ACE/ADE Twin models

Sarah Medland and Hermine Maes 2024

Today - sarah/2024/monday

We pickup from the saturated model

We will look at:

- Extending the modelling to estimate heritability

Important structural stuff

- openMx has a very fluid and flexible structure
- Each code snippet is being saved as an object
- We tend to reuse the object names in our scripts
  - There are very few ‘reserved’ names
  - Naming a matrix “mean” does not make it a mean.

Important structural stuff

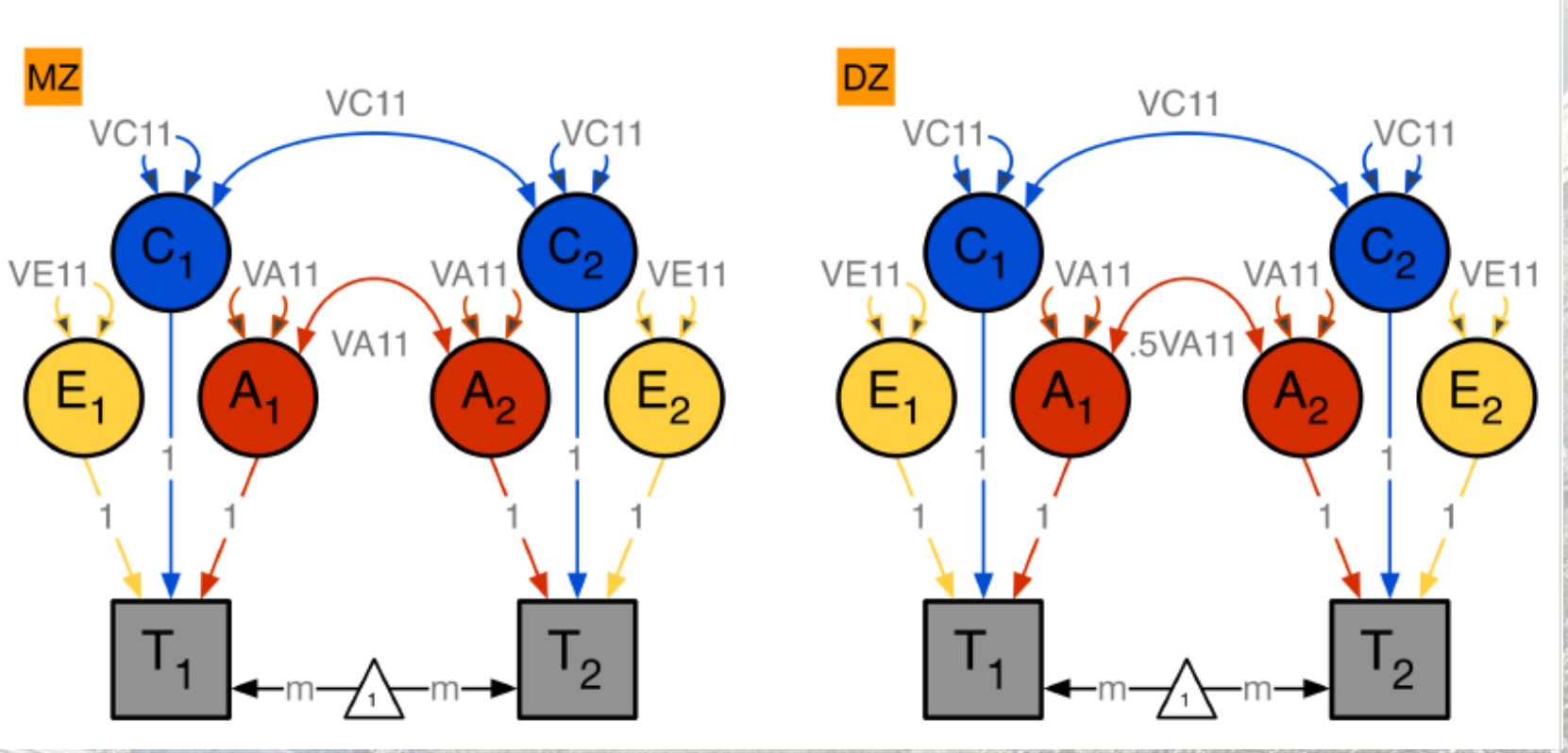
- No reserved names
  - We often use (and reuse) boring but meaningful names
    - make matrices `VA` `VC` `VE`
    - estimate `VP = VA + VC + VE`
  - But it would also work if we did this
    - make matrices `Coffee` `Milk` `Ice`
    - estimate `Frappe = Coffee + Milk + Ice`

Important structural stuff

- Because we tend to reuse the object names in our scripts you might need to remove these recycled objects from our work space to keep things tidy
  - `rm(list=ls())`
  - tends to freakout seasoned R uses – sorry
- Remember the project also contains the data so these files can become very large.
- Storing projects that contain data requires careful thinking about data security and can be an IRB risk if the project ‘leaves the building’

Today

- MZ and DZ pairs – estimating A, C and E



MZ

A+C+E	**A+C**
A+C	**A+C+E**

```
covP     <- mxAlgebra( expression= VA+VC+VE, name="V" )
covMZ    <- mxAlgebra( expression= VA+VC, name="cMZ" )
```

V	**cMZ**
cMZ	**V**

```
expCovMZ <- mxAlgebra( expression= rbind( cbind(V, cMZ),
                                          cbind(t(cMZ), V)),
                       name="expCovMZ" )
```

DZ

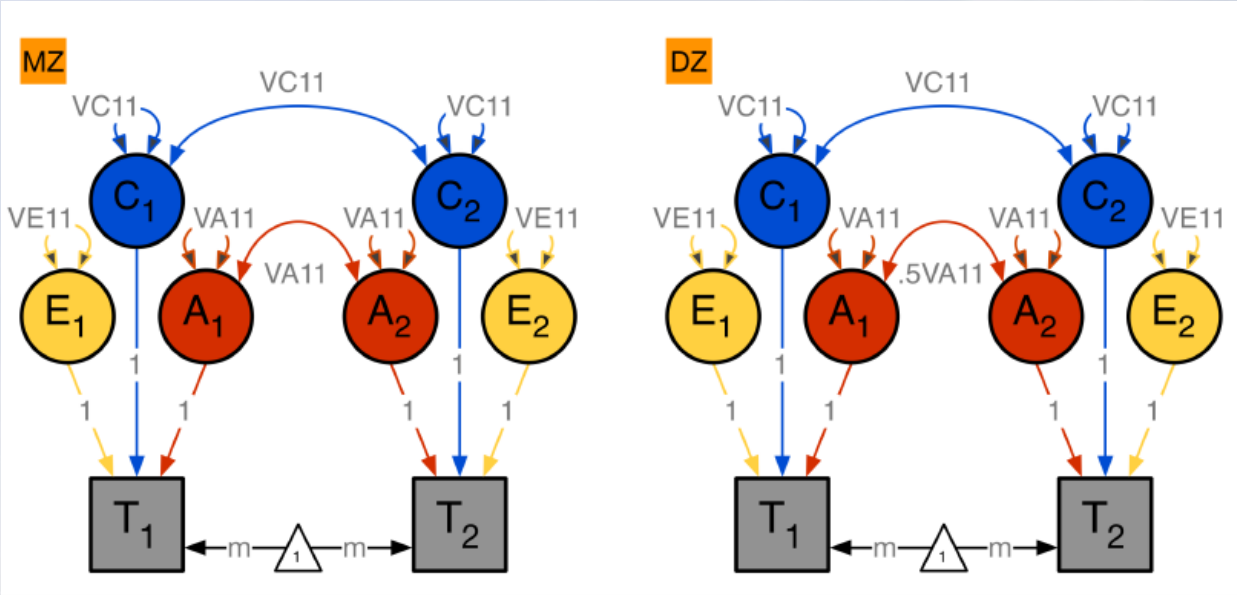
A+C+E	**.5⊗A+C**
.5⊗A+C	**A+C+E**

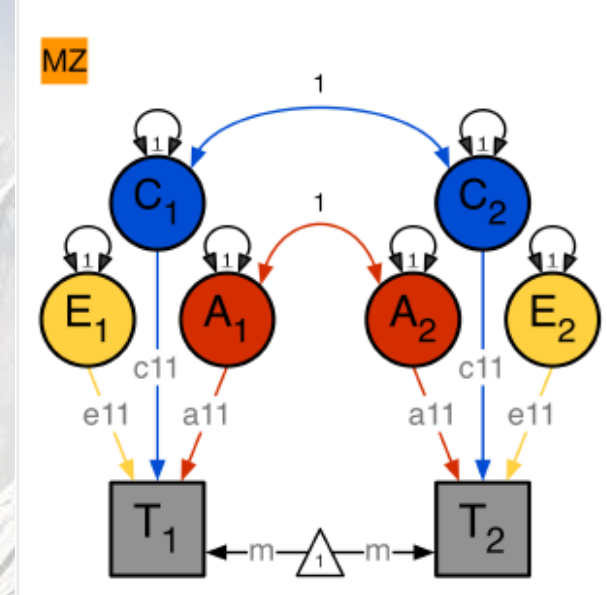
```
covP     <- mxAlgebra( expression= VA+VC+VE, name="V" )
covDZ    <- mxAlgebra( expression= 0.5%x%VA+VC, name="cDZ" )
```

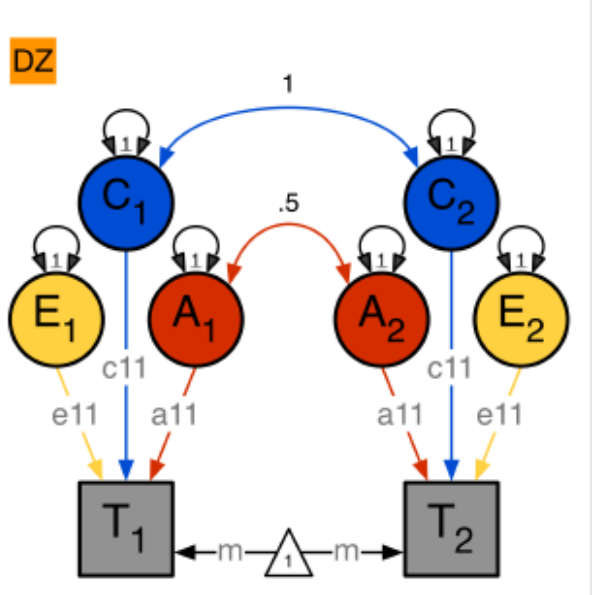
V	**cDZ**
cDZ	**V**

```
expCovDZ <- mxAlgebra( expression= rbind( cbind(V, cDZ),
                                          cbind(t(cDZ), V)),
                       name="expCovDZ" )
```

Change in approach







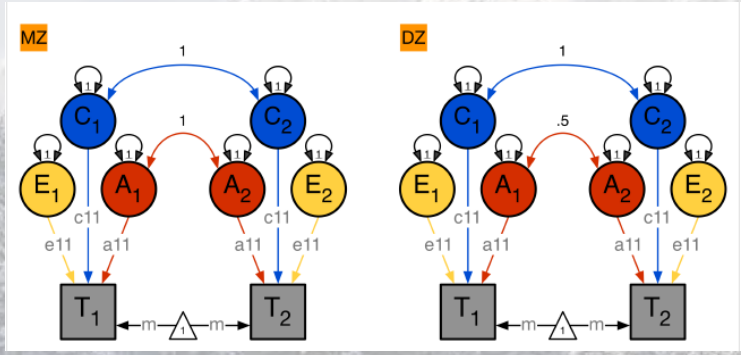
Two very useful papers in the ACE folder

Twin Research (1999) 2, 250–257

http://www.stockton-press.co.uk/tr

Genetic and environmental causes of variation in basal levels of blood cells

David M Evans[1], Ian H Frazer[2] and Nicholas G Martin[1]



ELSEVIER

BIOLOGICAL PSYCHOLOGY

Biological Psychology 61 (2002) 33–51

www.elsevier.com/locate/biopsycho

Biometrical genetics

David M. Evans *, N.A. Gillespie, N.G. Martin

Practical time

- In R studio
  - system("cp -R /faculty/sarah/2024/ACE/* ./ ")

- Qualtrics link is in ACE.txt

https://qimr.az1.qualtrics.com/jfe/form/SV_aXZTsTpDqACPQpM

Lets recap

- *The % variation in a trait attributable to genetic effects in a population*.
- The extent to which individual differences in genetics contribute to individual differences in observed behaviour in a large group of people
- Heritability should be thought about deterministically at the individual level
- These analyses don’t tell us what the genetic or environmental factors are.

For example

- About 75% of the variation in ADHD can be explained by genetic effects
- Heritability of 75%

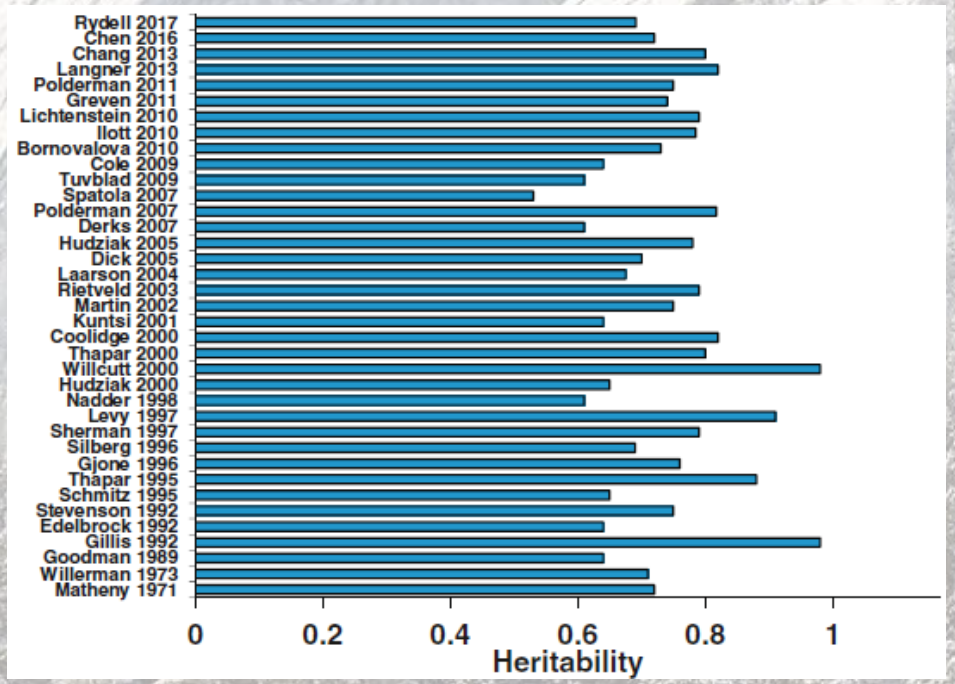
Molecular Psychiatry (2019) 24:562–575
https://doi.org/10.1038/s41380-018-0070-0

REVIEW ARTICLE

Genetics of attention deficit hyperactivity disorder

Stephen V. Faraone[1] · Henrik Larsson[2,3]

Received: 29 August 2017 / Revised: 31 January 2018 / Accepted: 19 February 2018 / Published online: 11 June 2018



This does not mean…

- That 75% of an individual's behaviour is due to their genetics and the other 25% is due to their environment
  - Genetic control 3am-9pm. Environmental control 9pm-3am
- That 75% of people have ADHD because of a genetic reason and 25% have ADHD because of an environmental reason
- A child of someone with ADHD has a 75% chance of developing ADHD

Important to remember

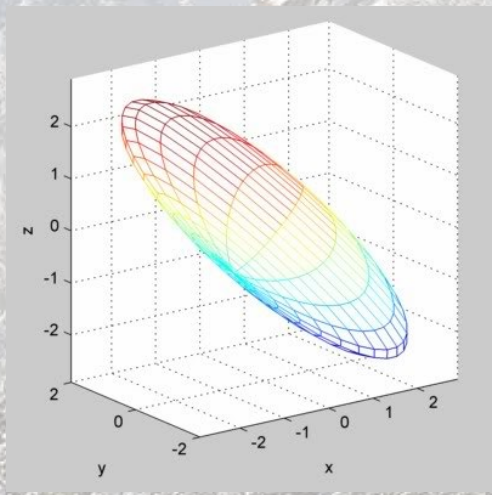
Our results are *estimates* based on the *data* we've analysed

- The won't necessarily generalize
  - Across time or space

Thinking out side the box…

Rather than thinking about estimates as fixed points I like to think about parameter space…

Imagine an ACE/ADE model as a solution space bounded by CIs



Important to remember

"Remember that all models are wrong; the practical question is how wrong do they have to be to not be useful"

George E P Box and Norman R Draper. 1986. *Empirical Model-Building and Response Surface*. John Wiley & Sons, Inc., New York, NY, USA.

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Questions?