Assessing aetiological overlap between child and adult attention-deficit hyperactivity disorder symptomatology using an extended family design

Luis Castro-de-Araujo[a]

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Virginia Institute for Psychiatric and Behavioral Genetics & The University of Melbourne

[a] Post-doc T32. luis.araujo@vcuhealth.org

- Several longitudinal studies have cast doubt on the aetiological overlap between child and adult attention-deficit hyperactivity disorder (ADHD). However, a lack of genetically sensitive data following children across adulthood precludes direct evaluation of aetiological overlap between child and adult ADHD

Aims

- Circumvent existing gap in longitudinal data by exploring genetic overlap between maternal (adult) and offspring (child) ADHD and comorbid symptoms in an extended family cohort.

- Data were drawn from the Norwegian Mother, Father, and Child Cohort Study (MoBa), a Norwegian birth registry cohort of 114,500 children and their parents. Medical Birth Registry of Norway (MBRN) data were used to link extended families.

- Mothers self-reported their own ADHD symptoms when children were aged 3, and reported children's ADHD symptoms at age 5, and children's ADHD, oppositional-defiant disorder (ODD), conduct disorder (CD), anxiety, and depression symptoms at age 8.

- Genetic correlations were derived using Multiple-Children-of-Twins-and-Siblings (MCoTS) and extended bivariate twin models.

- 25,469 mothers
- controlled for the effects of maternal age, parity (mothers' number of previous births), and children's year of birth on all variables, and the effects of child sex on child measures.

Supplementary Table S1. Frequencies of mothers and children stratified by maternal relatedness and child relatedness, for paired extended families and for unpaired nuclear families (i.e. singleton mothers with more than one child in MoBa).

Extended families (N = 19,201)

N stratified by the parent pairs used to identify extended families	rA	N
Identical twin pair	1.00	60
Full-sibling or fraternal twin pair	.500	12,085
Maternal or paternal half-sibling pair	.250	690
Cousin pair	.125	6,366

N stratified by mothers' relatedness in each extended family	rA	N
Identical twin pair	1.00	43
Full-sibling or fraternal twin pair	.500	4,074
Maternal or paternal half-sibling pair	.250	261
First cousin pair	.125	2,716
Unrelated sisters/cousins-in-law pair	0	12,107

Number of offspring pairs linked to each mother	rA	N
Full-sibling pair	.500	5,089
Maternal half-sibling pair	.250	41
Unpaired (singleton) offspring	---	20,339

Unpaired nuclear families (N = 4,565)

Number of offspring pairs linked to each mother	rA	N
Identical twin pair	1.00	172
Full-sibling or fraternal twin pair	.500	7,746
Maternal half-sibling pair	.250	32

**Adult ADHD symptoms (reported by mothers when children were aged 3)**
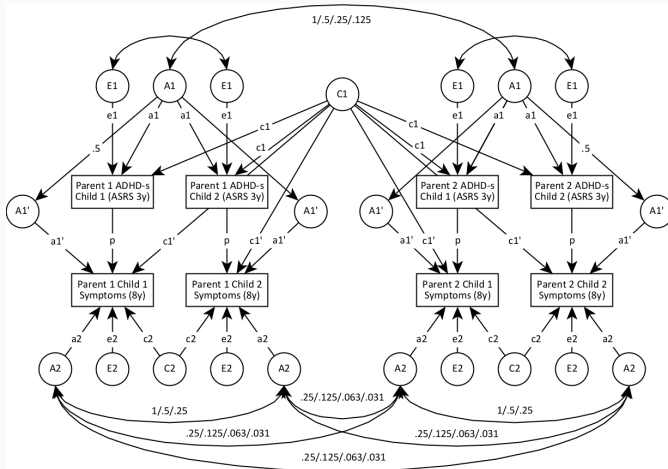
- Adult Self-Report Scale (ASRS)

Child ADHD symptoms at age 5

- Conners Parent Rating Scale-Revised (CPRS-R)
  - well-validated measure of parent-reported child ADHD symptoms

**Child ADHD and comorbid symptoms at age 8**

- Parent/Teacher Rating Scale for Disruptive Behavior (RS-DBD)
  - for ADHD, ODD and CD

Genetic correlations
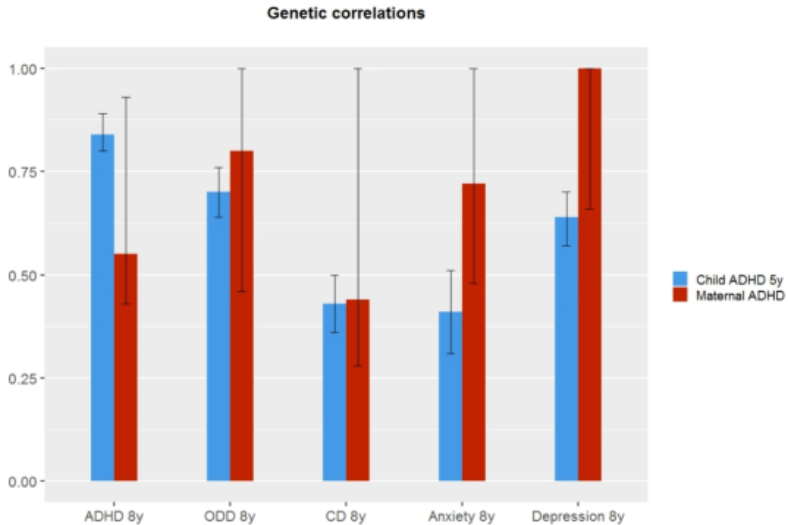
Supplementary Figure S3: Model specification for the MCoTS model. A1, C1 and E1 latent factors represent parental additive genetic, shared environmental and non-shared environmental variance components. A2, C2 and E2 factors represent the equivalent variance components for children. A1' latent factors represent genetic variance components that are shared between the parent and child phenotype. Paths a1', c1', and p represent the proportion of the parent-child association explained by genetic transmission, extended family environmental influence, and residual association indicating an influence of exposure to the parental phenotype. ADHD-s = ADHD symptoms.
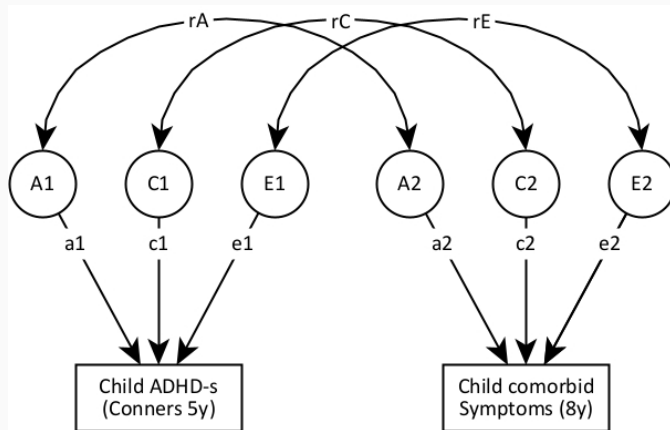
Model specification for the Extended Bivariate Twin Model. A1, C1 and E1 latent factors represent parental additive genetic, shared environmental and non-shared environmental variance components for child ADHD symptoms at age 5. A2, C2 and E2 factors represent the equivalent variance components for child comorbid symptoms at age 8. Paths rA, rC, and rE represent genetic, shared environmental, and nonshared environmental associations underpinning the total phenotypic association between the two measures. ADHD-s = ADHD symptoms. They had include sibling, half-sibling and cousin parents, and multiple children per parent
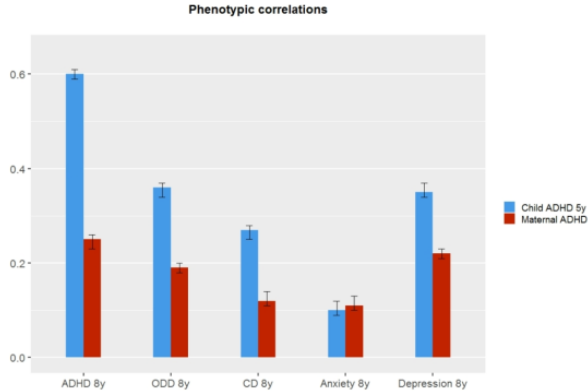
Figure 1. Bar plots displaying estimates (95% CI) of phenotypic correlations between each child symptom measure at age 8 (on X axis) and early child ADHD (blue bars) and adult ADHD (red bars).
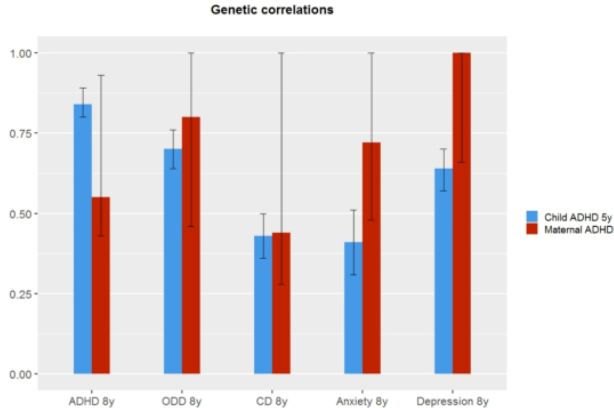
959x626mm (38 x 38 DPI)

Figure 2. Bar plots displaying estimates (95% CI) of genetic correlations between each child symptom measure at age 8 (on X axis) and early child ADHD (blue bars) and adult ADHD (red bars).

- genetically driven co-occurrence of adult ADHD symptoms in mothers and a typical pattern of ADHD-related symptomatology in their children

Team

- Michael C Neale.
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Contact

- **THANK YOU**