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Associations between genetic predisposition to mental health problems and academic achievement: a developmental perspective using two population-based cohorts

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Background: Children's cognitive abilities play an important role throughout their academic career, but recent studies highlight the negative impacts of aggression, inattention, and impulsivity on academic success. These behaviors and traits are central to most externalizing (EXT) and neurodevelopmental (NDD) problems, which are substantially genetically influenced. We examined the mechanisms by which high levels of genetic predispositions to EXT and NDD problems associate with elevated mental health symptoms and subsequently lead to lower levels of academic achievement in two developmental periods (i.e., childhood and adolescence). **Methods:** Analyses were performed on a subset of participants from the Generation R Study (N = 2,992) and the Avon Longitudinal Study of Parents and Children (ALSPAC) (N = 5,099). Using structural equation modeling, we simultaneously tested for indirect pathways between polygenic scores for externalizing and neurodevelopmental problems (PGS-EXT and PGS-NDD) and academic achievement (age 12 in the Generation R Study and age 16 in ALSPAC) via children's symptomatology for conduct, attention, social, and oppositional defiant problems reported by mothers during early childhood (Generation R Study) and from childhood to adolescence (ALSPAC study). Our models were adjusted for children's sex, exposure to adversity, cognitive abilities, early school achievement (only in ALSPAC), and genetic predisposition to educational attainment. **Results:** In both cohorts, we found that higher levels of PGS-NDD were associated with lower levels of academic achievement via higher attention problems. In adolescence only, we found that higher levels of PGS-NDD and PGS-EXT were associated with lower academic achievement via higher levels of conduct problems. **Conclusions:** Genetic predispositions to EXT and NDD were indirectly associated with academic achievement beyond the PGS for educational attainment, highlighting the need for sustained efforts to support children with attention problems in educational settings and to intervene on conduct problems, particularly during adolescence. **Pre-registration number:** Doi: 10.17605/OSF.IO/SQTJH. **Keywords:** Behavioral genetics; educational attainment; conduct disorder; attention-deficit-hyperactivity disorder.

Introduction

Low academic achievement and low levels of literacy are strong predictors of welfare dependence, stress, mental disorders, ill health, and premature mortality (Chetty et al., 2016; Jin, Shah, & Svoboda, 1995; Paul & Moser, 2009). Understanding the early predictors and developmental pathways that lead to academic success is, therefore, crucial. Several studies have shown that lower levels of genetic predisposition for education attainment are associated with reduced cognitive abilities and increased mental health problems, which, in turn, lead to academic underachievement (Belsky et al., 2016; Rabinowitz et al., 2020; Rea-Sandin et al., 2021). Alternatively, the developmental cascades to poor academic outcomes may stem from children's genetic predisposition to *mental health problems*, such as attention-deficit-hyperactivity disorder (ADHD). A meta-analysis of seven studies found that individuals with lower polygenic scores (PGS) for ADHD—indicating a lower genetic risk for the disorder—tend to achieve higher levels of academic success both during their school career and higher education attainment in adulthood (Ronald, de Bode, & Polderman, 2021). However, the additional predictive value of genetic predispositions for mental health problems over and above genetic predispositions for educational attainment has yet to be investigated.

Conflict of interest statement: No conflicts declared.

Both externalizing (EXT) and neurodevelopmental (NDD) problems are associated with psychosocial and behavioral problems that make children's school careers more challenging (Gray, Carter, Briggs-Gowan, Jones, & Wagmiller, 2014; Ramsook, Welsh, & Bierman, 2020; Schuurmans et al., 2022; Wang & Fredricks, 2014). Nonetheless, only a few studies have looked at how genetic predispositions for mental health problems associate with academic achievement via higher levels of symptomatology (e.g., Cabana-Domínguez et al., 2024; Jangmo et al., 2021), and these studies did not account for the co-occurrence and shared genetic etiology of mental health symptoms—that is, a common set of genes that express themselves pleiotropically (Mallard, Grotzinger, & Smoller, 2023). Horizontal pleiotropy happens when the same genetic variants predict multiple traits. As an example, the overlap among ADHD, ODD, and conduct disorder (CD) is predominantly due to common genetic influences (Dick, Viken, Kaprio, Pulkkinen, & Rose, 2005; Waldman, Rhee, Levy, & Hay, 2001). In the present study, we considered this shared genetic etiology between psychopathologies and the impact of their co-occurrence by investigating the developmental pathways from two higher-order polygenic scores for EXT and NDD problems and academic achievement via higher levels of psychopathological symptoms. These findings have the potential to inform early prevention efforts for poor academic achievement by highlighting intervention targets (e.g., early focus on attention, impulsivity, or conduct problems).

Relatedly, we were interested in the potential moderating effect of childcare attendance on these associations. We focus specifically on childcare attendance, defined as group-based childcare in settings such as nurseries and playgrounds because several studies previously showed that attending childcare for children from a more socio-economically deprived home environment was associated with lower levels of externalizing problems in adolescence (Larose, Côté, Ouellet-Morin, Maughan & Barker, 2021; Orri et al., 2019; Zachrisson & Dearing, 2015) and with reduced symptoms of hyperactivity, inattention, and aggression (Yamaguchi, Asai, & Kambayashi, 2018), as well as higher chances of graduating from mandatory school (Larose, Haeck, Ouellet-Morin, Barker & Coté, 2021). However, the moderating effect of childcare attendance on children's genetic predispositions for mental health problems has yet to be investigated.

Objectives

We examined whether children's symptomatology for conduct, attention, social, and oppositional defiant problems mediates the association between genetic predispositions for EXT and NDD problems and academic achievement. The analyses were performed in two independent population-based cohorts (i.e., the Generation R Study and ALSPAC) and covered two developmental periods (i.e., childhood and adolescence). We also tested the moderating role of childcare attendance on these developmental pathways.

Specifically, we hypothesized that the genetic predisposition to externalizing problems (PGS-EXT) will be associated with lower levels of academic achievement both directly and indirectly via higher levels of EXT problems (i.e., oppositional defiant disorder [ODD] and conduct problems [CD] in ALSPAC and aggression in The Generation R Study). Additionally, the PGS-EXT will associate indirectly with lower levels of academic achievement via higher levels of NDD problems.

We also anticipate that the genetic predisposition to neurodevelopmental disorders (PGS-NDD) will be associated with lower levels of academic achievement both directly and indirectly via higher levels of NDD problems (attention-deficit-hyperactivity disorder [ADHD] and emotionally reactive/social communication deficits). In addition, the PGS-NDD will be associated indirectly with lower levels of academic achievement via higher levels of EXT problems.

Moderating role of childcare attendance

We expect that childcare attendance will act as a buffering factor, which will decrease the strength of the hypothesized direct and indirect associations investigated.

Supplementary analysis

We also tested the incremental value of PGS-EXT and PGS-NDD in predicting academic achievement in young adulthood, above and beyond the PGS for educational attainment.

Methods

Amendment to pre-registered analysis

This study was pre-registered on an open registration platform; see Appendix S1 or DOI: 10.17605/OSF.IO/SQTJH. We followed the pre-registered analysis plan with a few exceptions, which are described in Appendix S2.

Samples

We used a subsample of the Generation R Study that included children for whom genome-wide genotypes, an academic achievement score at the end of primary school (i.e., 12 years old), and at least one maternal assessment of mental health problems between the ages of 1.5 and 6 were available ($N = 2{,}992$). The Generation R Study is an ongoing population-based prospective cohort from fetal life onwards (Kooijman et al., 2016) following 9,901 children born from 9,778 women residing in Rotterdam, The Netherlands, with an expected delivery date between April 2002 and January 2006. Written informed consent was obtained from the parents on behalf of the child. For data collected when the child was 12 years or older, the child also provided written informed

consent. The general design, research aims, and specific measurements of the Generation R Study have been approved by the Medical Ethical Committee of Erasmus MC, in accordance with the Declaration of Helsinki of the World Medical Association.

We also used a subsample of the Avon Longitudinal Study of Parents and Children (ALSPAC) (Fraser et al., 2013) that included children for whom genome-wide genotypes, academic scores at the end of mandatory school (i.e., 16 years old), and at least one maternal assessment of children's EXT and NDD symptoms between the ages of 7 and 13 were available (N = 5,099). ALSPAC is an ongoing epidemiological study of children born from 14,541 pregnancies to women residing in Avon, United Kingdom, with an expected delivery date between April 1991 and December 1992 (Boyd et al., 2013; Fraser et al., 2013), resulting in 13,988 children who were alive at 1 year of age. When the oldest children were approximately 7 years of age, an attempt was made to bolster the initial sample with eligible cases who had failed to join the study originally. The total sample size for analyses using any data collected after the age of seven is, therefore, 15,447 pregnancies, resulting in 14,901 children who were alive at 1 year of age. Informed consent to use the data collected via questionnaires and clinics was obtained from participants following the recommendations of the ALSPAC Ethics and Law Committee at the time. Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees (NHS Haydock REC: 10/H1010/70). Note that the study website contains details of all the data that are available through a fully searchable data dictionary (ALSPAC, 2025).

Measures

Polygenic scores. To account for the shared genetic etiology between psychopathologies, we used PGSs for higher-order factors of psychopathology. Previously, Waldman, Poore, Luningham, and Yang (2020) used genomic structural equation modeling (genomic SEM) of summary statistics from genome-wide association studies (GWAS) to identify a higher-order structure of psychopathology at the genetic level. Their best-fitting model included four higher-order psychopathology factors, which included EXT, NDD, internalizing, and thought problems. More specifically, the EXT factor included loadings for alcohol, cannabis, and nicotine dependence and antisocial behaviors, whereas the NDD factor included loadings for ADHD symptoms, autism spectrum disorder, and aggression (Waldman et al., 2020). Additionally, as their best-fitting model for the higher-order psychopathology structure included correlation between the higher-order factors, we decided to adjust our regression models with the two other higher-order PGS—in other words, internalizing and thought problems. Finally, as we aim to examine the additional value of genetic predispositions for psychopathologies over and above children's predisposition to educational attainment, we also computed this PGS.

To compute these five PGS (i.e., EXT, NDD, internalizing, thought problems, and educational attainment), we used the LDpred2-automatic model technique (Privé, Arbel, & Vilhjálmsson, 2021). We used the summary statistics generated from a multivariate GWAS conducted using genomic SEM on the higher-order structure of psychopathology described by Waldman et al. (2020) and the summary statistics from the latest GWAS of educational attainment (Okbay et al., 2022). We performed quality control (QC) on the summary statistics by removing duplicate Single Nucleotide Polymorphisms (SNPs) based on their rsID or chromosomal base pair position and selected only SNPs with a minor allele frequency >5%. We restricted the model to the Single Nucleotide Polymorphisms (SNPs) in common between the Generation R Study, the summary statistics for the higher-order psychopathology PGS or the educational attainment PGS, and the HapMap3 set of common variants (Altshuler et al., 2010). We replicated these steps in ALSPAC. Finally, we used the SNP-heritability estimates of each PGS based on the LD score regression as the initiation parameter for the calculation of the matrix of adjusted weights. The PGSs were created separately for each cohort.

After the PGSs were created, we adjusted them for children's sex and the first 10 genetic principal components. Of note, the Generation R Study is a population sample with children from European and non-European ancestry. We, therefore, computed two sets of PGS, one for the full sample and one restricted to the European sample. Importantly, the 10 principal components were estimated separately for the full sample and the European subsample. The description of how DNA was sampled, the genotyping, and the quality control procedure are described in Appendix S3 for both studies.

Mental health problems and social communication deficits. The Generation R Study: Emotionally reactive, aggressive, and attentive symptoms were assessed with maternal reports on the Child Behavior Checklist (CBCL/1.5–5), which is a validated and reliable measure for childhood mental health problems in the clinical and non-clinical range (Achenbach & Rescola, 2000). The three scales of the CBCL were assessed when children were 1.5, 3, and 6 years of age. The emotionally reactive scale consists of nine items, the aggressive symptoms scale consists of 19 items, and attentive symptoms were measured with five items.

ALSPAC: ODD, CD, and ADHD symptoms were assessed with maternal reports on the Development and Wellbeing Assessment (DAWBA) at ages 7, 10, and 13. DAWBA is a well-validated, semi-structured, DSM-IV-based questionnaire and interview evaluating a range of psychopathological symptoms (Goodman, Heiervang, Collishaw, & Goodman, 2011). The ADHD scale comprised 18 symptoms, ODD was assessed with nine symptoms, and CD was assessed with eight symptoms.

Social communication deficits were assessed using the 12-item Social Communication Disorder Checklist (SCDC) (Skuse, Mandy, & Scourfield, 2005), which is a validated screening instrument of social reciprocity and verbal/nonverbal communication with high sensitivity and specificity for autism. Mother-reported SCDC scores for children and adolescents were computed at ages 8, 11, and 14 years, with higher scores reflecting more social communication deficits (score range 0–24).

Academic achievement. The Generation R Study: We used children's results at 12 years old on a national examination at the end of primary school (i.e., Dutch Central Institute for Test Development [Cito] test) as the indicator of academic achievement at the end of middle school (Van Boxtel, Engelen, & De Wijs, 2010). The test consists of a total of 160 multiple-choice questions, which assess language and arithmetic skills. We used the standardized scores as raw scores are not comparable between different assessment years. Scores were collected either by national database linkage or by mother report.

ALSPAC: We used three indicators to create a latent score of academic achievement for each adolescent. The first indicator was the type of diploma obtained at the end of mandatory school (i.e., no certificate, Level 1 General Certificate of Secondary Education [GCSE; limited training], or Level 2 GCSE [qualification for academic post-16 education; high school diploma equivalent]). The second and third indicators were functional literacy in English and mathematics, which

were determined based on adolescents' results (achieved [1] or not [0]) on the functional English and mathematics tests taken at the Key Stage 4. These three indicators were combined in a latent variable using a confirmatory factor analysis to get a more refined evaluation of each participant's level of academic achievement (see Appendix S4).

Childcare attendance. The Generation R Study: Using maternal reports on childcare use (nursery, creche, and playground) when the child was 3 years of age, we created a categorical variable of childcare intensity: low childcare attendance (less than 8 h a week), part-time attendance (between 9 and 24 h a week), and full-time attendance (more than 25 h a week).

ALSPAC: Childcare attendance was reported by mothers when the child was 8 months, 15 months, 2 years, and 3 years old. Childcare attendance patterns have already been estimated (Larose, Côté, Ouellet-Morin, Maughan, & Barker, 2021) and have been categorized in three trajectories of attendance: low, part-time, and full-time attendance.

Covariates. The Generation R Study: We adjusted our model using the following covariates: child's sex, exposure to prenatal adversity (previously calculated for the Generation R Study and ALSPAC by Defina et al., 2024), and children's cognitive abilities. We adjusted for cognitive abilities (IQ) to examine the association between mental health symptoms and academic performance independent of cognitive abilities. This is motivated by phenotypic studies showing that mental health problems—especially ADHD symptomatology—associate with academic underachievement even when considering cognitive abilities (i.e., as quantified by IQ-achievement discrepancy) (Schuurmans et al., 2022).

The prenatal adversity index has been developed in collaboration between the Generation R and ALSPAC studies to better measure cumulative exposure to adversity. Specifically, the score comprises four cumulative domains (i.e., life events [e.g., death of a parent], contextual risk [e.g., financial difficulties], parental risk [e.g., parental psychopathology], and interpersonal risk [e.g., family conflicts]). Relevant items for each domain were dichotomized into 'risk' (1) or 'no risk' (0), and the mean was averaged to form the scores for each domain. Both the cumulative score and its four individual stress domains have been harmonized across the two cohorts in the present study.

Cognitive abilities were assessed using four subtests of the Wechsler Intelligence Scale for Children-Fifth Edition (WISC-V) (Wechsler, 2014). Cognitive abilities were assessed using four subtests of the Wechsler Intelligence Scale for Children-Fifth Edition (WISC-V) (Wechsler, 2014). We used Matrix reasoning to measure fluid reasoning, Digit Span for working memory, Coding for processing speed, and Vocabulary for verbal comprehension. The WISC-V was administered by a trained examiner during the research center visit when children had a mean age of 13.6 (*SD* = 0.3). The scores on the subtests were scaled and summed, and this sum score was converted to IQ using a conversion table that was created by Pearson (Blok et al., 2022).

ALSPAC: We adjusted our model with the following variables: child's sex, exposure to prenatal adversity (Defina et al., 2024), early academic achievement (i.e., results at Key Stage 1—to focus on the impact of mental health during adolescence), and children's cognitive abilities. Cognitive abilities were assessed when children were 8 years old during a half-day clinic, using a short form of the Wechsler Intelligence Scale for Children (WISC-III UK; Wechsler, Golombok, & Rust, 1992). A short form of the measure was employed to reduce the likelihood that the children would become fatigued and that this would affect their performance on the WISC-III UK. The WISC-III UK comprises five verbal subtests (information, similarities, arithmetic, vocabulary, and comprehension) and five performance subtests (picture completion, coding, picture arrangement, block design, and object assembly). Scores were age-normed in accordance with standard procedures. A child's general cognitive abilities score was created by Barker and colleagues by extracting the common variance from the verbal and performance tests in a latent factor (Barker et al., 2018). Finally, we adjusted for early academic achievement in the ALSPAC study to better isolate the role of mental health symptomatology during the teenage years regardless of children's levels of school readiness.

Finally, in both cohorts, we adjusted for genetic predispositions to internalizing and thought problems, educational attainment, and the first five genetic principal components to isolate the unique effects of PGS-EXT and NDD on academic achievement. Our adjustment strategy is illustrated in Figures S1 and S2.

Statistical analysis

Creation of the latent score of mental health symptomatology. The Generation R Study: We created three latent mental health scores representing the severity of symptoms for attention, aggression, and emotionally reactive by combining maternal ratings at 1.5, 3, and 6 years of age into three main latent variables.

ALSPAC: We created four latent mental health scores representing the severity of symptoms for ADHD, CD, ODD, and social communication deficits by combining maternal evaluation at 7, 10, and 13 years of age into four latent variables (i.e., one for each mental health problem).

Main analysis. We used multiple imputation by chained equation (van Buuren et al., 2023)—40 datasets over 40 iterations per dataset were generated—to impute missing data on covariates. Thereafter, using structural equation modeling, we simultaneously tested the direct and indirect associations between PGS-NDD/EXT and academic achievement via mental health problems. The direct and indirect effects and their associated 95% confidence intervals (CIs) were estimated using robust standard errors with a sandwich-type estimator. Specifically, academic achievement was predicted by children's PGS for EXT and NDD problems both directly and indirectly via children's latent scores for each form of psychopathology as mediators. We adjusted each regression with the following covariates: child's sex, exposure to prenatal adversity, children's cognitive abilities, early academic achievement [only in the ALSPAC study], and children's genetic predispositions to educational attainment, internalizing problems, and thought problems, as well as the first five genetic principal components.

Finally, we tested whether children's sex and attending childcare modified the strength of the direct and indirect associations previously examined using a multi-group strategy where model fit between the freely estimated and the constrained models was compared using an ANOVA. We used the R software with the following packages: *SemTools 0.5–6.933*, *lavaan 0.6–17*, and *MICE* (Jorgensen et al., 2022; Rosseel, 2012; van Buuren et al., 2023).

Sensitivity analysis

For the Generation R Study, we performed our analysis on the full sample and on two additional subsets based on participants ancestry—European and non-European—which was

determined with their genetic principal components (Medina-Gomez et al., 2015). Additionally, we ran our models without adjusting for cognitive abilities and early academic achievement (only for ALSPAC) to examine the robustness of our results.

Supplementary analysis

We examined the incremental value of the PGS-EXT and PGS-NDD in predicting academic achievement, above and beyond the PGS for educational attainment. First, we examined the variance explained only by our set of phenotypical covariates (i.e., exposure to adversity, cognitive abilities, child sex, and early academic achievement). Then, we added in subsequently: (a) the PGS-EXT as well as PGS-NDD together, (b) the PGS for educational attainment, (c) the PGS for internalizing problems, and (d) the PGS for thought problems. We provide the R^2 for each model to demonstrate the incremental value of each genetic predisposition over and above the contribution of the covariates and other genetic predispositions.

Results

Sample characteristics

Descriptive statistics and bivariate associations between the main study variables are presented in Table 1 (The Generation R Study) and Table 2 (ALSPAC) and in Tables S1 and S2. Representativeness of the sample was evaluated by comparing the baseline characteristics of the participants who first enrolled in the Generation R and ALSPAC studies to the ones that were included in our analysis. Briefly, participants who remained in our study had experienced less prenatal adversity, lower levels of mental health problems, and higher levels of academic achievement (see Tables S3 and S4 for more details in Supporting Information).

Table 1 Descriptive statistics of the analytic sample in The Generation R Study

Descriptive statistics	
	Analytical sample (N = 2,992)
Categorical variables	N (%)
Sex (boys)	1,445 (48.3)
European Ancestry (yes)	2,156 (72.1)
Childcare attendance during early childhood	
Low attendance (less than 8 h a week)	462 (20.7)
Part-time attendance (between 9 and 16 h a week)	634 (28.4)
Full-time attendance (more than 17 h a week)	1,138 (50.9)
	N = 2,234
Continuous variables	M (SD) [min–max]
Exposure to adverse prenatal life events	0.11 (0.09) [0–0.60] N = 2,322
Exposure to adverse prenatal contextual risks	0.19 (0.20) [0–1.00] N = 2,242
Exposure to adverse prenatal parental risks	0.04 (0.07) [0–0.50] N = 1,824
Exposure to adverse prenatal interpersonal risks	0.09 (0.13) [0–0.94] N = 2,534
Levels of inattention at 2 years old	2.03 (1.73) [0–9.00] N = 2,191
Levels of emotionally reactive problems at 2 years old	1.53 (1.74) [0–12.00] N = 2,174
Levels of aggression at 2 years old	8.14 (5.23) [0–30.00] N = 2,073
IQ	105.03 (12.79) [64.00–154.00] N = 2,601
Academic Achievement (Cito score)	539.46 (8.96) [501.00–550.00] N = 2,992

IQ, intelligence quotient; M, mean; SD, standard deviation.

Developmental pathways from early to late childhood: The generation R study results

We did not find a direct association between PGS-NDD and PGS-EXT and academic achievement after adjusting for the set of covariates, but we found that attention problems mediated the PGS-NDD and academic achievement association at 12 years old ($B_{\text{indirect effect}} = -0.014$, $p < .001$). More specifically, PGS-NDD was positively associated with aggression, attention problems, and emotionally reactive problems, and among these, only attention problems mediated the association with academic achievement. The fit indices of this model were very poor (CFI = 0.535, TLI = 0.332, RMSEA = 0.141, SRMR = 0.158) considering that many associations were estimated without explaining any additional variance in academic achievement (see Table S5 and Figure S3). Given this, we followed up this initial analysis with a simpler model in which we kept attention problems as the only mediator between PGS-EXT and PGS-NDD and academic achievement, which resulted in a considerably improved model fit (CFI = 0.963, TLI = 0.930, RMSEA = 0.041, SRMR = 0.023), which indicated that academic achievement decreased by 0.013 standard deviations for every one standard deviation in PGS-NDD via attention problems. Regression coefficients from this model are presented in Table 3 and in Figure 1.

Developmental pathways from middle childhood to the end of adolescence: ALSPAC Results

We did not find direct associations of PGS-NDD and PGS-EXT with academic achievement at the end of mandatory schooling after adjusting for covariates. However, we found that ADHD and CD both mediated the associations of PGS-NDD (via ADHD

Table 2 Descriptive statistics of the analytic sample in the ALSPAC Study

Descriptive statistics	
	Analytical sample (N = 5,099)
Categorical variables	N (%)
Sex (boys)	2,519 (49.4)
Childcare attendance during early childhood	
Low attendance (less than 8 h a week)	4,220 (88.0)
Part-time attendance (between 9 and 16 h a week)	362 (7.5)
Full-time attendance (more than 17 h a week)	213 (4.4)
	N = 4,795
Level achieved at Key Stage 4 (end of mandatory schooling)	
No level achieved	898 (17.6)
Level 1	896 (17.6)
Level 2	3,305 (64.8)
English literacy	
No level achieved	100 (2.0)
Level 1	948 (18.6)
Level 2	4,051 (79.4)
Mathematics literacy	
No level achieved	207 (4.1)
Level 1	1,171 (23.0)
Level 2	3,721 (73.0)
Continuous variables	M (SD) [min–max]
Exposure to adverse prenatal life events	0.21 (0.15) [0–1] N = 4,504
Exposure to adverse prenatal contextual risks	0.08 (0.14) [0–0.83] N = 4,859
Exposure to adverse prenatal parental risks	0.07 (0.10) [0–1] N = 4,884
Exposure to adverse prenatal interpersonal risks	0.09 (0.11) [0–1] N = 4,884
Levels of attention-deficit-hyperactivity symptoms at 7 years old	4.36 (6.20) [0–34] N = 4,356
Levels of social communication deficits at 7 years old	2.72 (3.55) [0–24] N = 4,349
Levels of conduct problems at 7 years old	0.53 (0.98) [0–8] N = 4,333
Levels of oppositional defiant symptoms at 7 years old	2.00 (3.02) [0–20] N = 4,344
Early academic achievement - results at Key Stage 1	10.13 (3.43) [0–15] N = 4,466
IQ	105.17 (16.16) [46–149] N = 4,117

M, mean; SD, standard deviation; IQ, intelligence quotient.

and CD) and PGS-EXT (via CD only) with academic achievement. As shown in Table S6 and Figure S4, we found that PGS-NDD was positively associated with all the suggested mediators (i.e., ADHD, CD, social communication deficit, and ODD), yet only ADHD and CD were negatively associated with academic achievement at 16 years old and played mediating roles between PGS-NDD and later academic achievement. We also identified a significant indirect effect between PGS-EXT and academic achievement via high levels of CD. As with the late childhood models, the fit indices of this model were poor (CFI = 0.663, TLI = 0.540, RMSEA = 0.107, SRMR = 0.148). We, therefore, followed up this analysis with a model in which only ADHD and CD were included as mediators, and the model fit considerably improved (CFI = 0.914, TLI = 0.872, RMSEA = 0.056, SRMR = 0.053), which indicated that academic achievement decreases by 0.011 standard deviations for every one standard deviation in PGS-NDD via ADHD problems and academic achievement decreased by 0.023 and 0.025 standard deviations for every one standard deviation in PGS-NDD and PGS-EXT, respectively, via CD problems. Standardized regression coefficients of this model are presented in Table 4 and in Figure 2.

Do sex and childcare attendance moderate the developmental cascade?

In both cohorts, we did not find that the indirect effects previously identified varied according to child sex (Generation R Study: F-$statistic$ = 0.630, df = 11, p = .804; ALSPAC: F-$statistic$ = 1.254, df = 14, p = .228, see Tables S7 and S8) or childcare attendance profiles (Generation R Study: F-$statistic$ = 0.990, df = 22, p = .478; ALSPAC: F-$statistic$ = 0.459, df = 28, p = .993, see Tables S9 and S10).

Sensitivity analysis

We conducted our analysis on the two subsamples of participants of the Generation R Study according to their ancestry. For the European sample, we did not find any meaningful differences between the associations reported using the full sample. However, when conducting the analysis with the non-European subsample, we did not find any association between the PGS-EXT and PGS-NDD and children's phenotypes, consistent with the non-transportability of PGS associations developed on a different ancestry (Martin et al., 2017, 2019). Regression coefficients per subsample according to ancestry are available in Tables S11 and S12.

We reran our models without adjusting for children's cognitive abilities and early academic achievement and found a similar pattern of results in both studies, with the exception that we found an additional indirect effect in the ALSPAC study between the PGS-EXT and academic achievement via higher levels of ADHD symptoms (see Tables S13 and S14).

Table 3 Regressions coefficients of the final mediational model between PGS-EXT and PGS-NDD and academic achievement at the end of childhood—Generation R Study

	Standardized estimate	*p*-Value	R^2
Academic achievement at 12 years old			
PGS neurodevelopmental problems	−0.014	.387	.463
PGS externalizing problems	0.016	.267	
Attention levels from 2 to 6 years old	−0.090	<.001	
Exposure to adversity in the prenatal period	−0.041	.033	
Cognitive abilities	0.517	<.001	
Child sex	−0.051	<.001	
PGS internalizing problems	−0.011	.468	
PGS thought problems	0.014	.339	
PGS educational attainment	0.172	<.001	
Attention levels from 2 to 6 years old			
PGS neurodevelopmental problems	0.14	<.001	.118
PGS externalizing problems	0.032	.153	
Exposure to adversity in the prenatal period	0.213	<.001	
Cognitive abilities	−0.105	<.001	
Child sex	−0.079	<.001	
PGS internalizing problems	−0.046	.049	
PGS thought problems	0.009	.668	
PGS educational attainment	−0.051	.027	
Indirect effects			
PGS neurodevelopmental problems → attention → academic achievement	−0.013	<.001	
PGS externalizing problems → attention → academic achievement	−0.003	.199	
Total effect			
PGS neurodevelopmental problems → attention → academic achievement	−0.027	.093	
PGS Externalizing problems → attention → academic achievement	0.014	.364	

Also adjusted for the first five genetic principal components. PGS, Polygenic Score.

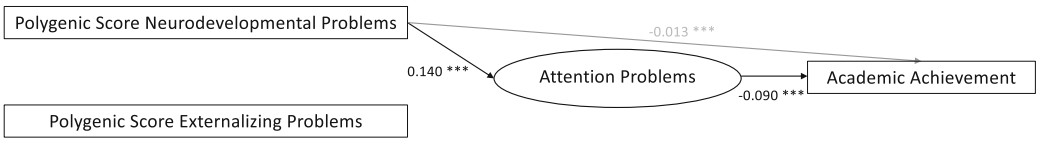

Figure 1 Mediational model between PGS-EXT and PGS-NDD and academic achievement at 12 years old via attention problems. Only significant associations are displayed. Standardized regression coefficients adjusted for: exposure to adversity, cognitive abilities, child sex, PGS internalizing problems, PGS thought problems, and PGS educational attainment as well as the first five genetic principal components. *p*-Values are displayed as *p = .05, **p = .01, ***p < .001. Black lines represent direct effects, and gray lines represent indirect effects. Of note, regression coefficients remain similar for the more complex model where attention, emotionally reactive, and aggression problems were the three mediators (see Table S5)

Supplementary analysis

We examined the incremental value of each PGS to the variance explained in academic achievement and mental health problems. In both ALSPAC and Generation R, adding PGSs did not substantially improve the variance explained for academic achievement beyond the phenotypic covariates, with R^2 increasing modestly from 42.2% to 44.6% in Generation R and from 42.7% to 44.1% in ALSPAC. In contrast, for aggression and conduct problems, PGSs provided a clearer incremental benefit, increasing explained variance from 8.3% to 12.2% in Generation R and from 11.4% to 15.7% in ALSPAC. Detailed results are shown in Tables S15 and S16.

Discussion

Using data from two population-based longitudinal cohorts, we examined how genetic predisposition for externalizing and neurodevelopmental problems can explain academic achievement in two developmental periods over and above children's genetic predispositions to educational attainment. First, we found that PGS-EXT was associated mainly with EXT symptoms in adolescence, while PGS-NDD was associated with various mental health problems across both developmental periods. Second, we found consistent evidence that attention problems (ADHD in ALSPAC) mediate the association between PGS-NDD and academic achievement. Additionally, CD was an important mediator between PGS-EXT and PGS-NDD and

Table 4 Regressions coefficients of the final mediational model between PGS-EXT and PGS-NDD and academic achievement at the end of adolescence—ALSPAC

	Standardized estimate	*p*-Value	R^2
Academic achievement at 16 years old			
PGS neurodevelopmental problems	0.016	.265	.440
PGS externalizing problems	−0.003	.831	
Attention-deficit-hyperactivity disorder levels from 7 to 13 years old	−0.089	<.001	
Conduct disorder levels from 7 to 13 years old	−0.169	<.001	
Exposure to adversity in the prenatal period	0.003	.821	
Early academic achievement at 7 years old	0.319	<.001	
Cognitive abilities	0.239	<.001	
Child sex	−0.062	<.001	
PGS internalizing problems	−0.038	.007	
PGS thought problems	0.021	.118	
PGS educational attainment	0.115	<.001	
Attention-deficit-hyperactivity disorder (ADHD) levels from 7 to 13 years old			
PGS neurodevelopmental problems	0.148	<.001	.193
PGS externalizing problems	0.027	.076	
Exposure to adversity in the prenatal period	0.116	<.001	
Early academic achievement at 7 years old	−0.298	<.001	
Cognitive abilities	−0.034	.093	
Child sex	0.151	<.001	
PGS internalizing problems	0.005	.767	
PGS thought problems	−0.002	.87	
PGS educational attainment	0.042	.008	
Conduct disorder (CD) levels from 7 to 13 years old			
PGS neurodevelopmental problems	0.131	<.001	.157
PGS externalizing problems	0.134	<.001	
Exposure to adversity in the prenatal period	0.214	<.001	
Early academic achievement at 7 years old	−0.147	<.001	
Cognitive abilities	−0.024	.285	
Child sex	0.068	<.001	
PGS internalizing problems	0.002	.926	
PGS thought problems	−0.022	.205	
PGS educational attainment	−0.033	.092	
Indirect effects			
PGS neurodevelopmental problems → ADHD → academic achievement	−0.013	<.001	
PGS externalizing problems → ADHD → academic achievement	−0.002	.112	
PGS neurodevelopmental problems → CD → academic achievement	−0.022	<.001	
PGS externalizing problems → CD → academic achievement	−0.023	<.001	
Total effect			
PGS neurodevelopmental problems → ADHD → academic achievement	0.003	.832	
PGS externalizing problems → ADHD → academic achievement	−0.005	.693	
PGS neurodevelopmental problems → CD → academic achievement	−0.025	.767	
PGS externalizing problems → CD → academic achievement	−0.006	<.001	

Also adjusted for the first five genetic principal components. ADHD, attention-deficit-hyperactivity disorder; CD, conduct disorder; PGS, Polygenic Score.

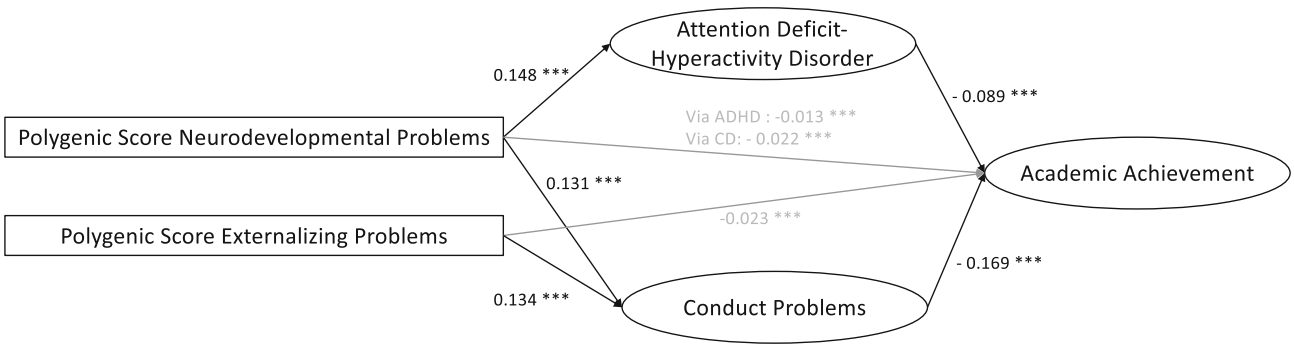

Figure 2 Mediational model between PGS-EXT and PGS-NDD and academic achievement at 16 years old via symptoms of attention-deficit-hyperactivity disorder and conduct problems. Only significant associations are displayed. Standardized regression adjusted for: exposure to adversity, cognitive abilities, child's sex and early academic achievement, PGS internalizing problems, PGS thought problems, and PGS educational attainment as well as the first five genetic principal components. *p*-Values are displayed as *p = .05, ** p = .01, ***p < .001. Black lines represent direct effects, and gray lines represent indirect effects. Of note, regression coefficients remain similar for the more complex model in which attention-deficit-hyperactivity disorder, oppositional defiant disorder, social communication deficits, and conduct problems were the four mediators (see Table S6)

academic achievement only in ALSPAC (i.e., from childhood to adolescence). Importantly, we did not find a direct effect of the PGS-NDD and EXT on academic achievement over and above the PGS for educational attainment and children's cognitive abilities, but we identified small significant indirect effects between PGS-NDD and EXT and academic achievement through higher levels of psychopathologies. Despite the small size of the indirect effects, uncovering the diverse genetic and phenotypic influences of early academic achievement is pivotal, as a deeper understanding of this educational milestone holds the potential to drive meaningful advances in both clinical practice and educational interventions (Andreassen, Hindley, Frei, & Smeland, 2023). Finally, we did not find that childcare attendance nor child sex moderated the associations between genetic predispositions to EXT and NDD and later academic achievement.

Predictive value of genetic predispositions to externalizing and neurodevelopmental symptoms in children and adolescents

PGS-NDD has widespread associations with mental health outcomes in the neurodevelopmental dimension (i.e., autism spectrum as well as attention problems) as well as externalizing psychopathology (i.e., aggression/conduct problems and oppositional defiant disorder). In contrast, PGS-EXT was only associated with mental health symptoms in ALSPAC, with the strongest association with CD. We found no significant association between PGS-EXT and mental health symptoms in the Generation R Study, which is surprising because we used the aggression subscale of the CBCL, which, similarly to the measure used in ALSPAC, includes early manifestations of CD and ODD, such as defiance, disobedience, and selfishness. However, these early behaviors may not be sufficiently associated with antisocial behavior and substance use (nicotine, alcohol, and cannabis) to show an early association with the PGS-EXT developed by Waldman et al. (2020). PGS-EXT appears to be better suited to predict rule-breaking behavior, and its predictive value may only emerge during adolescence, when teenagers display the specific behaviors on which the PGS was built (e.g., alcohol consumption), rather than the developmental precursors of these behaviors (e.g., being oppositional). We do not attribute the lack of association between PGS-EXT and early childhood mental health symptoms in Generation R to limited statistical power, as the near-zero or opposite-direction coefficients in bivariate analyses (Table S1) suggest a true absence of association rather than a power issue (Goertzen & Cribbie, 2010).

Highlighting the important role of attention problems for academic achievement

In this study, we found that attention problems were persistently associated with academic achievement from early childhood to the end of adolescence. The central role of attention problems in these associations is unsurprising, as it is a foundational precursor to academic success—independent of other cognitive skills, family adversity, and other behavioral skills (Cabana-Domínguez et al., 2024; Jangmo et al., 2021; Pingault et al., 2011; Schuurmans et al., 2022). Considering the high prevalence of attention problems from childhood to adulthood (Agnew-Blais et al., 2016), school-based interventions supporting children with attention problems (e.g., see for example DuPaul et al., 2021 and Evans, Owens, Wymbs, & Ray, 2018) are warranted for a lifelong impact on children's life opportunities.

Developmentally sensitive mechanisms

Interestingly, the mediating role of CD was only present in the ALSPAC study, which focuses on the adolescence period. The questionnaire used in ALSPAC had specific items on skipping school, threatening, or bullying others, as well as staying out late. These items correlate with the likelihood of early substance use, which may explain why we found an association with the PGS-EXT and later academic achievement. This result may also highlight developmentally sensitive mechanisms and may be related to parents' capacity to set limits on children displaying aggressive and disobedient behavior during childhood, but these compensatory strategies might not be as effective as children enter adolescence.

Contrary to our hypothesis, we did not find any association between social communication deficits or being emotionally reactive and later academic achievement in both developmental periods. This result echoes the ones presented by Cabana-Domínguez et al. (2024), suggesting a potential cancellation of effect when investigating the contribution of autism spectrum variants to academic achievement. This result might also be related to the use of population-based samples in which the severity of the symptoms is relatively low compared to a clinical sample.

Strengths and limitations

Strengths of this study include the use of two large population-based samples followed from pregnancy, and the analyses were conducted according to a preregistered analytical plan with few exceptions related to the psychometric properties of the scale (e.g., moving from the DSM scales to the symptom scales on the CBCL).

There are, however, a few limitations that may have constrained the study findings. First, although we examined academic achievement in both childhood and adolescence, each period was studied in a

separate cohort due to data availability. Future research should investigate these mechanisms within the same sample to determine whether the patterns replicate over time. Second, we were unable to perfectly match mediators between the two studies, and we only relied on maternal assessment of mental health symptoms. In the Generation R Study sample, the use of the CBCL prevented us from disentangling aggression and oppositional defiant disorder symptoms. Moreover, as we decided to use the symptom scales, we no longer had the hyperactivity component included in the latent factor for attention problems (compared to the ADHD scale used in ALSPAC). Also, we restricted our sample to participants who had been genotyped and who had data available on academic achievement as well as at least one assessment of mental health problems. Our samples are biased toward more socio-economically advantaged families; thus, results may differ in more at-risk samples. Finally, some individuals in the Generation R and ALSPAC Study have participated in two of the 14 GWAS used in the genomic SEM realized by Waldman et al. (2020). However, considering the small sample size of the two cohorts (N = 8,207) compared to the final sample size of the genomic SEM (N = 658,640), the influence of this overlap should not have a meaningful impact on our regression estimates. Replication in an independent, third sample is warranted, wherein mental health symptoms and academic achievement are assessed across childhood and adolescence.

Implications

To promote academic achievement, sustained efforts to ameliorate attention problems are necessary, while interventions on conduct problems might be most efficacious if taking place during adolescence. The findings on attention problems are to be considered in relation to recent findings by Cheesman et al. (2022), which highlighted that the association between PGS for ADHD and ADHD symptomatology is moderated by the quality of the school environment, where high-quality school environments have the potential to decrease or even render null the genetic association between PGS for ADHD and ADHD symptomatology.

Conclusions

Attention problems were consistently identified as a mediator of PGS-NDD effects on later academic achievement across two different population cohorts and developmental periods. Considering that low academic achievement can have substantial consequences on children's life opportunities, preventive and indicated school-based interventions focused on supporting children with attention problems are warranted.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article:

Appendix S1. Pre-registered analysis plan.

Appendix S2. Amendment to pre-registered analysis.

Appendix S3. Description of the genetic data.

Appendix S4. Description of the Key Stage 4 and academic achievement variable in ALSPAC.

Figure S1. Directed Acyclic Graphs of the associations between polygenic scores for neurodevelopmental and externalizing problems and academic achievement via mental health symptomatology—Generation R Study.

Figure S2. Directed Acyclic Graphs of the associations between polygenic scores for neurodevelopmental and externalizing problems and academic achievement via mental health symptomatology—ALSPAC Study.

Table S1. Correlation matrix of the main study variable in the Generation R Study.

Table S2. Correlation matrix of the main study variable in the ALSPAC.

Table S3. Descriptive statistics of the analytical sample compared to descriptive statistics of the sample excluded from the data analysis—Generation R Study.

Table S4. Descriptive statistics of the analytical sample compared to descriptive statistics of the sample excluded from the data analysis—ALSPAC Study.

Table S5. Regression coefficients of the full mediational model between PGS-EXT and PGS-NDD and academic achievement at the end of childhood: Generation R Study.

Figure S3. Mediational model between PGS-EXT and PGS-NDD and academic achievement at 12 years old via attention, aggression, and emotionally reactive problems.

Table S6. Regression coefficients of the full mediational model between PGS-EXT and PGS-NDD and academic achievement at the end of adolescence: ALSPAC study.

Figure S4. Mediational model between PGS-EXT and PGS-NDD and academic achievement at 16 years old via symptoms of oppositional defiant disorder, attention-deficit-hyperactivity disorder, conduct disorder and social communication deficits.

Table S7. Regression coefficients of the full mediational model between PGS-EXT and PGS-NDD and academic achievement at the end of childhood stratified by sex—Generation R Study.

Table S8. Regression coefficients of the full mediational model between PGS-EXT and PGS-NDD and academic achievement at the end of childhood stratified by sex—ALSPAC.

Table S9. Regression coefficients of the full mediational model between PGS-EXT and PGS-NDD and academic achievement at the end of childhood stratified by childcare attendance profile—Generation R Study.

Table S10. Regression coefficients of the full mediational model between PGS-EXT and PGS-NDD and academic achievement at the end of childhood stratified by childcare attendance trajectory—ALSPAC.

Table S11. Regression coefficients of the full mediational model between PGS-EXT and PGS-NDD and academic achievement at the end of childhood—European ancestry subsample of the Generation R Study.

Table S12. Regression coefficients of the full mediational model between PGS-EXT and PGS-NDD and academic achievement at the end of childhood—non-European ancestry subsample of the Generation R Study.
Table S13. Regression coefficients of the full mediational model between PGS-EXT and PGS-NDD and academic achievement at the end of childhood: Generation R Study—without adjustment for cognitive abilities.
Table S14. Regression coefficients of the full mediational model between PGS-EXT and PGS-NDD and academic achievement at the end of adolescence: ALSPAC study—without adjustment for cognitive abilities and early academic achievement.
Table S15. Incremental value of each polygenic score on the variance explained in academic achievement at the end of childhood—Generation R Study.
Table S16. Incremental value of each polygenic score on the variance explained in academic achievement at the end of adolescence—ALSPAC.

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The authors have declared that they have no competing or potential conflicts of interest. Open access publishing facilitated by Turun yliopisto, as part of the Wiley - FinELib agreement.

Ethical statement

This study was performed in line with the principles of the Declaration of Helsinki. For Generation R, study procedures were approved by the Medical Ethics Committee of the Erasmus University Medical Center in 2002, 2007, and 2012 (MEC 217.595/2002/202; MEC-2007-413; MEC-2012-165). Parents provided informed consent for their children in accordance with Dutch law.

For ALSPAC, informed consent to use the data collected via questionnaires and clinics was obtained from participants following the recommendations of the ALSPAC Ethics and Law Committee at the time (1989–1990) (IRB00003312). Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees (NHS Haydock REC: 10/H1010/70).

Data availability statement

The data that support the findings of this study are available from Generation R and ALSPAC. Restrictions apply to the availability of these data, which were used under license for this study.

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Key points

What's known?

- Academic achievement is facilitated by a suite of cognitive and psycho-emotional skills that allow children to thrive in the school context.

What's new?

- From early childhood to adolescence, attention problems played a mediating role in the associations between genetic predisposition to neurodevelopmental problems and academic achievement.

- Conduct problems only became a meaningful predictor of academic achievement from middle childhood to adolescence.

What's relevant?

- Sustained efforts to support children with attention problems in the school context are necessary to promote academic achievement throughout children's academic trajectory.

References

Achenbach, T.M., & Rescola, L. (2000). Manual for the ASEBA preschool forms & profiles. Research Center for Children, Youth, and Families, University of Vermont, USA.

Agnew-Blais, J.C., Polanczyk, G., Danese, A., Wertz, J., Moffitt, T.E., & Arseneault, L. (2016). Persistence, remission and emergence of ADHD in young adulthood: Results from a longitudinal, prospective population-based cohort. *JAMA Psychiatry*, *73*, 713–720.

ALSPAC. (2025). Avon Longitudinal Study of Parents and Children webpage. Available from: https://www.bristol.ac.uk/alspac/researchers/our-data/

Altshuler, D.M., Gibbs, R.A., Peltonen, L., Altshuler, D.M., Gibbs, R.A., Peltonen, L., … & McEwen, J.E. (2010). Integrating common and rare genetic variation in diverse human populations. *Nature*, *467*, 52–58.

Andreassen, O.A., Hindley, G.F., Frei, O., & Smeland, O.B. (2023). New insights from the last decade of research in psychiatric genetics: Discoveries, challenges and clinical implications. *World Psychiatry*, *22*(1), 4–24.

Barker, E.D., Cecil, C.A.M., Walton, E., Houtepen, L.C., O'Connor, T.G., Danese, A., … & Roberts, S. (2018). Inflammation-related epigenetic risk and child and adolescent mental health: A prospective study from pregnancy to middle adolescence. *Development and Psychopathology*, *30*, 1145–1156.

Belsky, D.W., Moffitt, T.E., Corcoran, D.L., Domingue, B., Harrington, H., Hogan, S., … & Caspi, A. (2016). The genetics of success: How single-nucleotide polymorphisms associated with educational attainment relate to life-course development. *Psychological Science*, *27*, 957–972.

Blok, E., Schuurmans, I.K., Tijburg, A.J., Hillegers, M., Koopman-Verhoeff, M.E., Muetzel, R.L., … & White, T. (2022). Cognitive performance in children and adolescents with psychopathology traits: A cross-sectional multicohort study in the general population. *Development and Psychopathology*, *35*, 1–940.

Boyd, A., Golding, J., Macleod, J., Lawlor, D.A., Fraser, A., Henderson, J., … & Davey Smith, G. (2013). Cohort profile: The 'Children of the 90s'—The index offspring of the Avon Longitudinal study of parents and children. *International Journal of Epidemiology*, *42*, 111–127.

Cabana-Domínguez, J., Bosch, R., Soler Artigas, M., Alemany, S., Llonga, N., Vilar-Ribó, L., … & Ribasés, M. (2024). Dissecting the polygenic contribution of attention-deficit/hyperactivity disorder and autism spectrum disorder on school performance by their relationship with educational attainment. *Molecular Psychiatry*, *29*, 3503–3513.

Cheesman, R., Eilertsen, E.M., Ayorech, Z., Borgen, N.T., Andreassen, O.A., Larsson, H., … & Ystrom, E. (2022). How interactions between ADHD and schools affect educational achievement: A family-based genetically sensitive study. *Journal of Child Psychology and Psychiatry*, *63*, 1174–1185.

Chetty, R., Stepner, M., Abraham, S., Lin, S., Scuderi, B., Turner, N., … & Cutler, D. (2016). The association between income and life expectancy in the United States, 2001-2014. *JAMA*, *315*, 1750–1766.

Defina, S., Woofenden, T., Baltramonaityte, V., Pariante, C.M., Lekadir, K., Jaddoe, V.W., … & EarlyCause Consortium. (2024). Effects of pre-and postnatal early-life stress on internalizing, adiposity, and their comorbidity. *Journal of the American Academy of Child & Adolescent Psychiatry*, *63*, 255–265.

Dick, D.M., Viken, R.J., Kaprio, J., Pulkkinen, L., & Rose, R.J. (2005). Understanding the covariation among childhood externalizing symptoms: Genetic and environmental influences on conduct disorder, attention deficit hyperactivity disorder, and oppositional defiant disorder symptoms. *Journal of Abnormal Child Psychology*, *33*, 219–229.

DuPaul, G.J., Evans, S.W., Owens, J.S., Cleminshaw, C.L., Kipperman, K., Fu, Q., & Benson, K. (2021). School-based intervention for adolescents with attention-deficit/hyperactivity disorder: Effects on academic functioning. *Journal of School Psychology*, *87*, 48–63.

Evans, S.W., Owens, J.S., Wymbs, B.T., & Ray, A.R. (2018). Evidence-based psychosocial treatments for children and adolescents with attention deficit/hyperactivity disorder. *Journal of Clinical Child & Adolescent Psychology*, *47*, 157–198.

Fraser, A., Macdonald-Wallis, C., Tilling, K., Boyd, A., Golding, J., Davey Smith, G., … & Lawlor, D.A. (2013). Cohort profile: The Avon longitudinal study of parents and children: ALSPAC mothers cohort. *International Journal of Epidemiology*, *42*, 97–110.

Goertzen, J.R., & Cribbie, R.A. (2010). Detecting a lack of association: An equivalence testing approach. *British Journal of Mathematical and Statistical Psychology*, *63*, 527–537.

Goodman, A., Heiervang, E., Collishaw, S., & Goodman, R. (2011). The 'DAWBA bands' as an ordered-categorical measure of child mental health: Description and validation in British and Norwegian samples. *Social Psychiatry and Psychiatric Epidemiology*, *46*, 521–532.

Gray, S.A.O., Carter, A.S., Briggs-Gowan, M.J., Jones, S.M., & Wagmiller, R.L. (2014). Growth trajectories of early aggression, overactivity, and inattention: Relations to second-grade reading. *Developmental Psychology*, *50*, 2255–2263.

Jangmo, A., Brikell, I., Kuja-Halkola, R., Feldman, I., Lundström, S., Almqvist, C., … & Larsson, H. (2021). The association between polygenic scores for attention-deficit/hyperactivity disorder and school performance: The role of attention-deficit/hyperactivity disorder symptoms, polygenic scores for educational attainment, and shared familial factors. *JCPP Advances*, *1*, e12030.

Jin, R.L., Shah, C.P., & Svoboda, T.J. (1995). The impact of unemployment on health: A review of the evidence. *CMAJ: Canadian Medical Association Journal*, *153*, 529–540.

Jorgensen, T.D., Pornprasertmanit, S., Schoemann, A.M., Rosseel, Y., Miller, P., Quick, C., … & Vanbrabant, L. (2022). semTools: Useful tools for structural equation modeling. Available from: https://cran.r-project.org/web/packages/semTools/index.html [last accessed 21 February 2024].

Kooijman, M.N., Kruithof, C.J., van Duijn, C.M., Duijts, L., Franco, O.H., van IJzendoorn, M.H., … & Jaddoe, V.W.V. (2016). The generation R study: Design and cohort update 2017. *European Journal of Epidemiology*, *31*, 1243–1264.

Larose, M.P., Côté, S.M., Ouellet-Morin, I., Maughan, B., & Barker, E.D. (2021). Promoting better functioning among

children exposed to high levels of family adversity: The protective role of childcare attendance. *Journal of Child Psychology and Psychiatry*, *62*, 762–770.
Larose, M.P., Haeck, C., Ouellet-Morin, I., Barker, E.D., & Côté, S.M. (2021). Childcare attendance and academic achievement at age 16 years. *JAMA Pediatrics*, *175*, 939–946.
Mallard, T.T., Grotzinger, A.D., & Smoller, J.W. (2023). Examining the shared etiology of psychopathology with genome-wide association studies. *Physiological Reviews*, *103*, 1645–1665.
Martin, A.R., Gignoux, C.R., Walters, R.K., Wojcik, G.L., Neale, B.M., Gravel, S., … & Kenny, E.E. (2017). Human demographic history impacts genetic risk prediction across diverse populations. *The American Journal of Human Genetics*, *100*, 635–649.
Martin, A.R., Kanai, M., Kamatani, Y., Okada, Y., Neale, B.M., & Daly, M.J. (2019). Clinical use of current polygenic risk scores may exacerbate health disparities. *Nature Genetics*, *51*, 584–591.
Medina-Gomez, C., Felix, J.F., Estrada, K., Peters, M.J., Herrera, L., Kruithof, C.J., … & Rivadeneira, F. (2015). Challenges in conducting genome-wide association studies in highly admixed multi-ethnic populations: The Generation R study. *European Journal of Epidemiology*, *30*, 317–330.
Okbay, A., Wu, Y., Wang, N., Jayashankar, H., Bennett, M., Nehzati, S.M., … & Esko, T. (2022). Polygenic prediction of educational attainment within and between families from genome-wide association analyses in 3 million individuals. *Nature Genetics*, *54*, 437–449.
Orri, M., Tremblay, R.E., Japel, C., Boivin, M., Vitaro, F., Losier, T., … & Côté, S.M. (2019). Early childhood child care and disruptive behavior problems during adolescence: A 17-year population-based propensity score study. *Journal of Child Psychology and Psychiatry*, *60*, 1174–1182.
Paul, K.I., & Moser, K. (2009). Unemployment impairs mental health: Meta-analyses. *Journal of Vocational Behavior*, *74*, 264–282.
Pingault, J.-B., Tremblay, R.E., Vitaro, F., Carbonneau, R., Genolini, C., Falissard, B., & Côté, S.M. (2011). Childhood trajectories of inattention and hyperactivity and prediction of educational attainment in early adulthood: A 16-year longitudinal population-based study. *American Journal of Psychiatry*, *168*, 1164–1170.
Privé, F., Arbel, J., & Vilhjálmsson, B.J. (2021). LDpred2: Better, faster, stronger. *Bioinformatics*, *36*, 5424–5431.
Rabinowitz, J.A., Kuo, S.I.-C., Domingue, B., Smart, M., Felder, W., Benke, K., … & Uhl, G. (2020). Pathways between a polygenic score for educational attainment and higher educational attainment in an African American sample. *Behavior Genetics*, *50*, 14–25.
Ramsook, K.A., Welsh, J.A., & Bierman, K.L. (2020). What you say, and how you say it: Preschoolers' growth in vocabulary and communication skills differentially predict kindergarten academic achievement and self-regulation. *Social Development*, *29*, 783–800.
Rea-Sandin, G., Oro, V., Strouse, E., Clifford, S., Wilson, M.N., Shaw, D.S., & Lemery-Chalfant, K. (2021). Educational attainment polygenic score predicts inhibitory control and academic skills in early and middle childhood. *Genes, Brain, and Behavior*, *20*, e12762.
Ronald, A., de Bode, N., & Polderman, T.J.C. (2021). Systematic review: How the attention-deficit/hyperactivity disorder polygenic risk score adds to our understanding of ADHD and associated traits. *Journal of the American Academy of Child & Adolescent Psychiatry*, *60*, 1234–1277.
Rosseel, Y. (2012). lavaan: An R package for structural equation modeling. *Journal of Statistical Software*, *48*, 1–36.
Schuurmans, I.K., Tamayo Martinez, N., Blok, E., Hillegers, M.H.J., Ikram, M.A., Luik, A.I., & Cecil, C.A.M. (2022). Child mental health problems as a risk factor for academic underachievement: A multi-informant, population-based study. *Acta Psychiatrica Scandinavica*, *145*, 578–590.
Skuse, D.H., Mandy, W.P.L., & Scourfield, J. (2005). Measuring autistic traits: Heritability, reliability and validity of the social and communication disorders checklist. *The British Journal of Psychiatry: the Journal of Mental Science*, *187*, 568–572.
Van Boxtel, H., Engelen, R., & De Wijs, A. (2010). *Wetenschappelijke verantwoording van de Eindtoets Basisonderwijs 2010 (scientific justification of the final test primary education 2010)*. The Netherlands: Cito.
van Buuren, S., Groothuis-Oudshoorn, K., Vink, G., Schouten, R., Robitzsch, A., Rockenschaub, P., … & Wade, S. (2023). mice: Multivariate imputation by chained equations. Available from: https://cran.r-project.org/web/packages/mice/index.html [last accessed 21 February 2024].
Waldman, I.D., Poore, H.E., Luningham, J.M., & Yang, J. (2020). Testing structural models of psychopathology at the genomic level. *World Psychiatry*, *19*, 350–359.
Waldman, I.D., Rhee, S.H., Levy, F., & Hay, D.A. (2001). Causes of the overlap among symptoms of attention deficit hyperactivity disorder, oppositional defiant disorder, and conduct disorder. In *Attention, genes and ADHD*. London: Psychology Press.
Wang, M.-T., & Fredricks, J.A. (2014). The reciprocal links between school engagement, youth problem behaviors, and school dropout during adolescence. *Child Development*, *85*, 722–737.
Wechsler, D. (2014). *WISC-V: Technical and interpretive manual*. Minneapolis: NCS Pearson.
Wechsler, D., Golombok, S., & Rust, J. (1992). *WISC-III UK Wechsler intelligence scale for children: UK manual*. Sidcup: The Psychological Corporation.
Yamaguchi, S., Asai, Y., & Kambayashi, R. (2018). How does early childcare enrollment affect children, parents, and their interactions? (SSRN Scholarly Paper No. ID 2932875). Rochester, NY: Social Science Research Network. Available from: https://papers.ssrn.com/abstract=2932875 [last accessed 28 March 2022].
Zachrisson, H.D., & Dearing, E. (2015). Family income dynamics, early childhood education and care, and early child behavior problems in Norway. *Child Development*, *86*, 425–440.

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