

Psych 3102
Introduction to Behavior Genetics
Lecture 12
Quantitative analysis
Covariance between relatives



Sources of covariance between relatives

covariance a measure of shared variance

(how similar the variation is between two samples or how well measurements in one sample predict those in the other)

correlation a standardized measure of covariance

- similarity between measurements of 2 samples of relatives for a trait will cause them to covary
- there will be no covariance between 2 samples of individuals picked at random from a population and measured for the trait

$$V_{(P)} = V_{(G)} + V_{(E)}$$

Substituting covariance for variance:

$$\text{COV}_{(P1)(P2)} = \text{COV}_{(G+E)(G+E)} \text{ where 1 and 2 are scores for relatives}$$

For relatives:

- only shared genes and shared environment can be sources of covariance (similarities)
- segregating genes and non-shared environment are sources of variance (differences)

$$\text{SO, } \text{COV}_{(P1)(P2)} = \text{COV}_{(Gc+Ec)(Gc+Ec)} \\ = \text{cov } Gc \times Gc + \text{cov } Ec \times Ec + 2\text{cov} GcEc \quad \left[\begin{array}{l} \text{cov of } Gc \text{ on } Gc = \text{var } Gc \\ \text{cov of } Ec \text{ on } Ec = \text{var } Ec \end{array} \right]$$

Ignoring G x E interactions and correlations, this simplifies to:

ie. the correlation between relatives for a trait equals the sum of the variances due to shared environmental effects and shared genetic effects

Additive and dominance genetic effects

- we can make some predictions about the additive and dominance effects of genes on variance for a trait and covariance between relatives:

Sources of phenotypic covariance V_A V_D V_{Ec}
between:

Parent/offspring (P/O)

Half-sibs (HS)

Full sibs (FS)

DZ twins $\left\{ \begin{array}{l} \text{reared together} \\ \text{reared apart} \end{array} \right.$

MZ twins $\left\{ \begin{array}{l} \text{reared together} \\ \text{reared apart} \end{array} \right.$

Other sources of covariance between relatives:

1. assortative mating

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-

2. epistasis

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-
-

★ MZ twin correlation gives best estimate of total genetic variance when either of these effects exist

Note on statistical significance

- when an effect reaches 'statistical significance' we usually assume it is a real effect, not occurring by chance
- very small but consistently-occurring effects can reach statistical significance
- we can expect small gene effects to reach significance if we use a large sample

Heritability

$$V_{\text{phenotype}} = V_{\text{genes}} + V_{\text{environment}}$$

heritability = the proportion of phenotypic variation accounted for by genetic variation

Heritability =

Effects of gene variation in a population are measured, NOT genetic effects in an individual

high heritability? low heritability? zero?

2 types of heritability:

broad heritability

- estimates all genetic effects

$$H^2_B = \frac{V_G}{V_P} \quad \text{where}$$

narrow heritability

- estimates only additive gene effects

$$h^2 = \frac{V_A}{V_P}$$

We will use twin correlations to estimate heritability:

$$r_{MZ} = H^2 \quad (+ c^2 \quad \text{if } c^2 \text{ exists)}$$

$$\text{and } r_{DZ} = \frac{1}{2} h^2 \quad (+ c^2 \quad \text{if it exists)}$$

$$\text{where } c^2 \text{ exists } \quad h^2 = 2(r_{MZ} - r_{DZ})$$

Heritability allows a comparison of the relative importance of genes and environment to the variation of traits

important in predicting response to selection in agriculture & evolutionary biology, & to prediction of risk in medicine

Family resemblance

- narrow heritability (h^2) determines most of the resemblance between relatives due to genes

Relationship	Examples	Estimate of additive gene effects	Estimate of h^2
Identical	MZ twins		
First degree	FS,DZ,P/O		
Second degree	HS,aunt/niece		
Third degree	cousins		
Non-genetic	spouses,in-laws parent/adoptedchild		

Effect of sample size

- large samples are optimal
- replication of studies is needed, especially when sample sizes are less than optimal

Example general cognitive ability
 from parent/offspring and siblings adopted-away
 correlation, $r = 0.24$ sample size = 203
 $h^2 =$

error measurement (standard error) is so large with this sample size that
 there is a 95% chance $r = 0.10 - 0.38$
 and estimate of $h^2 = 0.20 - 0.76$

extend sample size to 2000, $h^2 = 0.40 - 0.56$

Interpreting twin correlations

- r = correlation coefficient
- twins are reared together

Extreme cases:

If $r_{MZ} = r_{DZ} = 0$, this would indicate:

If $r_{MZ} = 2r_{DZ} = 1$, this would indicate

Never found in studies for behavioral traits

Measurement error always reduces correlations

Suppose $r_{MZ} > r_{DZ}$

Suppose $r_{MZ} = r_{DZ}$

Any time $r_{MZ} < 1$

If $r_{DZ} > \frac{1}{2} r_{MZ}$

If $r_{DZ} = \frac{1}{2} r_{MZ}$

If $r_{DZ} < \frac{1}{2} r_{MZ}$

Examples of reported twin correlations

Variable	MZ correlation	DZ correlation
BODY MASS INDEX <small>males aged ~20 years (Fabsitz et al., 1992, Int.J.of Obesity)</small>	.80	.42
GENERAL COGNITIVE ABILITY <small>average, many studies (see text page 140) (Bouchard, McGue, 1981, Science)</small>	.86	.60
EXTERNALIZING BEHAVIOR PROBLEMS (eg. CD, ODD) <small>rated by mother using CBCL, aged 12-16 (Hewitt et al. 1992, Behav. Genet)</small>	males .47 females .56	.40 .38
DUST ALLERGY <small>females (Duffy et al., 1992, Am.Rev.Resp.Diseases)</small>	.52	.21

For disorders:

- concordances instead of correlations
- cannot get estimates of heritability or variance components

MZ concordance > DZ concordance
 Evidence for genetic effects

Estimating variance components from twin correlations

- when $r_{DZ} \geq \frac{1}{2} r_{MZ}$ ie. NO non-additive gene effects

$$(V_D = 0)$$

$$\hat{V}_A = 2(r_{MZ} - r_{DZ})$$

$$\hat{V}_C = 2r_{DZ} - r_{MZ}$$

- when $r_{MZ} > 2r_{DZ}$ ie. non-additive gene effects are present

$$(V_C = 0)$$

$$V_A = 4r_{DZ} - r_{MZ}$$

$$V_D = 2r_{MZ} - 4r_{DZ}$$

- V_C and V_D can co-exist, but they cannot be estimated from twin correlation data if they do
- $H^2_{\text{broad}} = V_A + V_D$ $h^2_{\text{narrow}} = V_A$

What does an estimate of heritability tell us?

1. it applies only to the population studied
2. it estimates the proportion of variation in that population that is due to genetic variation
3. it can change over time if other influences change
4. estimates may be different even for the same trait
 - if environmental variance increases, heritability will decrease
 - if environmental variance decreases, heritability will increase
5. changes in environment that we all share may change the population mean but leave the variance unaffected, may still have a big effect on individuals
 - food, oxygen, technology
6. alleles for genes important in normal variation may not be the causes of disorders
7. finding a large genetic effect does not equal determinism

SUMMARY - sources of variation

ENVIRONMENTAL EFFECTS

	<u>Name</u>	<u>Symbol</u>	<u>Other names</u>	<u>Estimated by</u>
1. Effects that make family members similar	between family e	c^2	shared e common e	$2DZr - MZr$
2. Effects that make family members differ	within family e	e^2	non-shared e unique e	$1 - MZr$

GENETIC EFFECTS

1. all alleles for trait produce effect on phenotype	additive genetic	a^2	narrow heritability (h^2)	MZr when $MZr = 2DZr$
2. some alleles only have effect when heterozygous or with other genes	non-additive genetic	d^2 i^2	dominance epistasis	$2MZr - 4DZr$ when $MZr > 2DZr$