 + \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} e^2 \quad (4)$$

$$= \begin{pmatrix} a^2 & ra^2 \\ ra^2 & a^2 \end{pmatrix} + \begin{pmatrix} c^2 & c^2 \\ c^2 & c^2 \end{pmatrix} + \begin{pmatrix} e^2 & 0 \\ 0 & e^2 \end{pmatrix} \quad (5)$$

$$= \begin{pmatrix} a^2 + c^2 + e^2 & ra^2 + c^2 \\ ra^2 + c^2 & a^2 + c^2 + e^2 \end{pmatrix} \quad (6)$$

ACE Equations 2: Variance Component Model

$$\Sigma_r(\boldsymbol{\theta}) = \begin{pmatrix} 1 & r \\ r & 1 \end{pmatrix} \otimes a^2 + \begin{pmatrix} 1 & 1 \\ 1 & 1 \end{pmatrix} \otimes c^2 + \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} \otimes e^2 \quad (7)$$

$$= \begin{pmatrix} a^2 & ra^2 \\ ra^2 & a^2 \end{pmatrix} + \begin{pmatrix} c^2 & c^2 \\ c^2 & c^2 \end{pmatrix} + \begin{pmatrix} e^2 & 0 \\ 0 & e^2 \end{pmatrix} \quad (8)$$

$$= \begin{pmatrix} a^2 + c^2 + e^2 & ra^2 + c^2 \\ ra^2 + c^2 & a^2 + c^2 + e^2 \end{pmatrix} \quad (9)$$

Kronecker for Two Phenotypes

$$\begin{pmatrix} 1 & r \\ r & 1 \end{pmatrix} \otimes \begin{pmatrix} a_1^2 & a_{12} \\ a_{12} & a_2^2 \end{pmatrix} = \begin{pmatrix} 1 \begin{pmatrix} a_1^2 & a_{12} \\ a_{12} & a_2^2 \end{pmatrix} & r \begin{pmatrix} a_1^2 & a_{12} \\ a_{12} & a_2^2 \end{pmatrix} \\ r \begin{pmatrix} a_1^2 & a_{12} \\ a_{12} & a_2^2 \end{pmatrix} & 1 \begin{pmatrix} a_1^2 & a_{12} \\ a_{12} & a_2^2 \end{pmatrix} \end{pmatrix} \quad (10)$$

ACE Equations with Two Phenotypes

Variance Component Model

$$\begin{aligned}\Sigma_r(\boldsymbol{\theta}) &= \begin{pmatrix} 1 & r \\ r & 1 \end{pmatrix} \otimes \begin{pmatrix} a_1^2 & a_{12} \\ a_{12} & a_2^2 \end{pmatrix} \\ &+ \begin{pmatrix} 1 & 1 \\ 1 & 1 \end{pmatrix} \otimes \begin{pmatrix} c_1^2 & c_{12} \\ c_{12} & c_2^2 \end{pmatrix} \\ &+ \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} \otimes \begin{pmatrix} e_1^2 & e_{12} \\ e_{12} & e_2^2 \end{pmatrix} \end{aligned} \quad (11)$$

Genetic Correlation

What is a_{12} ?

Hint: Look at the title of the slide.

ACE Equations with Three Phenotypes

Variance Component Model

$$\begin{aligned}
 \Sigma_r(\boldsymbol{\theta}) = & \begin{pmatrix} 1 & r \\ r & 1 \end{pmatrix} \otimes \begin{pmatrix} a_1^2 & a_{12} & a_{13} \\ a_{12} & a_2^2 & a_{23} \\ a_{13} & a_{23} & a_3^2 \end{pmatrix} \\
 & + \begin{pmatrix} 1 & 1 \\ 1 & 1 \end{pmatrix} \otimes \begin{pmatrix} c_1^2 & c_{12} & c_{13} \\ c_{12} & c_2^2 & c_{23} \\ c_{13} & c_{23} & c_3^2 \end{pmatrix} \\
 & + \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} \otimes \begin{pmatrix} e_1^2 & e_{12} & e_{13} \\ e_{12} & e_2^2 & e_{23} \\ e_{13} & e_{23} & e_3^2 \end{pmatrix} \quad (12)
 \end{aligned}$$

ACE Equations with Three Phenotypes

$$\begin{aligned}
 \Sigma(\boldsymbol{\theta}) &= \begin{pmatrix} \Sigma_{MZ}(\boldsymbol{\theta}) & 0 \\ 0 & \Sigma_{DZ}(\boldsymbol{\theta}) \end{pmatrix} \\
 &= \underbrace{\begin{pmatrix} 1 & 1 & 0 & 0 \\ 1 & 1 & 0 & 0 \\ 0 & 0 & 1 & .5 \\ 0 & 0 & .5 & 1 \end{pmatrix}}_{R_A} \otimes \begin{pmatrix} a_1^2 & a_{12} & a_{13} \\ a_{12} & a_2^2 & a_{23} \\ a_{13} & a_{23} & a_3^2 \end{pmatrix} \\
 &+ \underbrace{\begin{pmatrix} 1 & 1 & 0 & 0 \\ 1 & 1 & 0 & 0 \\ 0 & 0 & 1 & 1 \\ 0 & 0 & 1 & 1 \end{pmatrix}}_{R_C} \otimes \begin{pmatrix} c_1^2 & c_{12} & c_{13} \\ c_{12} & c_2^2 & c_{23} \\ c_{13} & c_{23} & c_3^2 \end{pmatrix} + \underbrace{\begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix}}_{R_E} \otimes \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix}
 \end{aligned}$$

Modeling the Covariance

The model formerly known as the Cholesky

$$\begin{pmatrix} a_1^2 & a_{12} & a_{13} \\ a_{12} & a_2^2 & a_{23} \\ a_{13} & a_{23} & a_3^2 \end{pmatrix} = L_A L_A^T \quad (14)$$

L_A is $p \times p$ lower triangular matrix
 p = number of phenotypes

Modeling the Covariance

The Genetic Factor Model

$$\begin{pmatrix} a_1^2 & a_{12} & a_{13} \\ a_{12} & a_2^2 & a_{23} \\ a_{13} & a_{23} & a_3^2 \end{pmatrix} = L_A L_A^T \quad (15)$$

L_A is $p \times q$

p = number of phenotypes

q = number of factors Almost always $q = 1$ for this model, so

L_A is $p \times 1$: a column vector

Modeling the Covariance

The Independent Pathway Model

$$\begin{pmatrix} a_1^2 & a_{12} & a_{13} \\ a_{12} & a_2^2 & a_{23} \\ a_{13} & a_{23} & a_3^2 \end{pmatrix} = L_A L_A^T + U_A \quad (16)$$

L_A is $p \times q$ “factor loadings”

U_A is $p \times p$ and diagonal “factor residuals”

p = number of phenotypes

q = number of factors

Modeling the Covariance

The Common Pathway Model

$$\begin{pmatrix} a_1^2 & a_{12} & a_{13} \\ a_{12} & a_2^2 & a_{23} \\ a_{13} & a_{23} & a_3^2 \end{pmatrix} = L_F L_A L_A^T L_F + U_A \quad (17)$$

L_F is $p \times q$

L_A is $q \times 1$

U_A is $p \times p$ and diagonal

List of Multivariate Models

- ▶ Full ACE Covariance Model (Cholesky)
- ▶ Genetic Factor Model
- ▶ Independent Pathways Model
- ▶ Common Pathway Model

Other Models

Are these the *only* multivariate models in behavior genetics?

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Thank You

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Questions?

References

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