
Multivariate Mx Exercise

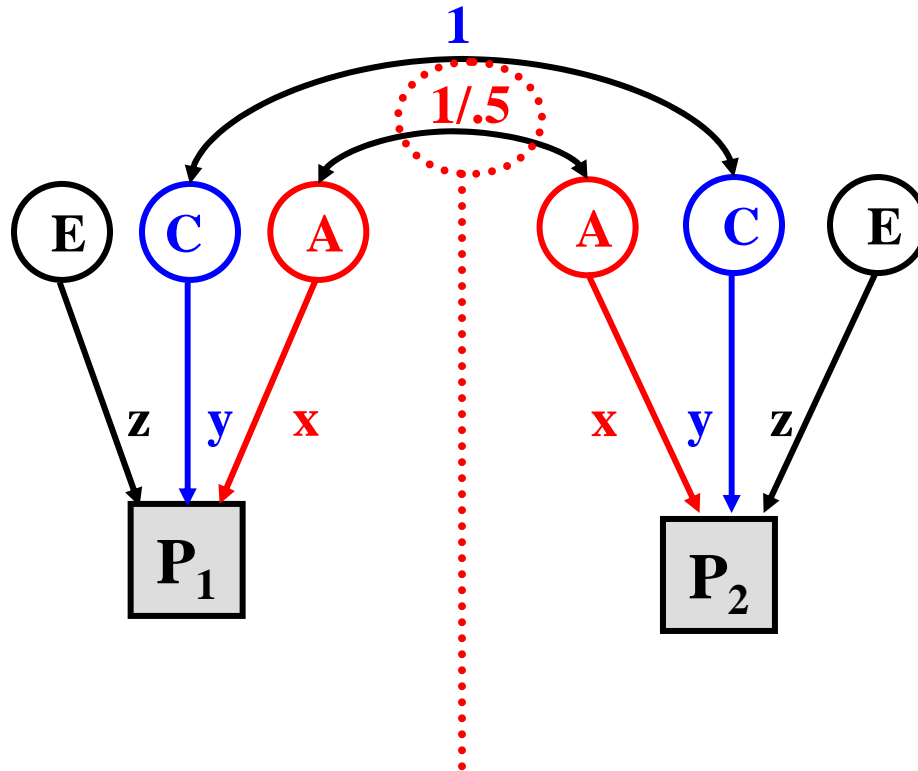
D Posthuma

Files: \\danielle\Multivariate

Short summary of terminology

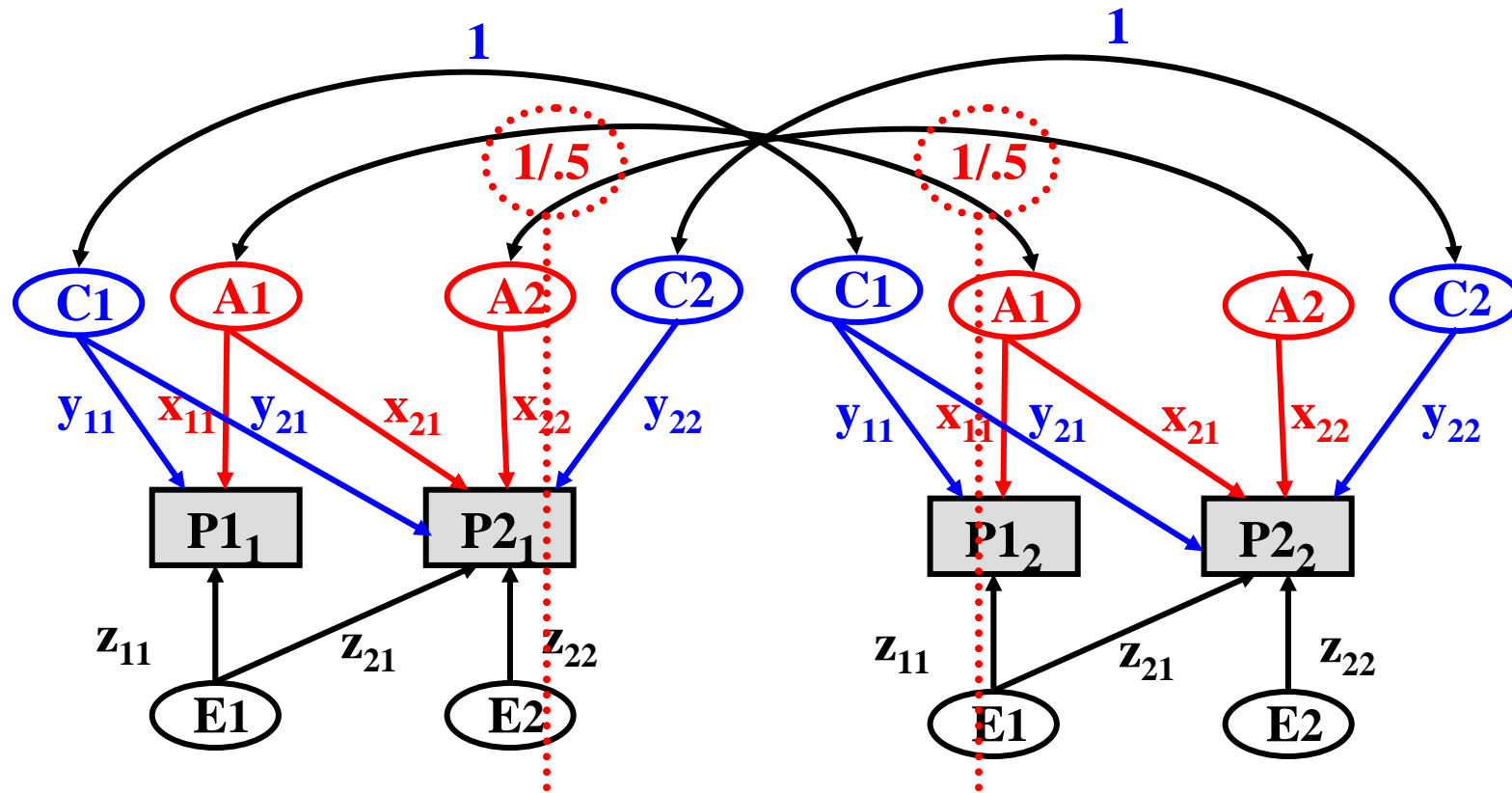
- Genetic correlation for MZ twins
- Genetic correlation for DZ twins
- Genetic correlation
- Proportion of the observed correlation (or covariance) explained by correlation at the genetic level

Univariate ACE Model for a Twin Pair



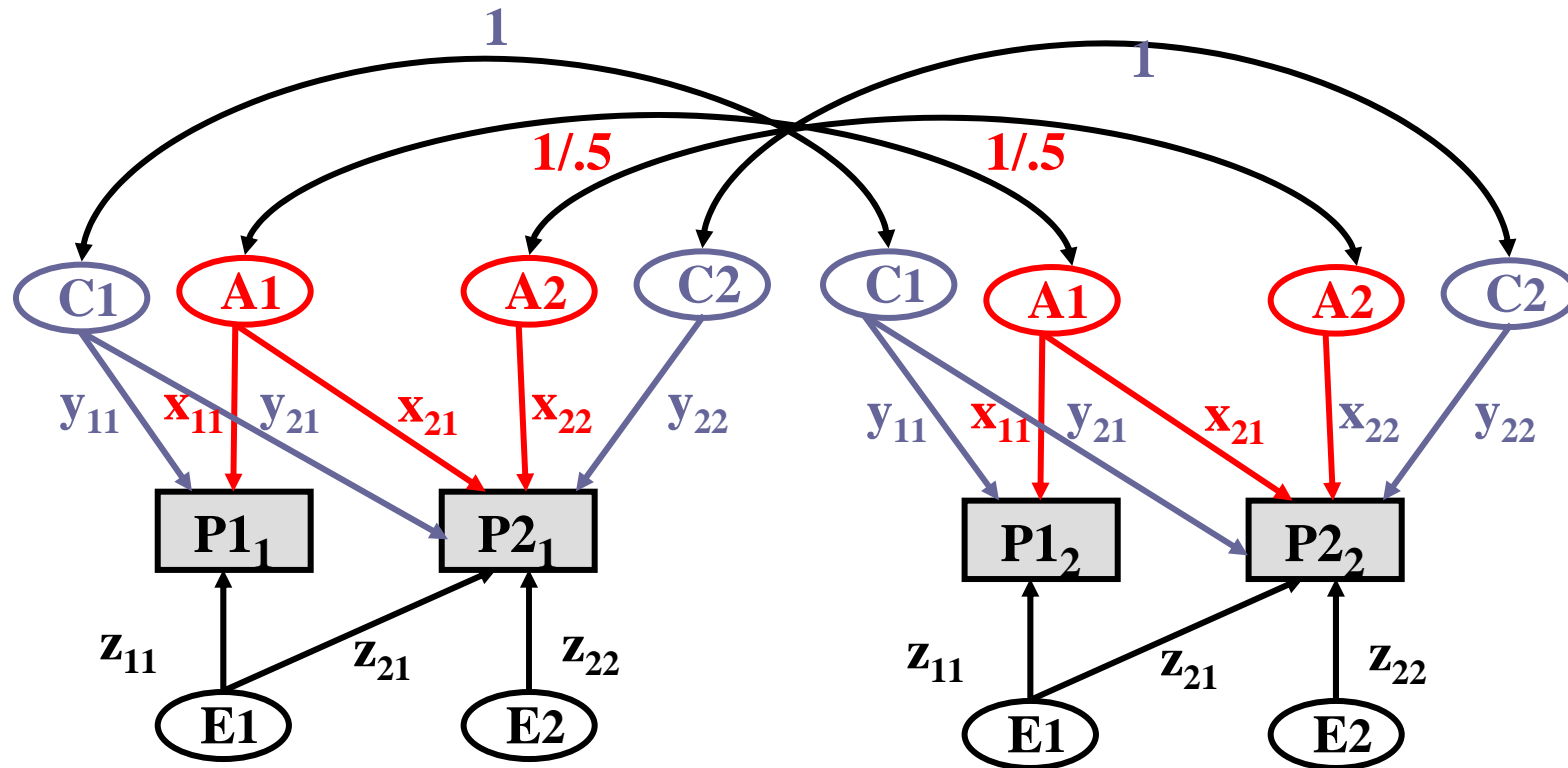
= Correlation between the sets of genes that influence the same trait in twin 1 and in twin 2. 1 for MZs as they share 100% of their genes, 0.5 for DZs as they share ~50% of their genes.

Bivariate ACE Model for a Twin Pair

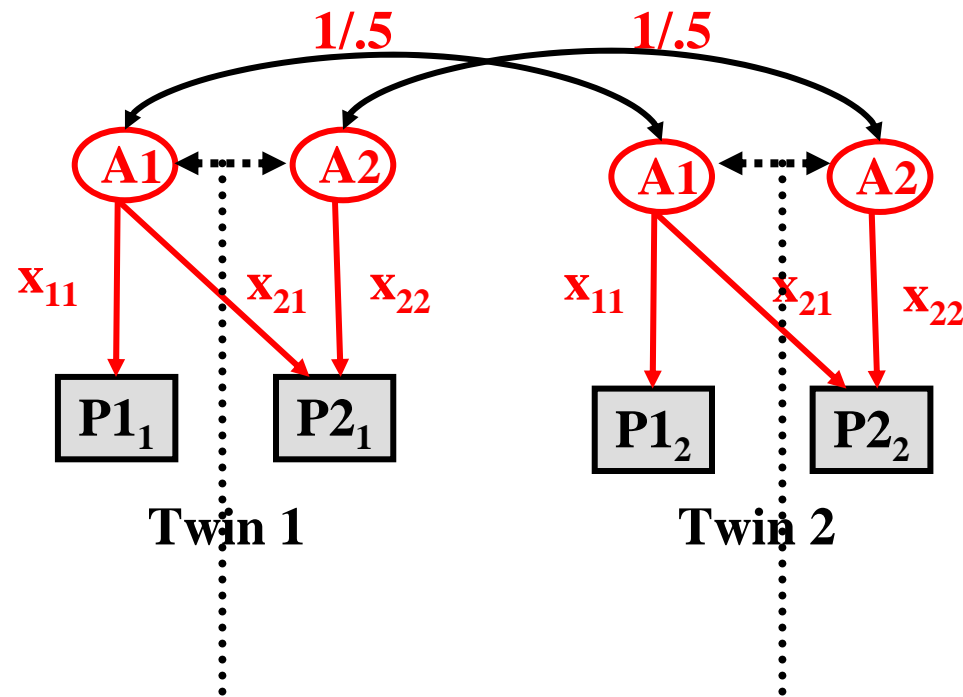


= Correlation between the sets of genes that influence the same trait in twin 1 and in twin 2. 1 for MZs as they share 100% of their genes, 0.5 for DZs as they share ~50% of their genes.

Bivariate ACE Model for a Twin Pair



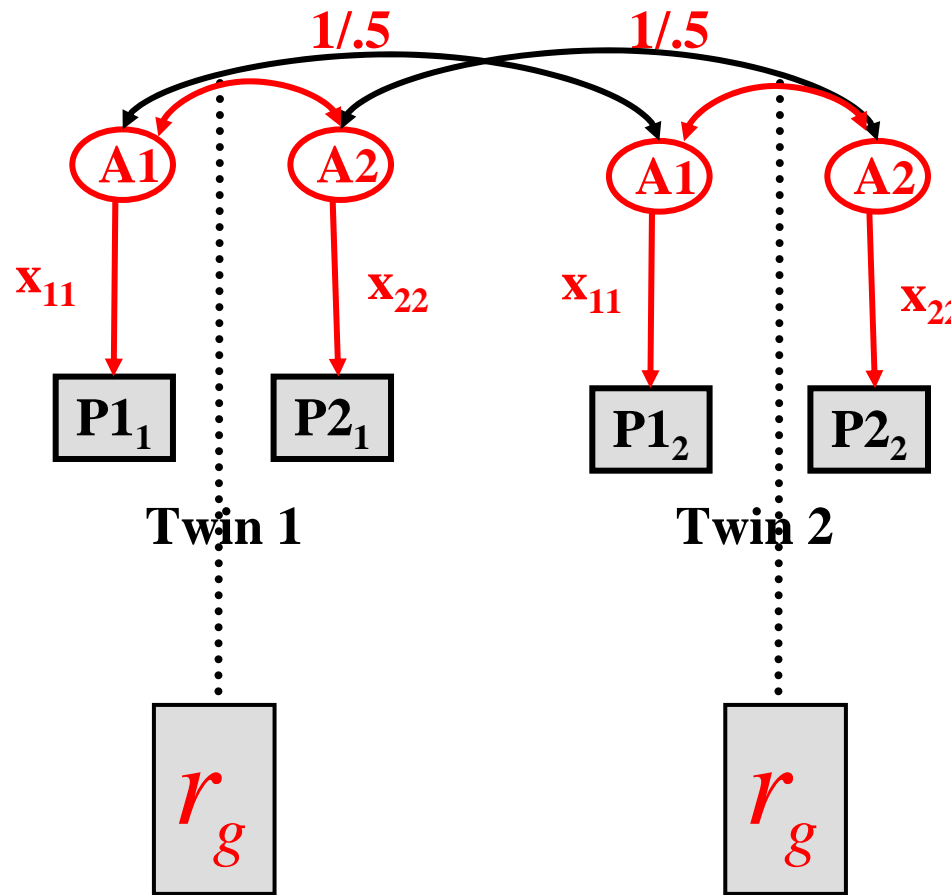
Genetic correlation



$$r_g = \frac{x_{21}x_{11}}{\sqrt{x_{11}^2 * (x_{21}^2 + x_{22}^2)}}$$

Matrix Function in Mx: $T = \text{std}(A)$

Standardized drawing or correlated factors solution



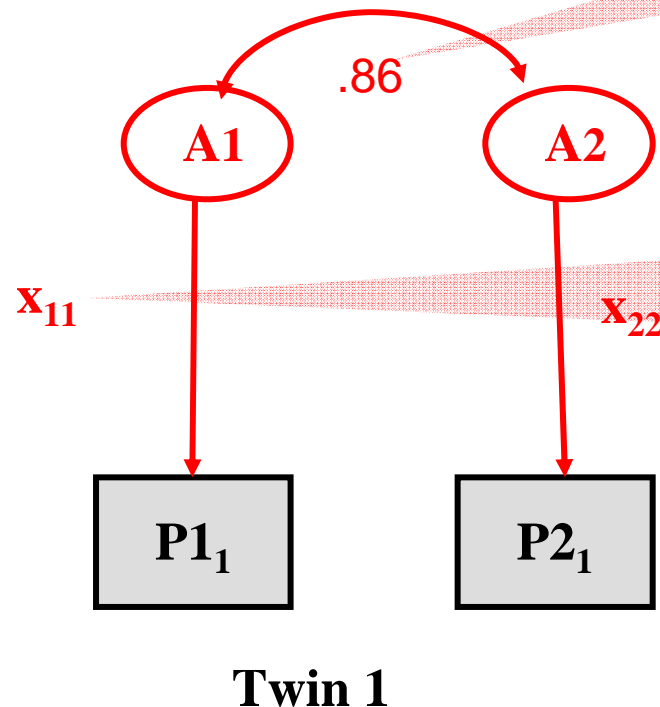
Genetic and (non-)shared environmental correlations

■ $T = \text{std}(A)$:
$$\begin{bmatrix} 1 & 0.86 \\ 0.86 & 1 \end{bmatrix}$$

■ $U = \text{std}(C)$:
$$\begin{bmatrix} 1 & 0.39 \\ 0.39 & 1 \end{bmatrix}$$

■ $V = \text{std}(E)$:
$$\begin{bmatrix} 1 & -0.02 \\ -0.02 & 1 \end{bmatrix}$$

Genetic correlation & contribution to observed correlation



If the $r_g = 1$, the two sets of genes overlap completely

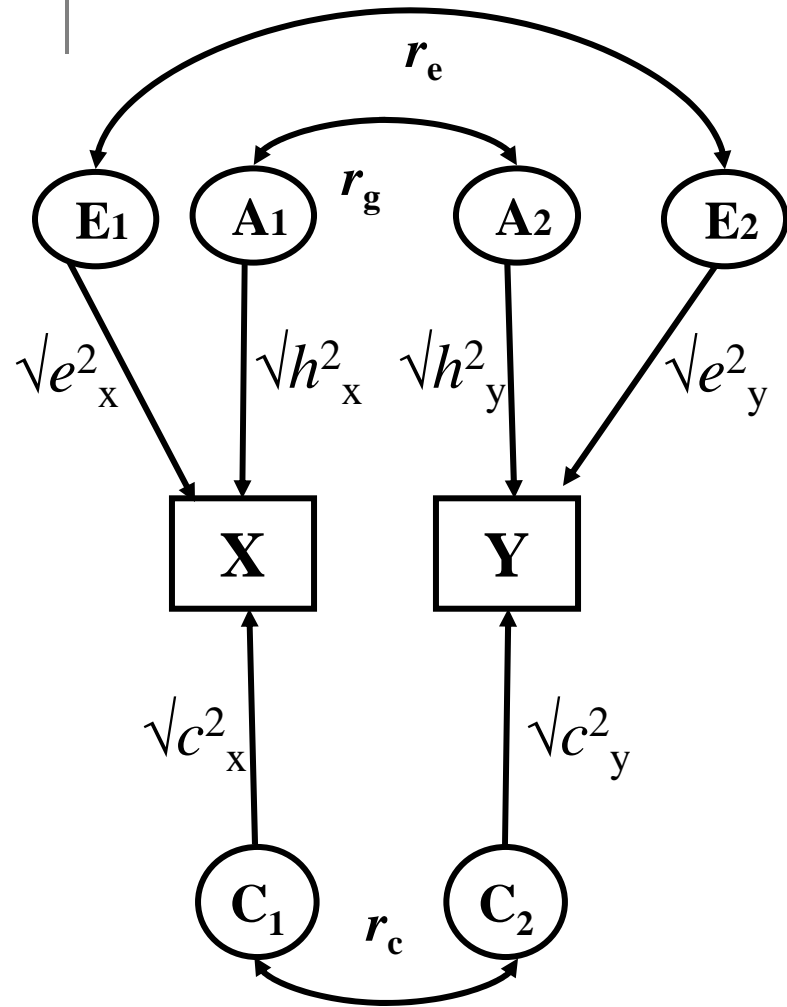
If however x_{11} and x_{21} are near to zero, genes do not contribute to the observed correlation

The contribution to the observed correlation is a function of both heritabilities and the r_g

Proportion of the observed correlation explained by correlation at the genetic level

Observed correlation is the result of correlation at

- The genetic level
- Common environmental level
- Unique environmental level



r_{ph} due to A

$$h^2_{x,y} = \sqrt{h^2_x} * r_g * \sqrt{h^2_y}$$

r_{ph} due to C

$$c^2_{x,y} = \sqrt{c^2_x} * r_c * \sqrt{c^2_y}$$

r_{ph} due to E

$$e^2_{x,y} = \sqrt{e^2_x} * r_e * \sqrt{e^2_y}$$

Genetic contribution to observed correlation (h^2_{xy}) is a function of r_g and both heritabilities

Observed correlation

$$\begin{aligned} r = & \sqrt{h_x^2} * r_g * \sqrt{h_y^2} \\ & + \sqrt{c_x^2} * r_c * \sqrt{c_y^2} \\ & + \sqrt{e_x^2} * r_e * \sqrt{e_y^2} \end{aligned}$$

Observed correlation and contributions

$$r =$$

$$\sqrt{h_x^2} * r_g * \sqrt{h_y^2}$$

$$+ \sqrt{c_x^2} * r_c * \sqrt{c_y^2}$$

$$+ \sqrt{e_x^2} * r_e * \sqrt{e_y^2}$$

$$.58 =$$

$$\sqrt{.45} * .86 * \sqrt{.56} = 0.43$$

$$+ \sqrt{.44} * 0.39 * \sqrt{0.36} = 0.16$$

$$+ \sqrt{.11} * -0.02 * \sqrt{0.08} = -.00$$

Proportion of the observed correlation (or covariance) explained by correlation at the genetic level: $0.43/0.58 = 0.74$

Proportion of the observed correlation (or covariance) explained by correlation at the shared environmental level: $0.16/0.58 = 0.27$

Proportion of the observed correlation (or covariance) explained by correlation at the non-shared environmental level: $0/0.58 = 0$

Percentage of correlation explained

MATRIX **S**

This is a computed FULL matrix of order 2 by 6
[=A%(A+C+E)|C%(A+C+E)|E%(A+C+E)]

	1	2	3	4	5	6
1	0.45	0.74	0.44	0.27	0.11	0.00
2	0.74	0.56	0.27	0.36	0.00	0.08

Proportion of observed correlation between P1 and P2 explained by genetic factors

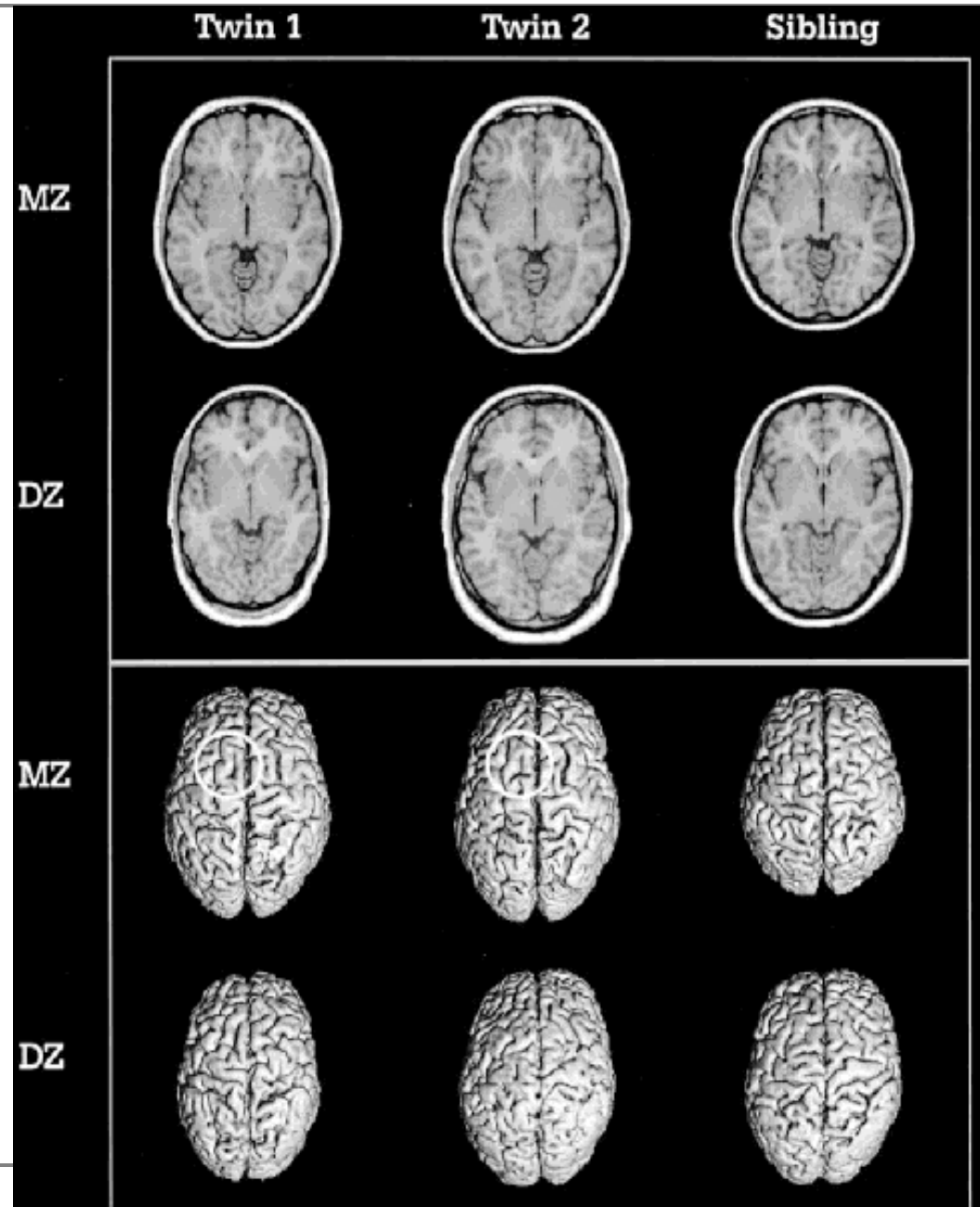
Proportion of observed correlation between P1 and P2 explained by shared environmental factors

Proportion of observed correlation between P1 and P2 explained by non-shared environmental factors

Exercise dataset: Brain volume

	Heritability
Grey Matter	0.82
White matter	0.87
Cerebellar Vol.	0.88

Baaré et al. Cer Cort 2001
Posthuma et al. Behav Genet 2000



Brain Volume (MRI)

Identical

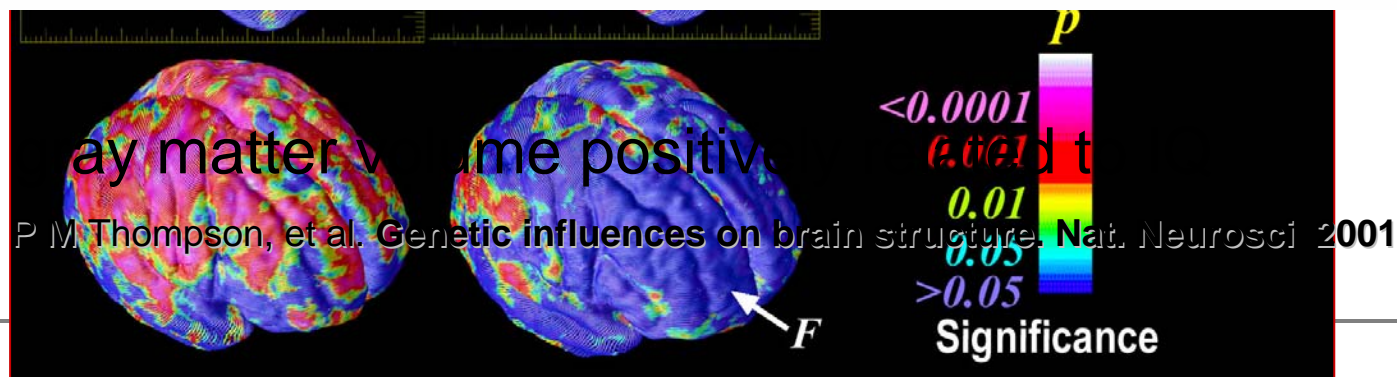
Fraternals

r^2

Table 1. Random effects analysis regressing individual regional gray matter measures on the IQ measure, Spearman's ρ ($n = 40$ subjects).

Measure	(a) Random effects analysis			Controlling for overall gray matter only		After controlling for other predictors	
	Regression coefficient (β)	Effect size (t)	Significance	$F_{1,33}$	Significance		
Whole brain gray matter volume	0.0037	1.73	0.046	3.92	0.0561		
Frontal gray matter volume	0.072	1.95	0.029**	9.37	0.0044**		
Temporal gray matter volume	0.039	0.23	0.411	3.77	0.0607		
Parietal gray matter volume	0.055	0.41	0.343	0.54	0.4690		
Occipital gray matter volume	0.033	0.15	0.439	0.04	0.8376		

Frontal gray matter volume positive



P M Thompson, et al. Genetic influences on brain structure. Nat. Neurosci 2001

Nature of the correlation?

		Grey matter – IQ	White matter – IQ
Observed correlation	Fe	0.25*	0.24*
MZ cross trait / cross twin correlation	T	0.26*	0.22*
DZ cross trait / cross twin correlation	v	0.14	0.19
Genetic contribution to observed correlation	se	100%	100%

Brain volume-IQ dataset

IQ: 688 subjects from 271 families
(twins and siblings)

MRI: 258 subjects from 111 families
(twins and siblings)

Overlapping: 135 subjects from 60 families

This example

We will use Brain volume-IQ dataset, but twins only,
no additional siblings

Variables: Grey matter, White matter, Working memory
dimension of the WAISIII IQ test

Data have been corrected for age and sex on SPSS

`\danielle\Multivariate`

Copy the files

Open Mx script

Now run it and open the output

Results

MATRIX S

This is a computed FULL matrix of order 2 by 6

[=A%(A+C+E)|C%(A+C+E)|E%(A+C+E)]

	A1	A2	C1	C2	E1	E2
GREYM	0.82	1.18	0.00	0.00	0.18	-0.18
WMEM	1.18	0.69	0.00	0.00	-0.18	0.31

heritabilities

Non-shared
environmentability

MATRIX T

This is a computed FULL matrix of order
2 by 2

$$[=\sqrt{I.A} \sim * A * \sqrt{I.A} \sim]$$

	1	2
1	1.00	0.36
2	0.36	1.00

Rg or genetic correlation between
grey matter and working memory

**Correlation due to A is a function of the
heritabilities and rg:**

$$\sqrt{a^2_{\text{grey}}} * R_g * \sqrt{a^2_{\text{wmem}}} =$$

$$\sqrt{.82} * .36 * \sqrt{.69} = .27$$

MATRIX V

This is a computed FULL matrix
of order 2 by 2

$$[=\sqrt{I.E} \sim * E * \sqrt{I.E} \sim]$$

	1	2
1	1.00	-0.18
2	-0.18	1.00

Re or environmental correlation between
grey matter and working memory

Correlation due to E:

$$\sqrt{e^2_{\text{grey}}} * Re * \sqrt{e^2_{\text{wmem}}} =$$

$$\sqrt{.18} * -.18 * \sqrt{.31} = -.04$$

Correlation due to A: **0.27**

Correlation due to E: **-0.04**

Total (phenotypic) correlation between
Grey Matter and Working Memory:
0.23

% due to A = $0.27/0.23 * 100 = 118\%$

% due to E = $-.04/0.23 * 100 = -18\%$

Results

MATRIX S

This is a computed FULL matrix of order 2 by 6

[=A%(A+C+E)|C%(A+C+E)|E%(A+C+E)]

	A1	A2	C1	C2	E1	E2
GREYM	0.82	1.18	0.00	0.00	0.18	-0.18
WMEM	1.18	0.69	0.00	0.00	-0.18	0.31

% contribution to the phenotypic correlation
due to A, and E

Exercise

- Add a third variable (white matter volume 'whitem')
- Fit the model in this order:

Grey matter - White matter - Working memory

Use these starting values:

Start 400 G 1 1 G 1 2

Start 70 G 1 3

st 18 X 1 1 Z 1 1 X 2 2 Z 2 2

st 4 X 3 3 Z 3 3

- If correctly: $-2ll = 8429.042$, $df = 929$

Exercise

- What are the genetic correlations between grey matter, white matter and working memory?
- What are the correlations of unique E factors?
- What are a^2 and e^2 ?
- What determines the phenotypic correlation?

A	Grey	White	Wmem
Grey	a^2	contrib	contrib
White	rg	a^2	contrib
Wmem	rg	rg	a^2

Contrib=bivariate heritability= $rg * \sqrt{a^2_1} * \sqrt{a^2_2}$

E	Grey	White	Wmem
Grey	e^2	contrib	contrib
White	re	e^2	contrib
Wmem	re	re	e^2

Contrib= bivariate environmentability= $re * \sqrt{e^2_1} * \sqrt{e^2_2}$

A	Grey	White	Wmem
Grey	.82	.68*sqrt.82*sqrt.87 = .57	.34*sqrt.82*sqrt.69 = .26
White	.68	.87	.21*sqrt.87*sqrt.69 = .16
Wmem	.34	.21	.69

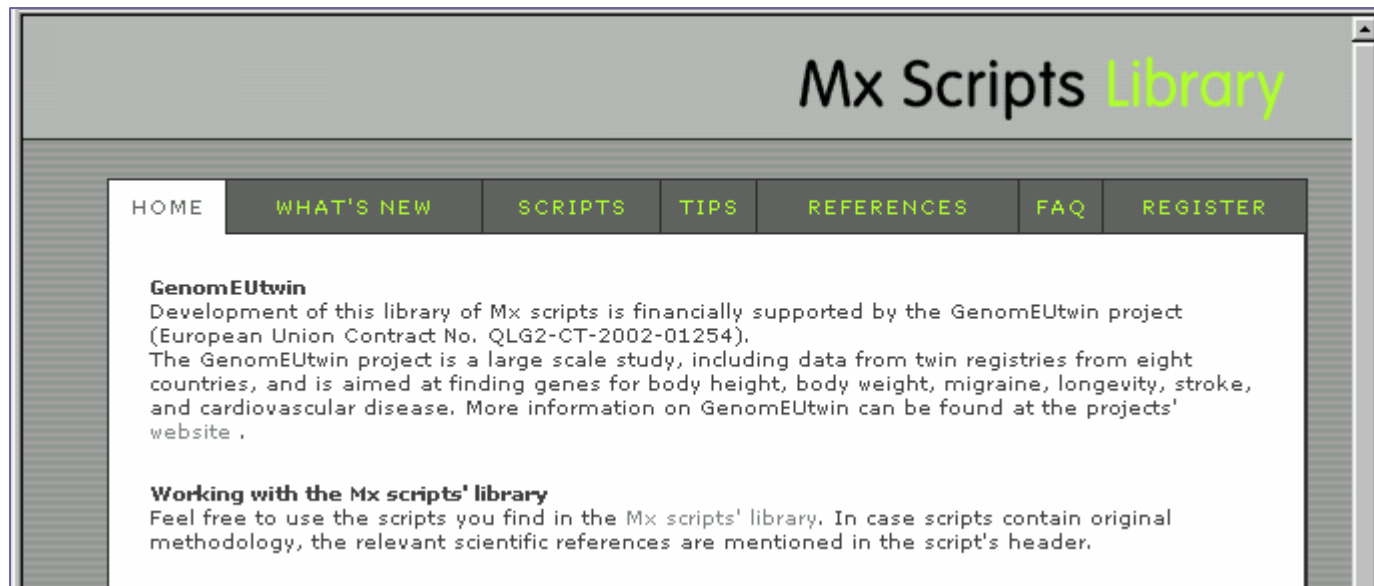
E	Grey	White	Wmem
Grey	.18	.0*sqrt.18*sqrt.13 = .00	-.15*sqrt.18*sqrt.31 = -.04
White	.00	.13	.02*sqrt.13*sqrt.31 = .00
Wmem	-.15	.02	.31

	Contr A	+	Contr E	= Pheno corr
Grey – White	0.57	+	0.00	= 0.57
Grey – Wmem	0.26	+	-.04	= 0.22
White – Wmem	0.16	+	0.00	= 0.16

You could further test whether the -.04 = zero, by constraining the re to be zero or by dropping the Z 2 1 parameter

Central place for Mx scripts genetic analyses

<http://www.psy.vu.nl/mxbib>



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