Heterogeneity II

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Heterogeneity Questions I

- <u>Standard Univariate Analysis</u>: What are the contributions of additive genetic, dominance/shared environmental and unique environmental factors to the variance?
- <u>Heterogeneity</u>: Are the contributions of genetic and environmental factors equal for different groups, such as sex, race, ethnicity, SES, environmental exposure, etc.?

Ways to Model Heterogeneity in Twin Data

- Multiple Group Models
 - Sex Effects
 - Divorced/Not Divorced
 - Young/Old cohorts
 - Urban/Rural residency
 - Etc...

Sex Effects

Females

Males



Sex Effects

Females





 $a_F = a_M ?$ $c_F = c_M ?$ $e_F = e_M ?$

Divorce Effects

Divorced

Not Divorced



 $a_D = a_{ND}$? $c_D = c_{ND}$? $e_D = e_{ND}$?

Problem:

- Many variables of interest do not fall into groups
 - Age
 - Socioeconomic status
 - Regional alcohol sales
 - Parental warmth
 - Parental monitoring
 - Grouping these variables into high/low categories may lose information

'Definition variables' in Mx

• <u>General definition</u>: Definition variables are variables that may vary per subject and that are not dependent variables

• <u>In Mx</u>: The specific value of the def var for a specific individual is read into a matrix in Mx when analyzing the data of that particular individual

'Definition variables' in Mx

create dynamic var/cov structure

- <u>Common uses</u>:
- 1. To model changes in variance components as function of some variable (e.g., age, SES, etc)
- 2. As covariates/effects on the means (e.g. age and sex)

Standard model

• Means vector

$$\begin{pmatrix} m & m \end{pmatrix}$$

• Covariance matrix

$$\begin{pmatrix} a^{2} + c^{2} + e^{2} \\ Za^{2} + c^{2} & a^{2} + c^{2} + e^{2} \end{pmatrix}$$

Model-fitting approach to GxE



Model-fitting approach to GxE



Individual specific moderators



E x E interactions



Definition Variables in Mx



• Classic Twin Model: Var (P) = $a^2 + c^2 + e^2$



• Moderation Model:

Var (P) = $(a + \beta_X M)^2 + (c + \beta_Y M)^2 + (e + \beta_Z M)^2$

Purcell 2002, Twin Research



Var (T) =
$$(a + \beta_X M)^2 + (c + \beta_Y M)^2 (e + \beta_Z M)^2$$

Where M is the value of the moderator and

Significance of β_X indicates genetic moderation Significance of β_Y indicates common environmental moderation Significance of β_Z indicates unique environmental moderation



Unstandardized versus standardized effects

	GROUP 1		GROUP 2	
	Unstandardized Variance	Standardized Variance	Unstandardized Variance	Standardized Variance
Genetic	60	0.60	60	0.30
Common environmental	35	0.35	70	0.35
Unique environmental	5	0.05	70	0.05
Total variance	100		200	

Matrix Letters as Specified in Mx Script



mu

'Definition variables' in Mx

create dynamic var/cov structure

- <u>Common uses</u>:
- 1. To model changes in variance components as function of some variable (e.g., age, SES, etc)
- 2. As covariates/effects on the means (e.g. age and sex)

Definition variables used as covariates

General model with age and sex as covariates: $y_i = \alpha + \beta_1(age_i) + \beta_2(sex_i) + \varepsilon$

Where y_i is the observed score of individual *i*, α is the intercept or grand mean, β_1 is the regression weight of age, **age**_i is the age of individual *i*, β_2 is the deviation of males (if sex is coded 0= female; 1=male), **sex**_i is the sex of individual *i*, and ε is the residual that is not explained by the covariates (and can be decomposed further into ACE etc).

Allowing for a main effect of *X*

• Means vector

$$\begin{pmatrix} m + \beta X_{1i} & m + \beta X_{2i} \end{pmatrix}$$

• Covariance matrix

$$\begin{pmatrix} a^{2} + c^{2} + e^{2} \\ Za^{2} + c^{2} & a^{2} + c^{2} + e^{2} \end{pmatrix}$$

Common uses of definition variables in the means model

• Incorporating covariates (sex, age, etc)

• Testing the effect of SNPs (association)

• In the context of GxE, controlling for rGE

Adding Covariates to Means Model



Matrix Letters as Specified in Mx Script

