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)

eg covariance between a sample of measurements from parents compared to a sample of measurements from their offspring

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
- both genes and environment shared will be sources of covariance between relatives living together

Variance   =   Variance   +   Variance
in phenotype   due to genes   due to environment

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

Substituting covariance for variance:

$cov_{(P1)(P2)} = cov_{(G+E)(G+E)}$ where 1 and 2 are scores for relatives

For relatives:

- only <u>shared</u> genes and <u>shared</u> environment can be sources of covariance (similarities)

both shared genes and shared environment will contribute to the covariance of scores between relatives

(segregating genes and non-shared environment are sources of variance (differences)

segregating genes and non-shared environment will not contribute to the covariance of scores between relatives)

so, $cov_{(P1)(P2)} = cov_{(Gc+Ec)(Gc+Ec)}$

[cov of Gc on Gc = var Gc

= cov GcxGc + cov EcxEc + 2covGcEc   cov of Ec on Ec = var Ec]

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

$$cov_{(P1)(P2)} = V_{Gc} + V_{Ec}$$

correlation (r) = standard form of covariance

<u>So, the correlation between relatives for a trait equals the sum of the variances due to shared environmental effects and genetic effects</u>

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 between:	V_A	V_D	V_{Ec}
Parent/offspring (P/O)	½	0	$V_{Ec\,(P/O)}$
Half-sibs (HS)	¼	0	$V_{Ec(HS)}$
Full sibs (FS)	½	¼	$V_{Ec(FS)}$
DZ twins reared together	½	¼	$V_{Ec(DZ)}$
DZ twins reared apart	½	¼	0
MZ twins reared together	1	1	$V_{Ec(MZ)}$
MZ twins reared apart	1	1	0

Other sources of covariance between relatives:

1. assortative mating

    - similarity between parents for a trait

    - increases covariance within a family

2. epistasis

   - interaction between genes

   - contributes in similar way to dominance

   - it reduces covariance between all relatives

     except between MZ twin pairs

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

Statistical significance

- when an effect reaches 'statistical significance' we usually assume it is a real effect, not occurring by chance

- significance does not tell us about <u>effect size</u>

- very small but consistently-occurring effects can reach statistical significance

Example: environmental effect of birth order on cognitive ability scores

Effect size

- the extent to which individual differences for the trait can be attributed to contributing factors (ie genes or environment)

- refers to the effect size in a <u>population,</u> not to any individual

- genetic and environmental effects can be very large for an individual but very small for a population

Example: Down syndrome has a large effect on an individual's IQ and this effect is almost entirely genetic, but since Down syndrome is rare, the genetic effect size of Down syndrome in the population is very small

Genetic effect sizes are usually very large, even though any one individual gene effect is extremely small

Genetic effect size tells us nothing about the size of individual gene effects

Heritability

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

Heritability is a measure of the genetic effect size or genetic variance(V_G)

It is estimated as the proportion of phenotypic variation accounted for by genetic variation

ie. how much of the variation in phenotype is due to variation in genes for the trait relative to the environment effect

$$Heritability \quad = \quad \frac{V_{genes}}{V_{phenotype}} \qquad \text{where } V_{phenotype} = V_{genes} + V_{environment}$$

Heritability is measured in a population , NOT in an <u>individual</u>

What does it mean when we find

high heritability?	low heritability?	zero?
genes account for most variation	environment accounts for most variation	no <u>variation</u> due to genes
low variation due to E	low genetic variation	
environmental effects on individual can be large	gene effects on individual can be large	sample population might all have same alleles for the trait

What would be the heritability of any trait measured in an inbred strain?

Can the same trait have different heritabilities in different situations?

IQ measurements in different environments, different populations

2 types of heritability:

broad heritability

    - an estimate of <u>all</u> genetic effects

$$H^2_B = \frac{V_G}{V_P} \quad \text{where } V_G = V_A + V_D + V_I$$

narrow heritability

    - an estimate of only <u>additive</u> gene effects

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

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

      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	1	h^2
First degree	FS,DZ,P/O	½	½ h^2
Second degree	HS,aunt/niece	¼	¼ h^2
Third degree	cousins	1/8	1/8 h^2
Non-genetic	spouses,in-laws adoptive relationships	0	0

Because we use correlations and correlations are standardized measures, the variance components we estimate are also standard and represent **proportions (and percentages)** of variance, total = 1 (100%)

$$e^2 + c^2 + a^2 = 1 \quad (100\%)$$

We will use twin correlations to estimate heritability:
h^2 = narrow heritability = a^2

So $r_{MZ} = h^2 + c^2$

and $r_{DZ} = \frac{1}{2} h^2 + c^2$

$h^2 = 2\,(r_{MZ} - r_{DZ})$ if c^2 not zero

$h^2 = r_{MZ}$ $h^2 = 2\,r_{DZ}$ if c^2 = zero

$c^2 = 2\,r_{DZ} - r_{MZ}$

Effect of sample size

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

<u>Example</u>   general cognitive ability

from parent/offspring and siblings adopted-away

   correlation, r = 0.24   sample size = 203

      $h^2 = 0.48$

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:

NO family resemblance

Shared genes and shared environments do not influence the trait $h^2 = 0$, $V_A = V_D = V_{Ec} = 0$

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

phenotype is controlled by additive genes $h^2 = 1$

$V_E = 0$

Never found in studies for behavioral traits

Measurement error always reduces correlations

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

> Evidence for genetic effects

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

> Resemblance between twins is due to shared e only
>
> $h^2 = 0$

Any time $r_{MZ} < 1$

> Evidence for non-shared environmental effects (+error)

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

> Evidence for shared e as well as genetic effects
>
> $h^2 = 2 (r_{MZ} - r_{DZ})$

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

> No evidence for shared e and gene effects are additive only
>
> $h^2 = r_{MZ}$ or $h^2 = 2 (r_{DZ})$

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

> Evidence for non-additive genetic effects
>
> $H^2 = r_{MZ}$

Examples of reported twin correlations

Variable	MZ correlation	DZ correlation
BODY MASS INDEX	.80	.42

males aged ~20 years   (Fabsitz et al.,1992, Int.J.of Obesity)

GENERAL COGNITIVE ABILITY	.86	.60

average, many studies (see text page 140) (Bouchard,McGue,1981,Science)

EXTERNALIZING BEHAVIOR	males	.47	.40
PROBLEMS (eg. CD,ODD)	females	.56	.38

rated by mother using CBCL, aged 12-16 (Hewitt et al.1992,Behav.Genet)

DUST ALLERGY	.52	.21

females (Duffy et al., 1992, Am.Rev.Resp.Diseases)

For disorders:

- concordances instead of correlations

- for twins studies, % concordance = % of second twins who have the disorder when the first twin has the disorder

- concordance has to be compared to prevalence before we can say a family resemblance is present

- cannot get estimates of heritability or variance components

But,   if MZ concordance > DZ concordance

　　　Evidence for genetic effects

Estimating variance components from twin correlations

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

$$(\quad V_D = 0)$$

$$\hat{V_A} = 2 \ (r_{MZ} - r_{DZ})$$
$$\hat{V_C} = 2 \ r_{DZ} - \ r_{MZ}$$

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

$$(V_C = 0)$$

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

- V_C and V_D can co-exist, but they cannot be estimated from twin correlation data if they do

- $H^2_{broad} = \ V_A + \ V_D$ $h^2_{narrow} = \ V_A$

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 for the same trait if different samples are used

   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, but not heritability

   Flynn effect on IQ measurements   recent increase in BMI

6. 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

	Name	Symbol	Other names	Estimated by
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

	Name	Symbol	Other names	Estimated by
1. all alleles influencing trait produce effect on phenotype	additive genetic	a^2	narrow heritability (h^2)	MZr when MZr =2DZr
2. some alleles only have effect when homozygous or with other genes	non-additive genetic	d^2 i^2	dominance epistasis	2MZr – 4DZr when MZr>2DZr