**Genetic and environmental contribution to the overlap between ADHD and ASD trait dimensions in young adults: a twin study.**

Laura Ghirardi1; Erik Pettersson1, Mark Taylor1, Christine M. Freitag4, Barbara Franke5, Philip Asherson6, Henrik Larsson1,7, Ralf Kuja-Halkola1

1Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden.

2Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, University Hospital Frankfurt, Goethe University, Frankfurt am Main, Germany.

3Department of Human Genetics and Psychiatry, Donders Institute for Brain, Cognition and Behaviour, Nijmegen, The Netherlands.

4MRC Social, Genetic and Developmental Psychiatry Centre, Institute of Psychiatry, Psychology, and Neuroscience, King's College London, London, UK.

5School of Medical Sciences, Örebro University, Örebro, Sweden.

Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, 171 77, Stockholm, Sweden

[laura.ghirardi@ki.se](mailto:laura.ghirardi@ki.se)

**Supplementary Material**

**Table of contents**

Suppelementary analysis 1. Differences between participants and non-participants

Supplementary table 1. Main characteristics of participants and non-participants

Supplementary table 2. Factors predicting non-response

Supplementary analysis 2. Accuracy of the scales

Supplementary table 3. Accuracy of the scales

Supplementary table 4. List of items for ASD and ADHD traits

Supplementary table 5. Distribution of the data for the variables under study

Supplementary table 6. Saturated models and submodels for assumption testing by trait (univariate)

Supplementary table 7. Saturated model and submodels for assumption testing (multivariate)

Supplementary table 8. AE models testing sex differences

Supplementary table 9. ACE models

Supplementary table 10. ADE models after exclusion of individuals with clinical diagnosis

Supplementary table 11. ADE models alowing for variance difference across zygosity groups

References

**Supplementary analysis 1. Differences between participants and non-participants**

Using a linkage of Swedish national registers via the unique personal identification number (Ludvigsson *et al.*, 2009), we created a cohort based on the same inclusion and exclusion criteria as the ones defining the target population of the survey conducted by the Swedish Twin Registry (Lichtenstein *et al.*, 2002, Lichtenstein *et al.*, 2006, Magnusson *et al.*, 2012) in order to compare participants to non-participants to the study on a set of variables available from the registers. Specifically, we first identified 18,379 twins born in Sweden between May 1st 1985 and June 30th 1992 using the Total Population Register (Ludvigsson *et al.*, 2016). After excluding individuals who had migrated or died before or during February 2013 (when the survey was conducted), the target population consisted of 17,266 individuals, and among these 6,838 had responded to the survey. Twenty-eight individuals who had responded to the survey were not identified in our cohort. Main characteristics of participants and non-participants are reported in Supplementary table 1.

Being born 1990 or later was associated with an increased probability of not participating to the study (OR=1.27; 1.17 -1.38).

We retrieved information on several socio-economic variables referring to year 2013 (when the survey was conducted) from the LISA (Longitudinell Integrationsdatabas för Sjukförsäkrings- och Arbetsmarknadsstudier) Database (Statistics Sweden, https://www.scb.se/lisa/).

Since several of the socio-economic characteristics examined were correlated with age (highest education achieved, employment status and annual disposable income), we examined the association between such variables and the probability of not responding to the survey, while controlling for year of birth as a categorical variable.

After adjusting for year of birth categorized as being born on 1990 or later and before 1990, several socio-economic characteristics considered were significantly associated with the probability of not responding to the survey. For example, having completed upper secondary or post-secondary education, as compared to primary or lower secondary, was associated with a decreased probability of being non-participant (OR=0.32; 95% CI: 0.28 - 0.38). The probability of not responding was decreased in those employed, as compared to those unemployed (OR=0.92; 95% CI: 0.85 - 0.99), and it was increased in those receiving unemployment benefit (OR= 1.21; 95% CI: 1.04 - 1.40), income support (OR= 1.87; 95% CI: 1.57 - 2.23) or sickness benefit (OR= 1.15; 95% CI: 1.00 - 1.31).

We retrieved information on psychiatric diagnoses from the National Patient Register (Ludvigsson *et al.*, 2011). We used the following codes from the International Classification of Diseases, Ninth Revision (ICD-9; 1987-1996) and ICD-10 (1997-2013):

* ICD-9 codes 299 – 319 and ICD-10 codes F00-F99 for all psychiatric diagnoses;
* ICD-9 code 314 and ICD-10 code F90 for ADHD;
* ICD-9 code 299A and ICD-10 codes F840, F841, F845 for Autism Spectrum Disorder (ASD).

After adjusting for year of birth categorized as being born on 1990 or later and before 1990, having any psychiatric diagnosis was associated with an increased probability of not responding to the survey (OR= 1.33; 95%CI: 1.21 - 1.46). When we examined diagnoses of ADHD and ASD, the association was stronger with ADHD diagnosis (OR=1.82; 95% CI: 1.45 - 2.29), but it was not statistically significant with ASD (OR= 1.28; 95% CI: 0.95 - 1.72).

**Supplementary table 1. Main characteristics of participants and non-participants**

|  |  |  |
| --- | --- | --- |
|  | **Participants** | **Non-participants** |
|  | *Number(%)/ Mean(SD)* | *Number(%)/ Mean(SD)* |
| *Year of birth* |  |  |
| 1985 | 462 (6.76) | 653 (6.26) |
| 1986 | 828 (12.11) | 1,171 (11.23) |
| 1987 | 882 (12.90) | 1,107 (10.62) |
| 1988 | 1,032 (15.09) | 1,357 (13.01) |
| 1989 | 966 (14.13) | 1,464 (14.04) |
| 1990 | 1,021 (14.93) | 1,667 (15.99) |
| 1991 | 1,068 (15.62) | 1,865 (17.88) |
| 1992 | 579 (8.47) | 1,144 (10.97) |
| *Residential status* |  |  |
| Times of moving residency within Sweden | 0.39 (0.61) | 0.37 (0.61) |
| *Highest completed education* |  |  |
| Primary and lower secondary | 233 (3.41) | 1,012 (9.70) |
| Upper secondary and post-secondary | 6,547 (95.74) | 9,164 (87.88) |
| Missing | 58 (0.85) | 252 (2.42) |
| *Study income* |  |  |
| Present | 2,750 (40.22) | 2,837 (27.21) |
| Absent | 4,068 (59.49) | 7,540 (72.31) |
| Missing | 20 (0.29) | 51 (0.49) |
| *Employment status* |  |  |
| Employed | 4,723 (69.07) | 7,295 (69.96) |
| Unemployed | 2,095 (30.64) | 3,082 (29.56) |
| Missing | 20 (0.29) | 51 (0.49) |
| *Unemployment benefit* |  |  |
| Present | 315 (4.61) | 568 (5.45) |
| Absent | 6,503 (95.10) | 9,809 (94.06) |
| Missing | 20 (0.29) | 51 (0.49) |
| *Sickness or employment injury benefit* |  |  |
| Present | 407 (5.95) | 684 (6.56) |
| Absent | 6,411 (93.76) | 9,693 (92.95) |
| Missing | 20 (0.29) | 51 (0.49) |
| Number of days | 3.12 (22.21) | 4.00 (25.53) |
| *Disposable income* |  |  |
| Individual | 1,647.92 (863.25) | 1,655.93 (940.99) |
| Family | 3,635.11 (3,897.73) | 4,098.37 (4,874.36) |
| *Income support* |  |  |
| Present | 214 (3.13) | 602 (5.77) |
| Absent | 6,604 (96.58) | 9,775 (93.74) |
| Missing | 20 (0.29) | 51 (0.49) |
| *Psychiatric disorders* |  |  |
| Any psychiatric diagnosis | 966 (14.13) | 1,869 (17.92) |
| ADHD | 115 (1.68) | 320 (3.07) |
| ASD | 75 (1.09) | 146 (1.40) |

**Supplementary table 2. Factors predicting non-response**

|  |  |
| --- | --- |
|  | **ORs/Coefficient (95%CIs)** |
| Birth in 1990 or after | 1.27 (1.17 - 1.38) |
| Moved within Sweden at least oncea | 0.94 (0.88 - 1.01) |
| Upper secondary or post-secondary educationa | 0.32 (0.28 - 0.38) |
| Employeda | 0.92 (0.85 - 0.99) |
| Presence of unemployment benefita | 1.21 (1.04 - 1.40) |
| Presence of sickness benefita | 1.14 (1.00 - 1.31) |
| Individual disposable incomea | 1.00 (1.00 - 1.00) |
| Family disposable incomea | 1.00 (1.00 - 1.00) |
| Presence of income supporta | 1.87 (1.56 - 2.23) |
| Presence of any psychiatric diagnosisa | 1.33 (1.21 - 1.46) |
| Presence of ADHD diagnosisa | 1.82 (1.45 - 2.29) |
| Presence of ASD diagnosisa | 1.28 (0.95 - 1.72) |

Note: aestimates are adjusted for year of birth categorized as being born on 1990 or later and before 1990.

**Supplementary analysis 2. Accuracy of the scales**

Using a linkage of Swedish national registers via the unique personal identification number, we identified diagnosis of ADHD and ASD in the National Patient Register (Ludvigsson *et al.*, 2011) according to the following codes from the International Classification of Diseases, Ninth Revision (ICD-9; 1987-1996) and ICD-10 (1997-2013):

* ICD-9 code 314 and ICD-10 code F90 for ADHD;
* ICD-9 code 299A and ICD-10 codes F840, F841, F845 for ASD;

We identified 115 (1.67%) individuals with a diagnosis of ADHD and 75 individuals with a diagnosis of ASD (1.09%).

We used logistic regression to evaluate whether the scales under study were predicting the probability of having a diagnosis of ADHD and ASD in the National Patient Register and we computed the area under the curve (AUC). Results are reported in Supplementary Table 3.

**Supplementary table 3. Accuracy of the scales**

|  |  |  |
| --- | --- | --- |
|  | **ORs (95% CI)** | **AUC** |
| *ADHD* |  |  |
| IA | 1.19 (1.16 - 1.22) | 0.81 |
| HI | 1.20 (1.16 - 1.22) | 0.79 |
| *ASD* |  |  |
| SIC | 2.36 (2.06 - 2.72) | 0.88 |
| RRB | 3.28 (2.61 - 4.13) | 0.81 |

Abbreviations: ORs=odds ratio; 95% CIs= 95% Confidence Intervals; AUC= area under the curve, area under receiver operation characteristic curve; IA= Inattention; HI= hyperactivity; RRB= repetitive and restricted behaviours; SIC= social interaction and communication. Note: ORs represent the increase in odds for a diagnosis of ADHD or ASD per unit increase in the scales (that is, IA, HI, RRB, SIC). Traits related to ADHD (that is, IA and HI) and traits ASD (that is, SIC and RRB) were assessed using different scales, with different means and variances. Hence the ORs are not directly comparable across ADHD and ASD.

**Supplementary table 4. List of items for ADHD and ASD traits**

|  |  |
| --- | --- |
| **ASRS** | |
| *How often during the last 6 months have you felt or acted in the following way?* | |
| **Items** | **Subscale** |
| How often do you have trouble wrapping up the final details of a project, once the challenging parts have been done? | IA |
| How often do you have difficulty getting things in order when you have to do a task that requires organization? | IA |
| How often do you have problems remembering appointments or obligations? | IA |
| When you have a task that requires a lot of thought, how often do you avoid or delay getting started? | IA |
| How often do you fidget or squirm with your hands or feet when you have to sit down for a long time? | HI |
| How often do you feel overly active and compelled to do things, like you were driven by a motor? | HI |
| How often do you make careless mistakes when you have to work on a boring or difficult project? | IA |
| How often do you have difficulty keeping your attention when you are doing boring or repetitive work? | IA |
| How often do you have difficulty concentrating on what people say to you, even when they are speaking to you directly? | IA |
| How often do you misplace or have difficulty finding things at home or at work? | IA |
| How often are you distracted by activity or noise around you? | IA |
| How often do you leave your seat in meetings or other situations in which you are expected to remain seated? | HI |
| How often do you feel restless or fidgety? | HI |
| How often do you have difficulty unwinding and relaxing when you have time for yourself? | HI |
| How often do you find yourself talking too much when you are in social situations? | HI |
| When you’re in a conversation, how often do you find yourself finishing the sentences of the people you are talking to, before they can finish themselves? | HI |
| How often do you have difficulty waiting your turn in situations when turn taking is required? | HI |
| How often do you interrupt others when they are busy? | HI |
|  |  |
| **A-TAC** |  |
| *In order to get as complete a picture as possible we would like you to answer the following questions from a life perspective but with extra emphesize on childhood and young adulthood. We all act and function different from each other at different ages and in different situations. Answer the questions how you function compared to most people of the same age as you.* |  |
| **Items** | **Subscale** |
| Do you have difficulties expressing emotions and reactions with facial gestures, pronunciation, or body language? | SIC |
| Have you difficulties to get and keep friends? | SIC |
| Are you disinterested in sharing joy, interests, and activities with others? | SIC |
| Can you only be with other people on your terms? | SIC |
| Was your language development delayed? | SIC |
| Do you have difficulties participating in discussions with others? | SIC |
| Do you like to repeat words and expressions or do you use words in a way other people find strange? | SIC |
| Do you have difficulty imitating other people or to play charades? | SIC |
| Do you get absorbed by your interests in such a way as being repetitive or too intense? | RRB |
| Do you get absorbed by routines in such a way as to produce problems for yourself or for others? | RRB |
| Have you some body movements that come automatically when you are happy or upset? | RRB |
| Do you get absorbed by details? | RRB |

Abbreviations: IA= Inattention; HI= hyperactivity; RRB= repetitive and restricted behaviours; SIC= social interaction and communication difficulties.

**Supplementary table 5. Distribution of the data for the variables under study**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Skewness** | | | | **Kurtosis** | | | |
|  | **IA** | **HI** | **SIC** | **RRB** | **IA** | **HI** | **SIC** | **RRB** |
| Untransformed | 0.61 | 0.62 | 1.67 | 1.47 | 3.32 | 3.44 | 6.87 | 5.41 |
| Logarithmic transformation | -1.26 | -1.18 | 0.41 | 0.58 | 5.21 | 4.76 | 2.38 | 2.41 |
| Square-root transformed | -0.51 | -0.50 | 0.10 | 0.20 | 3.68 | 3.60 | 2.23 | 1.87 |

Abbreviations: IA= Inattention; HI= hyperactivity; RRB= repetitive and restricted behaviours; SIC= social interaction and communication.

**Supplementary table 6. Saturated models and submodels for assumption testing by trait (univariate)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **-2LL** | **DF** | **Δ -2LL** | **Δ DF** | **p-value** | **AIC** |
| **IA** |  |  |  |  |  |  |
| Saturated Model | 16968.14 | 5872 |  |  |  | 5224.14 |
| Model 1 | 16973.62 | 5876 | 5.48 | 4 | 0.24 | 5221.62 |
| Model 2 | 16977.31 | 5878 | 3.69 | 2 | 0.16 | 5221.31 |
| Model 3 | 16994.13 | 5881 | 16.82 | 3 | 0.00 | 5232.13 |
| Model 4 | 16999.03 | 5885 | 4.90 | 4 | 0.30 | 5229.03 |
| Model 5 | 16999.22 | 5887 | 0.19 | 2 | 0.91 | 5225.22 |
| Model 6 | 16999.22 | 5888 | 0.00 | 1 | 0.99 | 5223.22 |
| Model 7 | 17002.95 | 5890 | 3.73 | 2 | 0.15 | 5222.95 |
| Model 8 | 17003.05 | 5891 | 0.10 | 1 | 0.75 | 5221.05 |
| Model 9 | 17003.69 | 5892 | 0.64 | 1 | 0.42 | 5219.69 |
| Model 10 | 17004.5 | 5893 | 0.81 | 1 | 0.37 | 5218.50 |
| **HI** |  |  |  |  |  |  |
| Saturated Model | 16525.04 | 5868 |  |  |  | 4789.041 |
| Model 1 | 16530.44 | 5872 | 5.39896067 | 4 | 0.25 | 4786.44 |
| Model 2 | 16553.93 | 5874 | 23.49412501 | 2 | 0.00 | 4805.934 |
| Model 3 | 16580.14 | 5877 | 26.20269233 | 3 | 0.00 | 4826.137 |
| Model 4 | 16593.69 | 5881 | 13.55634844 | 4 | 0.01 | 4831.693 |
| Model 5 | 16600.7 | 5883 | 7.003954067 | 2 | 0.03 | 4834.697 |
| Model 6 | 16600.73 | 5884 | 0.03421694 | 1 | 0.85 | 4832.732 |
| Model 7 | 16601.05 | 5886 | 0.321792454 | 2 | 0.85 | 4829.053 |
| Model 8 | 16601.17 | 5887 | 0.113614092 | 1 | 0.74 | 4827.167 |
| Model 9 | 16601.23 | 5888 | 0.06356321 | 1 | 0.80 | 4825.231 |
| Model 10 | 16608.94 | 5889 | 7.711897179 | 1 | 0.01 | 4830.943 |
| **RRB** |  |  |  |  |  |  |
| Saturated Model | 7940.344 | 4954 |  |  |  | -1967.66 |
| Model 1 | 7948.662 | 4958 | 8.31816106 | 4 | 0.08 | -1967.34 |
| Model 2 | 7962.138 | 4960 | 13.47631638 | 2 | 0.00 | -1957.86 |
| Model 3 | 7979.29 | 4963 | 17.15212964 | 3 | 0.00 | -1946.71 |
| Model 4 | 7979.631 | 4967 | 0.341222037 | 4 | 0.99 | -1954.37 |
| Model 5 | 7979.658 | 4969 | 0.02640769 | 2 | 0.99 | -1958.34 |
| Model 6 | 7980.098 | 4970 | 0.440207397 | 1 | 0.51 | -1959.9 |
| Model 7 | 7980.282 | 4972 | 0.183545321 | 2 | 0.91 | -1963.72 |
| Model 8 | 7980.567 | 4973 | 0.285012637 | 1 | 0.59 | -1965.43 |
| Model 9 | 7980.58 | 4974 | 0.013686554 | 1 | 0.91 | -1967.42 |
| Model 10 | 7981.169 | 4975 | 0.588487496 | 1 | 0.44 | -1968.83 |
| **SIC** |  |  |  |  |  |  |
| Saturated Model | 10223.78 | 5428 |  |  |  | -632.218 |
| Model 1 | 10227.31 | 5432 | 3.532200277 | 4 | 0.47 | -636.686 |
| Model 2 | 10233.77 | 5434 | 6.460384244 | 2 | 0.04 | -634.226 |
| Model 3 | 10239.75 | 5437 | 5.974955155 | 3 | 0.11 | -634.251 |
| Model 4 | 10240.92 | 5441 | 1.174718181 | 4 | 0.88 | -641.076 |
| Model 5 | 10241.28 | 5443 | 0.358951232 | 2 | 0.84 | -644.717 |
| Model 6 | 10242.41 | 5444 | 1.124086764 | 1 | 0.29 | -645.593 |
| Model 7 | 10242.99 | 5446 | 0.581735601 | 2 | 0.75 | -649.011 |
| Model 8 | 10243.53 | 5447 | 0.545691978 | 1 | 0.46 | -650.466 |
| Model 9 | 10246.66 | 5448 | 3.122900874 | 1 | 0.08 | -649.343 |
| Model 10 | 10246.98 | 5449 | 0.324426704 | 1 | 0.57 | -651.018 |

Abbreviations: -2LL= -2LogLikelihood; DF= degrees of freedom; Δ -2LL= difference in -2LogLikelihood between the two models compared; difference in degrees of freedom between the two models compared; p-value= p-values for Chi square test for the difference in -2LogLikelihood between the two models compared. Legend for the models: 1) Means constrained to be equal across twin order (opposite-sex twins excluded); 2) Means constrained to be equal across females and males (opposite-sex twins excluded); 3) Means constrained to be equal across all zygosity groups; 4) Variances constrained to be equal across twin order (opposite-sex twins excluded); 5) Variances constrained to be equal across MZ and DZ (exclude opposite sex); 6) Variances constrained to be equal across females and males (opposite-sex twins excluded): 7) Variances constrained to be equal across all zygosity groups; 8) Correlations constrained to be equal between females and males in MZ; 9) Correlations constrained to be equal between females and males in same-sex DZ; 10) Correlations constrained to be equal across same-sex and opposite-sex DZ twins.  
Note: Each model from Model 1 to Model 10 was compared to the one preceding it in the list, that is, Model 1 was compared to Saturated Model, Model 2 was compared to Model 1 and so on. The models were based on means corrected on age.

**Supplementary table 7. Saturated model and submodels for assumption testing (multivariate)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Model** | **-2LL** | **DF** | **Δ -2LL** | **Δ DF** | **P-value** | **AIC** |
| Saturated Model | 46976 | 22002 |  |  |  | 2971.996 |
| Model 1 | 46997.69 | 22018 | 21.69 | 16 | 0.15 | 2961.688 |
| Model 2 | 47019 | 22034 | 21.31 | 16 | 0.17 | 2951.004 |
| Model 3 | 47050.54 | 22058 | 31.54 | 24 | 0.14 | 2934.539 |
| Model 4 | 47083.67 | 22082 | 33.13 | 24 | 0.10 | 2919.669 |
| Model 5 | 47092.36 | 22088 | 8.69 | 6 | 0.19 | 2916.36 |
| Model 6 | 47097.46 | 22096 | 5.1 | 8 | 0.75 | 2905.458 |
| Model 7 | 47104.57 | 22108 | 7.11 | 12 | 0.85 | 2888.575 |
| Model 8 | 47131.44 | 22118 | 26.87 | 10 | 0.00 | 2895.442 |

Abbreviations: -2LL= -2LogLikelihood; DF= degrees of freedom; Δ -2LL= difference in -2LogLikelihood between the two models compared; difference in degrees of freedom between the two models compared; p-value= p-values for Chi square test for the difference in -2LogLikelihood between the two models compared. Legend for the models: 1) Means constrained to be equal across twin order (opposite-sex twins excluded); 2) Variances constrained to be equal across twin order (opposite-sex twins excluded); 3) Phenotypic correlations constrain to be equal in the two members of the twin pair (opposite-sex twins excluded); 4) CTCT constrained to be symmetrical (opposite-sex twins excluded); 5) CTCT correlations constrained to be symmetrical in opposite-sex twins; 6) ICC constrained to be equal across sexes (opposite-sex twins excluded); 7) CTCT correlations constrained to be equal across females and males (opposite-sex twins excluded); 8) ICC and CTCT correlations constrained to be equal across same-sex and opposite-sex DZ twins. Note: Each model from Model 1 to Model 8 was compared to the one preceding it in the list, that is, Model 1 was compared to Saturated Model, Model 2 was compared to Model 1 and so on. The models were based on means corrected on age.

**Supplementary table 8 . AE models testing sex differences**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Model** | **-2LL** | **DF** | **Δ -2LL** | **Δ DF** | **P-value** | **AIC** |
| AE qualitative and quantitative sex differences | 47179.41 | 22164 |  |  |  | 2851.41 |
| AEa only quantitative sex differences | 47197.63 | 22174 | 18.22 | 10 | 0.05 | 2849.63 |
| AEa no sex differences | 47210.12 | 22190 | 30.71 | 26 | 0.24 | 2830.12 |

Abbreviations: -2LL= - 2LogLikelihood; DF= degrees of freedom; Δ -2LL= difference in -2LogLikelihood between the two models compared; difference in degrees of freedom between the two models compared; p-value= p-values for Chi square test for the difference in -2 loglikelihood between the two models compared. Note: aCompared to AE allowing for qualitative and quantitative sex differences. The models were based on means corrected on age.

**Supplementary table 9. ACE models**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Model Fitting** | | | | | | |
|  | **-2LL** | **DF** | **Δ -2LL** | **Δ DF** | **P-value** | **AIC** |
| ACE qualitative and quantitative sex differences | 47165.54 | 22144 |  |  |  | 2877.54 |
| ACE only quantitative sex differences | 47172.27 | 22154 | 6.73 | 10 | 0.75 | 2864.27 |
| ACE no sex differences | 47209.08 | 22180 | 36.81 | 26 | 0.08 | 2849.08 |
| AE no sex differences | 47210.12 | 22190 | 1.04 | 10 | 1.00 | 2830.12 |
| E no sex differences | 47795.91 | 22200 | 585.79 | 10 | 0.00 | 3395.91 |
| **Results from AE Model no sex differences** | | | | | | |
|  | **IA-HI** | **IA-RRB** | **IA-SIC** | **HI-RRB** | **HI-SIC** | **RRB-SIC** |
| rP | 0.61  (0.59-0.62) | 0.33  (0.31-0.36) | 0.32  (0.29-0.34) | 0.38  (0.35-0.40) | 0.24  (0.21-0.27) | 0.39  (0.36-0.41) |
| A | 45%  (38-51) | 53%  (42-64) | 50%  (38-60) | 51%  (41-61) | 49%  (34-64) | 49%  (38-59) |
| E | 55%  (49-62) | 47%  (36-58) | 50%  (40-62) | 49%  (39-59) | 51%  (36-66) | 51%  (41-62) |
| rG | 0.66  (0.60-0.71) | 0.48  (0.39-0.58) | 0.42  (0.33-0.51) | 0.56  (0.46-0.65) | 0.33  (0.23-0.43) | 0.59  (0.49-0.70) |
| rE | 0.57  (0.53-0.61) | 0.25  (0.19-0.30) | 0.26  (0.21-0.31) | 0.28  (0.23-0.33) | 0.19  (0.14-0.24) | 0.29  (0.24-0.35) |

Abbreviations: -2LL= - 2LogLikelihood; DF= degrees of freedom; Δ -2LL= difference in -2LogLikelihood between the two models compared; difference in degrees of freedom between the two models compared; p-value= p-values for Chi square test for the difference in -2 loglikelihood between the two models compared; IA= Inattention; HI= hyperactivity; RRB= repetitive and restricted behaviours; SIC= social interaction and communication; rP= phenotypic correlation; A= Additive genetic contribution; E= non-shared environmental contribution; rA= additive genetic correlation; rA= unique environmental correlation. Note: The models were based on means corrected on age. A and E refer to the proportions of the phenotypic correlation explained by additive genetics and non-shared environment.

**Supplementary table 10. ADE models after exclusion of individuals with clinical diagnosis**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Model Fitting** | | | | | | |
|  | **-2LL** | **DF** | **Δ -2LL** | **Δ DF** | **P-value** | **AIC** |
| ADE qualitative and quantitative sex differences | 46271.02 | 21828 |  |  |  | 2615.024 |
| ADE only quantitative sex differences | 46283.16 | 21838 | 12.13858 | 10 | 0.28 | 2607.163 |
| ADE no sex differences | 46305.03 | 21864 | 21.86242 | 26 | 0.70 | 2577.025 |
| AE no sex differences | 46313.49 | 21874 | 8.462506 | 10 | 0.58 | 2565.488 |
| E no sex differences | 46872.47 | 21884 | 558.9775 | 10 | 0.00 | 3104.465 |
| **Results from AE Model no sex differences** | | | | | | |
|  | **IA-HI** | **IA-RRB** | **IA-SIC** | **HI-RRB** | **HI-SIC** | **RRB-SIC** |
| rP | 0.60  (0.58-0.61) | 0.32  (0.29-0.35) | 0.30  (0.28-0.33) | 0.37  (0.35-0.39) | 0.23  (0.20-0.25) | 0.38  (0.35-0.40) |
| A | 44%  (37-50) | 51%  (40-63) | 47%  (35-58) | 50%  (39-60) | 49%  (33-64) | 47%  (36-58) |
| E | 56%  (50-63) | 49%  (37-60) | 53%  (42-65) | 50%  (40-61) | 51%  (36-67) | 53%  (42-64) |
| rG | 0.65  (0.59-0.70) | 0.46  (0.36-0.56) | 0.39  (0.29-0.48) | 0.55  (0.45-0.65) | 0.32  (0.22-0.43) | 0.58  (0.46-0.69) |
| rE | 0.56  (0.53-0.60) | 0.25  (0.19-0.30) | 0.26  (0.21-0.31) | 0.28  (0.23-0.33) | 0.18  (0.12-0.23) | 0.29  (0.23-0.34) |

Abbreviations: -2LL= - 2LogLikelihood; DF= degrees of freedom; Δ -2LL= difference in -2LogLikelihood between the two models compared; difference in degrees of freedom between the two models compared; p-value= p-values for Chi square test for the difference in -2 loglikelihood between the two models compared; IA= Inattention; HI= hyperactivity; RRB= repetitive and restricted behaviours; SIC= social interaction and communication; rP= phenotypic correlation; A= Additive genetic contribution; E= non-shared environmental contribution; rA= additive genetic correlation; rA= unique environmental correlation. Note: The models were based on means corrected on age. A and E refer to the proportions of the phenotypic correlation explained by additive genetics and non-shared environment.

**Supplementary table 11. ADE models alowing for variance difference across zygosity groups**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Model Fitting** | | | | | | |
|  | **-2LL** | **DF** | **Δ -2LL** | **Δ DF** | **P-value** | **AIC** |
| ADE qualitative and quantitative sex differences | 47161.69 | 22136 |  |  |  | 2889.69 |
| ADE only quantitative sex differences | 47173.84 | 22146 | 12.14 | 10 | 0.28 | 2881.84 |
| ADE no sex differences | 47198.59 | 22172 | 24.76 | 26 | 0.53 | 2854.59 |
| AE no sex differences | 47206.99 | 22182 | 8.39 | 10 | 0.59 | 2842.99 |
| E no sex differences | 47791.82 | 22192 | 584.84 | 10 | 0.00 | 3407.82 |
| **Results from AE Model no sex differences** | | | | | | |
|  | **IA-HI** | **IA-RRB** | **IA-SIC** | **HI-RRB** | **HI-SIC** | **RRB-SIC** |
| rP | 0.61  (0.59-0.62) | 0.33  (0.31-0.36) | 0.32  (0.29-0.34) | 0.38  (0.35-0.40) | 0.24  (0.21-0.27) | 0.39  (0.36-0.41) |
| A | 45%  (38-51) | 53%  (42-64) | 50%  (38-60) | 51%  (41-61) | 49%  (34-64) | 49%  (38-59) |
| E | 55%  (0.49-0.62) | 47%  (36-58) | 0.50%  (40-62) | 49%  (39-59) | 51%  (36-66) | 51%  (41-62) |
| rG | 0.66  (0.60-0.71) | 0.48  (0.39-0.58) | 0.42  (0.33-0.51) | 0.56  (0.46-0.65) | 0.33  (0.23-0.43) | 0.59  (0.49-0.70) |
| rE | 0.57  (0.53-0.61) | 0.25  (0.19-0.30) | 0.26  (0.21-0.31) | 0.28  (0.23-0.33) | 0.19  (0.14-0.24) | 0.29  (0.24-0.35) |

Abbreviations: -2LL= - 2LogLikelihood; DF= degrees of freedom; Δ -2LL= difference in -2LogLikelihood between the two models compared; difference in degrees of freedom between the two models compared; p-value= p-values for Chi square test for the difference in -2 loglikelihood between the two models compared; IA= Inattention; HI= hyperactivity; RRB= repetitive and restricted behaviours; SIC= social interaction and communication; rP= phenotypic correlation; A= Additive genetic contribution; E= non-shared environmental contribution; rA= additive genetic correlation; rA= unique environmental correlation. Note: The models were based on means corrected on age. A and E refer to the proportions of the phenotypic correlation explained by additive genetics and non-shared environment.

**References**

**Lichtenstein, P, De Faire U, Floderus B, Svartengren M, Svedberg P & Pedersen NL** (2002). The Swedish Twin Registry: a unique resource for clinical, epidemiological and genetic studies. *Journal of Internal Medicine* **252**, 184 - 205.

**Lichtenstein, P, Sullivan PF, Cnattingius S, Gatz M, Johansson S, Carlstrom E, et al.** (2006). The Swedish Twin Registry in the third millennium: an update. *Twin Research Human Genetetic* **9**, 875 - 82.

**Ludvigsson, JF, Otterblad-Olausson P, Pettersson BU & Ekbom A** (2009). The Swedish personal identity number: possibilities and pitfalls in healthcare and medical research. *European Journal of Epidemiology* **24**, 659 - 67.

**Ludvigsson, JF, Andersson E, Ekbom A, Feychting M, Kim J-L, Reuterwall C, et al.** (2011). External review and validation of the Swedish national inpatient register. *BMC Public Health* **11**, 450.

**Magnusson, PKE, Almqvist C, Rahman I, Ganna A, Viktorin A, Walum H, et al.** (2012). The Swedish Twin Registry: Establishment of a Biobank and Other Recent Developments. *Twin Research and Human Genetics* **16**, 317-29.

**Ludvigsson, JF, Almqvist C, Bonamy A-KE, Ljung R, Michaëlsson K, Neovius M, et al.** (2016). Registers of the Swedish total population and their use in medical research. *European Journal of Epidemiology* **31**, 125 - 36.