# Behaviour problems and co-occurring developmental conditions: genes, environments and their interplay.

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of the Degree of Doctor of Philosophy

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# Statement of originality

I, Agnieszka Gidziela, confirm that the research included within this thesis is my own work or that where it has been carried out in collaboration with, or supported by others, that this is duly acknowledged below, and my contribution indicated. Previously published material is also acknowledged below.

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# Abstract

Individual differences in developmental psychopathology are influenced by complex genetic and environmental factors, as well as their interplay. The first research study of the present thesis aims to clarify the state of knowledge on the genetic and environmental aetiology of neurodevelopmental disorders, their co-occurrence, and their association with disruptive disorders during childhood and adolescence, through a large-scale meta-analysis. The remaining three studies focus on investigating polygenic prediction of behaviour problem symptomatology and identifying environmental conditions that combine with genetic propensity to result in individual variation in behavioural traits. Longitudinal phenotypes and DNA data came from the Twins Early Development Study sample, consisting of more than 10,000 twin pairs born in England and Wales. Results of the meta-analysis showed that neurodevelopmental disorders in childhood and adolescence are highly heritable, and their pattern of co-occurrence is complex— while some are closely related, other show little genetic overlap, along with moderate-to-strong overlap with other developmental conditions. Research into polygenic prediction revealed modest predictive power of polygenic scores, accounting for up to 5% of the variance in child and adolescent behaviour problems and suggested that DNA-based prediction models can explain more variance by employing cross-trait, longitudinal and trans-situational approaches, and by using multiple polygenic scores to predict developmentally aggregated measures. In the search for specific early environments that predict behaviour problem outcomes, preschool, primary, and secondary school environments were not observed to have a major environmental impact, the strongest predictive processes were genetic. These insights laid the foundation for analysing how genes and environments correlate and interact in shaping adolescent psychopathology, revealing that both contribute to its development, though their interactions are modest. Research conducted as part of this thesis provides evidence to inform clinical and educational procedures and practice. It also discusses strategies to improve prediction of behaviour problems and developmental psychopathology.

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# Chapter 1— General Introduction

Developmental psychopathology is a multidisciplinary field of study that explores the complex interplay between psychological development and the emergence of psychiatric disorders across the lifespan (Cicchetti et al., 1989; Cicchetti & Cohen, 1995). Rooted in developmental psychology, this field seeks to understand how biological, psychological, and social factors interact dynamically to influence the course of normal and abnormal development (Cicchetti et al., 1989; Cicchetti & Cohen, 1995; Sroufe & Rutter, 1984). Researchers and clinicians in developmental psychopathology investigate the origins, risk factors, and protective factors associated with various mental health conditions, emphasising the importance of considering development as a continuous and interactive process. The field integrates insights from psychology, psychiatry, neuroscience, genetics and other related disciplines to provide a comprehensive understanding of the complexities involved in the manifestation and progression of psychological disorders from infancy through adulthood (Cicchetti & Toth, 2006).

Symptoms of developmental psychopathology in childhood and adolescence comprise problems in the behavioural domain, such as impulse-control disorders, attention-deficit hyperactivity disorder (ADHD) and conduct disorder, mood, and anxiety disorders, as well as thought disorders like autism spectrum disorder (ASD) and schizophrenia. However, the latter commonly onsets later in life and early-onset schizophrenia, i.e., diagnosed in childhood or adolescence, is considered rare (Clemmensen et al., 2012). Research adopting the developmental psychopathology perspective highlights the importance of evaluating behaviour in comparison to normative development to discern atypical or problematic nature (Drabick & Kendall, 2010; Rutter & Sroufe, 2000; Steinberg, 2008). However, challenges arise in distinguishing normative from atypical behaviour, particularly given the broad spectrum of what is considered "typical" across various developmental periods (Drabick & Kendall, 2010). Furthermore, while acknowledging the crucial role of environmental factors, such as parent-child dynamics and peer influences, the developmental psychopathology perspective highlights the oversight of these contextual influences in traditional diagnoses and proposes individual×context interactions (Boyce et al., 1998; Deater-Deckard, 2001; Drabick & Kendall, 2010; D. Hart & Marmorstein, 2009). According to the developmental psychopathology perspective, these reciprocal processes between individuals and their

environments shape psychopathology outcomes (Drabick & Kendall, 2010; Rutter & Sroufe, 2000).

One line of research in the field of developmental psychopathology explores genetic and environmental variables underlying individual differences in longitudinal trajectories of typical and atypical development (Masten & Curtis, 2000; Rutter & Sroufe, 2000). In relation to behaviour genetics, developmental psychopathology is concerned with the genetic and environmental aetiology, developmental manifestation of genetic and environmental risk and mechanisms underlying the continuous distribution of emotional, behavioural, and cognitive functioning (Plomin, 2004; Rende & Plomin, 1990; Rutter & Sroufe, 2000). In this thesis, developmental psychopathology will broadly refer to the comprehensive study of the development of psychological disorders and behaviour problems in children and adolescents, specifically focusing on neurodevelopmental disorders. Neurodevelopmental disorders are early-onset impairments in the development of the nervous system, affecting cognitive, motor, communication, and social functioning (APA, 2022; Thapar et al., 2015). These disorders often follow lifelong trajectories and can result in diminished independence throughout the lifespan (Faraone et al., 2006; McDowell & Lesslie, 2018; McGovern & Sigman, 2005).

The importance of studying developmental psychopathology is underscored by increases in the number of children and adolescents reporting behavioural and psychological challenges, as well as the rising prevalence of neurodevelopmental disorders. For instance, the prevalence of ASD has shown a marked increase over the years. According to the Autism and Developmental Disabilities Monitoring (ADDM) Network report in 2018, the estimated prevalence of ASD among children aged 8 years was 1 in 59, which represents a 15% increase compared to previous estimates (Baio et al., 2018). Similarly, ADHD diagnoses have also witnessed a substantial rise. The National Comorbidity Survey-Adolescent Supplement reported a prevalence rate of major depression and ADHD among adolescents aged 13 to 18 years at 11.4% and 9.0%, respectively (Avenevoli et al., 2015). This surge in statistics might suggest an expanded scope of diagnoses, warranting the urgent need to understand the underlying factors contributing to these conditions and develop effective interventions.

Developmental psychopathology phenotypes are complex traits influenced by a combination of nature, nurture and the interplay between the two (Knopik et al., 2017; Plomin, 2019;

Plomin et al., 1977; Rutter & Silberg, 2002). Psychiatric phenotypes rarely develop in isolation, and about half of the time, they co-occur with other psychiatric traits (Caspi et al., 2014; Kessler et al., 2005; Newman et al., 1998). The development of these phenotypes in childhood and adolescence is therefore defined by a complex network of interrelationships between psychological traits and between genetic and environmental factors underlying their aetiology and that of their co-occurrences. The present thesis aims to investigate the complex aetiology of individual differences in the development of psychopathology, with a particular focus on behaviour problems and their co-occurrences.

This chapter introduces developmental psychopathology, as well as the main methods that have been adopted across the four empirical chapters, namely quantitative genetic and genomic methods. I will first outline the main branches of analytical methods used in behaviour genetics, starting from the fundamentals of the twin method and the concepts of broad-sense heritability, shared and nonshared environment, moving on to DNA-based methods to estimate narrow-sense heritability. I will provide an overview of the technological advances brought by the era of genome-wide association (GWA) studies, highlighting the emergence of genome-wide polygenic scores (PGSs). Subsequently, I will illustrate the importance of thinking about psychopathology as a continuous distribution of symptoms, rather than uniform diagnoses. Next, I will describe the genetic and environmental aetiology of the main symptom categories investigated in the present thesis. This will be followed by a brief review of research on the complex interplay between nature and nurture and a discussion of how PGSs can be used to predict individual differences in complex developmental phenotypes. Lastly, I will discuss the origins of the co-occurrence between key developmental psychopathology phenotypes and provide an outline of the chapters that follow.

## Quantitative genetics and genomics

### *Twin heritability*

Twin heritability is an estimate of the relative contribution of genetic factors to individual variation in a trait or disorder and can be assessed using twin and pedigree methods, including the classical twin design. The twin design allows for the decomposition of

individual differences in a trait into genetic and environmental sources of variance by capitalising on the genetic relatedness between monozygotic twins, who share approximately 100% of their genetic makeup, and dizygotic twins, who share on average 50% of the genes that differ between individuals (Knopik et al., 2017). A trait can be assumed heritable, if monozygotic within-pair similarity is greater than dizygotic similarity, assuming that the environments experienced by monozygotic twins are not more similar than those experienced by dizygotic twins (Knopik et al., 2017; Rijsdijk & Sham, 2002). In twin studies, heritability is estimated using the Falconer's formula, expressed as a doubled difference between monozygotic and dizygotic twin correlations (Falconer, 1996). The twin model further partitions the variance in a trait into a shared environment, which describes the extent to which twins raised in the same family resemble each other beyond their shared genetic variance, and a non-shared environment, which describes environmental variance that does not contribute to similarities between twins and siblings. The twin model measures broad-sense heritability, including additive and non-additive genetic effects, such as gene-gene interactions (Knopik et al., 2017).

*Genome-wide association (GWA) studies*

Quantitative genomics aims to identify genetic variation correlated with differences in phenotypic traits. Early attempts to identify gene-trait associations via candidate gene studies proved unsuccessful and failed to replicate (Border et al., 2019; Caspi et al., 2003), thereby initiating the search for genetic signals at a genome-wide level (Visscher & Goddard, 2019). Scientific advances introduced by the DNA chip technology gave rise to GWA studies that employ a hypothesis-free methodology to explore the entire genome and identify genetic variation associated with phenotypic differences. Genome-wide association studies enabled behaviour geneticists to investigate how genetic variation relates to individual phenotypic variation in complex traits, such as psychiatric disorders and personality (Plomin, 2019; Visscher & Goddard, 2019). The success of these studies is reflected in their ability to uncover numerous trait-associated genetic loci, with improvements observed as sample sizes increase. For instance, successive iterations of GWA studies of schizophrenia with larger sample sizes have led to the discovery of a growing number of significant loci associated with the disorder, from 5 loci identified in the first iteration (Ripke et al., 2011), to 287 significant loci identified in the fourth iteration (Trubetskoy et al., 2022). The difficulty in identifying all genetic variants associated with phenotypic variation indicated that the genetic

effects on behavioural traits were more subtle than initially assumed (Chabris et al., 2015) and that complex traits are highly polygenic, meaning that they are influenced by thousands of genetic variants of small effects (Plomin et al., 2016; Visscher et al., 2017, 2021; Visscher & Goddard, 2019).

*Single nucleotide polymorphism (SNP) heritability*

Genome-wide approaches allowed for estimation of single nucleotide polymorphism (SNP) heritability– i.e., the proportion of phenotypic variation accounted for by variation in single nucleotide polymorphisms (SNPs). Single nucleotide polymorphism heritability can be estimated using individual-level genotype data, as well as summary results of existing GWA studies (Baselmans et al., 2021; Bulik-Sullivan et al., 2015; J. Yang et al., 2011). The issue of polygenicity of complex traits implies that their heritability emerges as a function of the cumulative influence of numerous loci, including not only common variants in the general population, but also rare variants (Visscher et al., 2021). Although SNP-based methods are at present only capable of estimating narrow-sense heritability, that is the influence of common additive genetic variation on phenotypic differences, it has been demonstrated that heritability of complex traits, such as height and body mass index (BMI) is, at least in part, attributable to rare variants (Wainschtein et al., 2022). This implies that rare variants may play a crucial role in accounting for the unexplained proportion of broad-sense heritability estimated by family-based designs (Wainschtein et al., 2022).

*Genome-wide polygenic scores (PGSs)*

Another application of GWA data, next to the estimation of SNP heritability, is the construction of PGSs. Genome-wide polygenic scores use results from GWA studies and aggregate information from hundreds of thousands of SNPs across the genome into a single composite index summarising genetic influence on a phenotype (D. W. Belsky & Harden, 2019; Dudbridge, 2013). They are calculated as the sum of all SNPs weighted by the effect size of their association with a target trait (Dudbridge, 2013). Just as twin heritability is the ceiling for SNP heritability, SNP heritability is the ceiling for PGS prediction (Plomin & Von Stumm, 2018). The most predictive PGSs have been derived from GWA studies of educational attainment (Okbay et al., 2022) and height (Yengo et al., 2022), with PGS predictions of 16% and 40%, respectively, with the latter estimate reaching the goal of accounting for the trait SNP heritability. Nonetheless, PGS prediction is modest for

neurodevelopmental disorders, such as ASD (2.5%) (Grove et al., 2019) and ADHD (3.3%) (Ronald et al., 2021), and even weaker for childhood psychopathology (less than 1%) (Akingbuwa et al., 2020), despite significant SNP heritability (Cheesman et al., 2017; Demontis et al., 2023; Grove et al., 2019). The power of PGSs to predict psychiatric disorders are linked to the discovery sample size, the ratio of causal variants, heritability of the phenotype, and differences in genetic ancestry leading to heterogeneity between the discovery and target samples (Albiñana et al., 2023; L. Duncan et al., 2019; A. R. Martin, Kanai, et al., 2019; Privé et al., 2022). Another aspect of this heterogeneity between samples pertains to the prevalent use of adult samples in GWA studies, leading to decreased predictive power for child and adolescent traits (Gidziela, Rimfeld, et al., 2022).

## Clinical diagnoses and quantitative dimensions

*Dimensions and DNA*

A fundamental argument in developmental psychopathology research refers to categorical and dimensional models in comprehending psychological disorders among youth, recognising the limitations of a solely categorical approach and advocating for the integration of dimensional models (Drabick & Kendall, 2010). Child and adolescent developmental disorders and psychopathology vary in severity and reflect a normal distribution of symptoms, with clinical diagnoses laying on the low extreme of this distribution (Plomin et al., 2009, 2016). For example, the ASD diagnosis is at the low end of the autism spectrum, whereas neurotypicality reflects the high end of the continuum (Happé, 1999; Ronald, Happé, Price, et al., 2006).

DNA research addressing the relationship between genes, diagnoses, and continuous dimensions provided evidence for the utility of dimensional models of developmental psychopathology (Plomin et al., 2016). Genetic influences associated with psychiatric disorders were found to be associated with continuous phenotypes (Plomin et al., 2009, 2016; Plomin & Kovas, 2005). For example, a PGS derived from a case-control GWA study of ADHD was found to successfully predict quantitative measures of ADHD in the general population (Gidziela et al., 2021; Groen-Blokhuis et al., 2014; J. Martin et al., 2014). This bidirectional relationship was also demonstrated for a PGS derived from a GWA study of ADHD trait dimensions and phenotypic measure of ADHD diagnosis, emphasising the

continuous nature of genetic influences on both dimensions and disorders (Plomin et al., 2016; Stergiakouli et al., 2015).

*Is abnormal normal?*

The hypothesis that psychiatric disorders are at the genetic extreme of the spectrum of normal trait variation gains support from the understanding that heritability arises from numerous genes of small effect contributing to a quantitative distribution— referred to as trait polygenicity (Plomin et al., 2016; Visscher et al., 2017, 2021; Visscher & Goddard, 2019). This perspective challenges the notion of discrete disorders, suggesting that what is traditionally labelled as abnormal is, in fact, a quantitative variation of the same genetic factors influencing the phenotype in a broader population (Plomin et al., 2009, 2016). This finding echoes the recently adopted NIMH Research Domain Criteria strategy, emphasising dimensional models of psychopathology over rigid diagnostic categories (Insel et al., 2010).The dimensional nature of child and adolescent psychopathology makes it possible to investigate behaviour problems and psychopathology in a general population, not limiting the phenotypic variation to formal diagnoses and categories based on clinical cut-offs. This thesis, therefore, focuses on a broad spectrum of symptom patterns assessed quantitatively, moving beyond case/control group classifications.

## Genetic influences on developmental psychopathology

*Neurodevelopmental disorders (NDDs)*

Neurodevelopmental disorders (NDDs) are multidimensional conditions characterised by impairments in cognitive and/or motor development and difficulties in communication and behavioural adaptation (APA, 2022; Thapar et al., 2015). The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (APA, 2022) recognises seven distinct NDD categories, including intellectual disabilities, communication disorders, ASD, ADHD, specific learning disorders, motor disorders, and other NDDs. These disorders are characterised by early onset and lifetime progression (APA, 2022; Gillberg, 2010; Hyman et al., 2020). Childhood NDD diagnoses increase the risk of reduced independence throughout the life course, socioeconomic difficulties, as well as incidence of other psychiatric disorders later in life (Faraone et al., 2006; Hechtman et al., 2016; McCauley et al., 2020; McGovern & Sigman, 2005; Roux et al., 2013). For instance, ADHD diagnosis in childhood can lead to impaired occupational functioning and increased risk for risky sexual behaviour and mood

disorders in adulthood (Hechtman et al., 2016). Similarly, individuals with ASD diagnosis experience more difficulties finding employment and tend to earn less than the average wages for young adults (Roux et al., 2013).

Twin studies have consistently demonstrated substantial heritability of 70%-74% for the two most widely researched NDDs— ASD and ADHD (Burt, 2009; Faraone & Larsson, 2019; Tick et al., 2016). Expanding on the genetic basis of NDDs, it is also important to consider the specific heritability estimates for intellectual disabilities, communication disorders, specific learning disorders, and motor disorders, although they have not been systematically reviewed. For example, intellectual disabilities were found to be highly heritable, with genetic influences accounting for 73%- 94% of the variance (Du Rietz et al., 2021a; M. J. Taylor et al., 2019a). On the other hand, specific language impairment has shown heritability estimates ranging from 36% to 97%, with binary phenotypes reflecting disorder status resulting in higher estimates of heritability, compared to continuous measurement (Bishop & Hayiou-Thomas, 2008). Specific learning disorders, such as dyslexia, dyscalculia, and dysgraphia, also have a notable genetic component. Heritability estimates range from 60%-65% for dyslexia (Hensler et al., 2010; Kovas et al., 2007; Willcutt et al., 2019), 38%- 65% for dyscalculia (Oliver et al., 2007) and 70% for dysgraphia (Oliver et al., 2007). Motor disorders, including developmental coordination disorder (DCD) and Tourette's syndrome, exhibit moderate to high heritability estimates. Twin studies have reported heritability estimates of around 69%-70% for DCD (Lichtenstein et al., 2010; N. C. Martin, Piek, et al., 2006), 77% for Tourette's syndrome (Mataix-Cols et al., 2015) and 56%- 57% for tic disorder (Lichtenstein et al., 2010; M. J. Taylor et al., 2019a).

The heritability estimates derived from DNA data are generally lower than those obtained from twin and family studies for all complex phenotypes, including NDDs (Cheesman et al., 2017). The shortfall in identifying the DNA variants accounting for the twin heritability is known as the 'missing heritability' gap (Manolio et al., 2009). This unexplained variance arises due to several factors, including methods to estimate trait heritability not taking into account rare variants, complex gene interactions or the intricate interplay between genetics and the environment (Manolio et al., 2009). The two largest studies conducted thus far have reported SNP heritability estimates of 12% for ASD (Grove et al., 2019) and 14% for ADHD (Demontis et al., 2023). Single nucleotide polymorphism heritability of some of the other NDD categories has also been estimated in child and adolescent samples. These analyses

revealed that common SNPs account for 25%-35% of the variance in communication disorders (Cheesman et al., 2017; Trzaskowski, Dale, et al., 2013; Trzaskowski, Davis, et al., 2013; Verhoef et al., 2021) and 20%-25% in dyslexia (Gialluisi et al., 2021). Similar to twin heritability, higher SNP heritability estimates were typically reported for case-control neurodevelopmental phenotypes, rather than traits measured on a continuum (Gidziela, Ahmadzadeh, et al., 2023).

*Other symptoms of developmental psychopathology*

Childhood developmental psychopathology encompasses a range of psychological conditions, including anxiety disorders, mood disorders, and behaviour problems like conduct disorder. Anxiety and conduct disorders typically emerge during childhood or adolescence, affecting approximately 6-7% of children and adolescents globally (Kessler et al., 2005; Polanczyk et al., 2015). Studies have shown that the symptoms of these disorders often persist into adulthood and can serve as predictors of mental health disorders in later life (Reef, Diamantopoulou, et al., 2010).

Twin and family research has provided substantial evidence for a strong genetic component underlying various forms of psychopathology during childhood and adolescence. Symptoms of anxiety disorders exhibit heritability estimates of 38% to 55%, while estimates for depression range from 26% to 67%, depending on the source of reporting (Cheesman et al., 2017). On the other hand, conduct problems have heritability estimates ranging from 36% to 62% (Anckarsäter et al., 2011; Cheesman et al., 2017). Substantially less variance was explained using DNA-based methods— 5%-6% for anxiety, 0%-5% for depression (Cheesman et al., 2017) and 1%-13% for conduct problems (Cheesman et al., 2017; Tielbeek et al., 2022).

## Environmental influences on developmental psychopathology

Findings from behaviour genetics research highlight the strong genetic aetiology of developmental psychopathology, both through twin studies that emphasise broad heritability estimates and through GWA studies that identify specific genetic variants associated with the disorders (Gidziela, Ahmadzadeh, et al., 2023; Visscher et al., 2017). It is important to note that twin studies have consistently demonstrated that environmental factors also play a role in

the development of these phenotypes, accounting for roughly half of the variation (Burt, 2009; Eley et al., 2003; Gidziela, Malanchini, et al., 2023; Lau & Eley, 2006).

*Shared environment*

The shared environmental basis of developmental psychopathology refers to environmental factors that contribute to similarities in individuals growing up in the same family (Knopik et al., 2017). Shared environment denotes what is usually meant by the word nurture—environmental influences that make children growing up in the same family similar, for example, home environment and parenting (Harris, 1998). If a trait is influenced by environmental factors shared by both twins, dizygotic within-pair similarity would be greater than half of monozygotic similarity, due to dizygotic twins sharing ~50% genes (Falconer, 1996; Knopik et al., 2017). Studies have shown that shared environmental factors play a limited role in the development of externalizing psychopathology during childhood and adolescence, as opposed to internalizing psychopathology, such as symptoms of depression and anxiety, in case of which modest to moderate shared environmental influences were observed (Burt, 2009; Gidziela, Ahmadzadeh, et al., 2023; Gidziela, Malanchini, et al., 2023). Rather, genetic influences and unique environmental factors have been found to have a more substantial impact on the manifestation of these phenotypes (Gidziela, Ahmadzadeh, et al., 2023; Gidziela, Malanchini, et al., 2023). While shared environmental factors may contribute to some degree (10-30%), the overall influence appears to be relatively small compared to genetic and nonshared environmental influences (Burt, 2009).

*Nonshared environment*

The nonshared environment refers to environmental factors that do not contribute to sibling similarities (Knopik et al., 2017; Plomin, 2011; Plomin & Daniels, 1987). Examples of nonshared environmental effects include the distinct treatment that twins receive from their parents and variations in external factors, such as classroom or peer group environments. The nonshared environmental impact is indicated by both the monozygotic and dizygotic correlations being lower than the unity (Falconer, 1996; Knopik et al., 2017).Twin studies conducted with children and adolescents have estimated that these nonshared environmental influences play a significant role in the environmental effects on developmental psychopathology. The nonshared environment has been found to account for about half of the variance in mood disorders (Eley et al., 2003; Lau & Eley, 2006) and about a third of

variance in neurodevelopmental and conduct disorders (Anckarsäter et al., 2011; Burt, 2009; Colvert et al., 2015).

Similar to the concept of the 'missing heritability' gap, there is a corresponding 'missing nonshared environment' gap (Turkheimer, 2011). This gap refers to the difficulty in identifying specific environments that contribute to the nonshared environmental component of complex traits. When analysing the nonshared environmental variance, which includes unique experiences, personal interactions, and individual circumstances, it becomes challenging to pinpoint and quantify the specific environmental factors that contribute to the differences observed between twins. Despite extensive investigation, researchers thus far have not explained large proportions of nonshared environmental variance in developmental psychopathology, generally accounting for less than 5% of the variance (Pike, Hetherington, et al., 1996; Pike, McGuire, et al., 1996; Turkheimer & Waldron, 2000). The ‘missing nonshared environment’ gap arises because it is difficult to capture and measure the full range of unique environmental influences that shape an individual's development (Gidziela, Malanchini, et al., 2023; Plomin & Daniels, 2011).

## Gene-environment interplay in developmental psychopathology

The gene-environment interplay examines how genetic predispositions and environmental influences dynamically interact to shape the emergence and course of developmental psychopathology (Rutter & Silberg, 2002). Two prominent types of gene-environment interplay that have been extensively studied are gene-environment correlation (rGE) and gene-environment interaction (G×E) (Plomin et al., 1977).

### *Gene-environment correlation (rGE)*

The gene-environment correlation suggests that genetic factors influence the likelihood of exposure to specific environmental contexts or experiences, which, in turn, shape individual outcomes and characteristics, such as psychopathology (Plomin et al., 1977). Gene-environment correlation can be classified into three categories: evocative, active, and passive (Plomin, 2014). Evocative rGE occurs when an individual’s genetic tendencies evoke specific external environmental responses. For example, a child's genetic predisposition towards lower BMI has been observed to lead parents to exert pressure on the child to eat, subsequently resulting in the child refusing food (Selzam et al., 2018). Likewise, children

with a higher genetic risk for antisocial behaviour were found to elicit harsher punishment from their parents, compared to children with a lower genetic risk (O'Connor et al., 1998). Active rGE refers to individuals actively selecting or creating environments that align with their genetic propensities. In the event of active rGE, the individual's genetic characteristics influence their choices and experiences in the environment, like when individuals with a higher genetic inclination for educational attainment actively seek out learning opportunities (Abdellaoui et al., 2019). Passive rGE takes place when children encounter environments that align with their genotypes, primarily due to growing up with parents who not only transmit genetic predispositions, but also influence their offspring's environments partly based on their own genotypes. For example, males inheriting a genetic risk for developing antisocial behaviour may also be exposed to environmental conditions linked to parental conduct disorder, including substance abuse (D'Onofrio et al., 2007).

*Gene-environment interaction G×E*

Gene-environment interaction recognises that genetic factors interact with environmental exposures to create susceptibility or vulnerability to certain disorders, i.e., these environmental factors can modify or trigger the expression of these genetic propensities (Domingue et al., 2022). Investigating G×E provides valuable insights into the intricate mechanisms through which nature and nurture collaboratively contribute to the development of psychopathology during various stages of life (Plomin et al., 2022). By unravelling these complex interactions, we aim to gain a deeper understanding of the aetiology, risk factors, and potential avenues for intervention and prevention in developmental psychopathology.

Multiple research studies have examined the phenomenon of G×E in developmental psychopathology (J. Belsky et al., 2007). A seminal study was conducted to examine the interaction between the risk of depression and the presence of stressful life events in individuals with a specific variation of the 5-HTT gene (Caspi et al., 2003). The findings of the study indicated that individuals with this specific polymorphism were more susceptible to depression when exposed to stressful life events (Caspi et al., 2003). Despite initial findings suggesting an association between diminished 5-HTT expression and anxiety and depression, especially in the aftermath of stressful life events, subsequent attempts to replicate these results have been unsuccessful (Border et al., 2019). This lack of replication extends to much

of the early research on candidate genes and G×E (Border et al., 2019; Hirschhorn et al., 2002; López-León et al., 2008).

Beyond mental health conditions, candidate gene framework was also employed in investigation of G×E in the context of antisocial behaviour (Caspi et al., 2002). It was observed that individuals who possessed both low-activity MAOA variant and experienced early maltreatment displayed a higher likelihood of engaging in antisocial behaviour (Caspi et al., 2002). Despite some studies not replicating these results (Haberstick et al., 2005), the aggregated meta-analytic evidence provided support for the association between child maltreatment and mental health problems in males with the low-activity MAOA genotype (Cicchetti et al., 2012; Kim-Cohen et al., 2006). Another study examined the interplay between genetic susceptibility and parenting practices in the development of externalizing behaviour in children (Bakermans-Kranenburg & Van IJzendoorn, 2007). The results revealed that children with the 7-repeat DRD4 allele and insensitive mothers exhibited higher externalizing behaviour levels than children without that allele, irrespective of maternal sensitivity (Bakermans-Kranenburg & Van IJzendoorn, 2007). Conversely, children with the 7-repeat DRD4 allele and sensitive mothers showed the lowest levels of externalizing behaviour (Bakermans-Kranenburg & Van IJzendoorn, 2007). These findings suggest that viewing the 7-repeat DRD4 allele solely as a risk factor may be misguided, as this genetic variant appears to heighten susceptibility to a wide range of environments (J. Belsky et al., 2007). In other words, supportive contexts are assumed to promote positive outcomes, while risky contexts contribute to negative outcomes (J. Belsky et al., 2007).

*Genome-wide polygenic scores (PGSs) in G×E research*

With the development of PGSs that allow researchers to calculate a composite index representing an individual's partial genetic propensity for a specific trait (Dudbridge, 2013), there has been a shift towards considering polygenicity in investigations of gene-environment interplay. Polygenic scores enabled researchers to test how much variance can be explained by these interactions via directly incorporating them in prediction models and estimating the increase in predictive power, after accounting for the main effects of the PGSs and environmental measures (Plomin et al., 2022). This has led to a growing body of research that utilises PGSs as a measure of genetic disposition to explore the intricate dynamics between genes and the environment (Plomin et al., 2022; Plomin & Viding, 2022).

Initial research on G×E using PGSs focused on the interplay between PGSs of major depressive disorder (MDD) and childhood experiences in predicting depression later in life (Mullins et al., 2016; Nelemans et al., 2021; Peyrot et al., 2014, 2018). While some studies found a significant association between MDD PGSs and childhood trauma in predicting adult MDD diagnosis (Coleman et al., 2020; Mullins et al., 2016; Peyrot et al., 2014), these findings were not consistently replicated using other PGSs constructed from GWA studies with varying statistical power (Peyrot et al., 2018). Recent studies have extended the investigation of G×E in developmental psychopathology using PGSs of adult psychiatric disorders (Plomin et al., 2022). For example, one study exploring G×E in mood disorders suggested that the genetic susceptibility to MDD increases the risk of depressive symptoms in adolescents exposed to critical parenting (Nelemans et al., 2021). Additional investigations explored the G×E effects of PGSs of alcohol dependence, ADHD, risky behaviours and neuroticism, interacting with childhood maltreatment (He & Li, 2022; Ksinan et al., 2022), environmental stressors (Bares et al., 2020; Plomin et al., 2022) and parental discipline (Plomin et al., 2022) in the prediction of adolescent externalizing and internalizing problems. Nevertheless, the observed G×E effects exhibited relatively small effect sizes, explaining less than 0.5% of the overall variance (Plomin et al., 2022).

The replicability of G×E research utilizing PGSs remains a complex and evolving challenge. Gene-environment interaction research has primarily focused on adult psychiatric disorders, yet solidly replicated G×E findings remain elusive (Arnau-Soler et al., 2019; Bogdan et al., 2018; Colodro-Conde et al., 2018; Kandaswamy et al., 2022; Plomin et al., 2022; N. Robinson & Bergen, 2021). Although the previously discussed reports in developmental psychopathology hinted at G×E for childhood adversity predicting adult depression, subsequent studies failed to replicate these findings (Mullins et al., 2016; Peyrot et al., 2014, 2018). Although recent research in developmental psychopathology has shown promise, with reports of significant G×E with regard to critical parenting and depression (Nelemans et al., 2021) or environmental stress influencing conduct problems (Bares et al., 2020), an equal number of studies have reported no significant G×E effects (Armitage et al., 2022; He & Li, 2022; Ksinan et al., 2022).

Another fundamental issue in G×E research refers to examining rGE, which is vital for a comprehensive understanding of how genetic and environmental factors interplay in shaping

developmental psychopathology outcomes (Plomin & Viding, 2022). Acknowledging and considering rGE alongside G×E is crucial because it highlights that individuals, based on their genetic predispositions, might actively seek or shape environments aligned with their genetic tendencies. Failing to account for rGE introduces complexity in interpreting G×E effects, potentially leading to misinterpretations and hindering the identification of genuine G×E effects. Achieving adequate statistical power in G×E research is a formidable challenge, as emphasised by the fact that large G×E effects typically contribute to only about 1% of the variance, whereas to detect such effects with 80% power, sample sizes of approximately 600 are required (L. E. Duncan & Keller, 2011; Plomin et al., 2022). The situation becomes even more demanding for moderate G×E effects, accounting for 0.1 percent of the variance, where tens of thousands of participants are necessary to attain 80% power (Plomin et al., 2022). Notably, the power of PGSs is intricately tied to the sample size of the underlying GWA studies, accentuating the critical role of larger and more robust datasets to enhance the reliability of G×E findings. The limited power of individual G×E interactions to account for significant proportions of variance in developmental psychopathology suggests the need for a methodological refinement to improve predictive capacity of both the genes and the environments. Combining multiple PGSs with environmental measures in a multivariable framework has shown promise in improving the prediction of educational achievement and may be valuable for enhancing the prediction of developmental psychopathology from G×E interactions (Allegrini, Karhunen, et al., 2020).

## Co-occurrence in developmental psychopathology

*Neurodevelopmental disorders (NDDs)*

There is a high homotypic co-occurrence rate among NDDs, meaning that different NDD diagnoses often coexist (Brimo et al., 2021; Pettersson et al., 2013), and this co-occurrence within the neurodevelopmental diagnostic category leads to greater severity of NDD-associated impairments (Rasmussen & Gillberg, 2000). Later life disadvantage becomes more salient for individuals diagnosed with more than one NDD, for example children diagnosed with ADHD and DCD are more likely to be affected by antisocial personality disorder, alcohol abuse, delinquency, reading difficulties and poor educational outcomes in early adulthood (Rasmussen & Gillberg, 2000).

The majority of studies that have focused on examining genetic correlations, which represent the extent to which the same genetic variants contribute to the observed co-occurrence between pairs of disorders (Knopik et al., 2017), explored the genetic relationship between ASD and ADHD specifically. Meta-analytic studies incorporating twin and family data have estimated an aggregated genetic correlation of 0.50 between autistic traits and ADHD (Andersson et al., 2020), which is greater than the SNP-based genetic correlation estimated as 0.35 (Grove et al., 2019; Z. Yang et al., 2021). Nevertheless, the comparison between genetic correlations derived from twin studies and those based on DNA data can be challenging due to the fact that GWA studies often employ case-control phenotypic measures of disorders, while twin studies more often utilize quantitative symptom scales in the general population (Andersson et al., 2020). In addition, while SNP-based genetic correlations primarily encompass contributions from common genetic variants, correlations derived from twin and family studies also consider rare variant influences (Andersson et al., 2020).

In contrast, the aetiology of co-occurrence between other NDDs has not been extensively meta-analysed. However, individual studies have consistently pointed to a moderate to strong shared liability between ASD/ADHD and other NDDs, including specific learning disorders (Lichtenstein et al., 2010; Paloyelis et al., 2010a), communication disorders (Dworzynski et al., 2008; L. J. Taylor et al., 2014) and motor disorders (Lichtenstein et al., 2010; N. C. Martin, Piek, et al., 2006). Additional investigations are needed to comprehensively evaluate the genetic and environmental influences underlying the co-occurrence of NDDs beyond ASD and ADHD.

*Disruptive, impulse control and conduct disorders (DICCs)*

Another cluster of conditions defined by childhood onset and developmental progression is the DSM-5 category of disruptive, impulse control and conduct disorders (DICCs) (APA, 2022). Disorders classified as DICCs are defined by a set of common behavioural characteristics, including impulsivity, aggression, and frequent rule violation. The DICC category comprises eight distinct disorders: Oppositional Defiant Disorder, Intermittent Explosive Disorder, Conduct Disorder, Antisocial Personality Disorder, Pyromania, Kleptomania, Other Specified DICC Disorders, and Unspecified DICC Disorders (APA, 2022). Disruptive, impulse control and conduct disorders are associated with poor social and

educational outcomes (Frick & Loney, 1999; Offord et al., 1992), such as delinquency and imprisonment (Frick, 1998; Lahey & Loeber, 1994).

The investigation of the co-occurrence between NDDs and DICCs during childhood and adolescence is particularly valuable due to the developmental nature of these conditions. The fact that NDDs and DICCs commonly co-occur constitutes an example of heterotypic co-occurrence, i.e., co-occurrence between different categories of disorders (Bayard et al., 2020; N. C. Martin, Levy, et al., 2006; Thorell & Wåhlstedt, 2006). Among the various examples of symptom overlap between NDDs and DICCs, the relationships between ADHD and conduct disorder and between ADHD and oppositional defiant disorder have received significant attention in research, with genetic correlations of 0.43 and 0.49, respectively (Tuvblad et al., 2009). This overrepresentation is likely due to the DSM-IV classifying these disorders under the same category of Attention-deficit and disruptive behaviour disorders (APA, 1994). With the fifth edition of the DSM (APA, 2022), the classification was changed, and ADHD was included in the NDD category.

Shared symptomatology has also been observed between ASD and antisocial behaviour (Bronsard et al., 2010; Moffitt et al., 2009). However, it is important to note that studies investigating the association between NDDs and DICCs exhibit considerable heterogeneity and inconsistencies across different co-occurring conditions (Jones et al., 2009; O'Nions et al., 2015). For example, one study found that individual differences in ASD and callous-unemotional traits are explained by largely independent genetic influences, with a genetic correlation of 0.31 for social interaction impairments and 0.23 for social communication impairments (O'Nions et al., 2015). Another study reported moderate genetic correlation of 0.43 between autistic traits and psychopathic tendencies (Jones et al., 2009). Such variations highlight the need for further research to enhance our understanding of the complex relationships between NDDs and DICCs, their shared features, and the factors contributing to their co-occurrence.

*The p factor*

The p factor, a latent general psychopathology factor, has emerged as a concept in developmental psychopathology, providing a framework for understanding the common underlying vulnerabilities shared across various mental health disorders (Caspi et al., 2014;

Lahey & Loeber, 1994). This latent factor represents a pervasive liability to psychopathology, suggesting a continuum of risk that transcends traditional diagnostic boundaries and is associated with diverse psychiatric conditions, including mood disorders, anxiety disorders, and behaviour problems (Allegrini, Cheesman, et al., 2020; Caspi et al., 2014; Gidziela, Rimfeld, et al., 2022; Lahey & Loeber, 1994). The p factor offers a holistic perspective, highlighting the shared aetiological factors that contribute to the co-occurrence between multiple disorders (Allegrini, Cheesman, et al., 2020; Caspi et al., 2014; Lahey & Loeber, 1994).

The genetic underpinnings of the p factor are substantial, with heritability estimates ranging from 50% to 60% (Allegrini, Cheesman, et al., 2020). These genetic influences manifest consistently throughout childhood and adolescence and across multiple raters, suggesting stability over time and contexts (Allegrini, Cheesman, et al., 2020). Notably, the ability to predict childhood p using PGSs derived from case-control GWA studies involving adult samples implies continuous manifestations of genetic risk for adult psychiatric disorders in young children, supporting the notion that early-onset behavioural and emotional problems serve as early indicators of psychiatric genetic risk (Allegrini, Cheesman, et al., 2020). The recognition of a common factor amid diverse aspects of childhood psychopathology has crucial implications, not only for genomic research, but also for early detection of risk in the general population (Allegrini, Cheesman, et al., 2020).

## The thesis aims and objectives

The present thesis has four core aims, addressed by the four consecutive chapters (Chapters 2-5). First (Chapter 2), to illustrate the current state of understanding of the genetic and environmental underpinnings of child and adolescent neurodevelopmental phenotypes and their co-occurrence with other developmental disorders. Second (Chapter 3), to clarify the extent to which DNA-based indices of genetic propensity can predict individual variation in behaviour problem symptomatology. Third (Chapter 4), to identify environmental candidates that can predict symptoms of behaviour problems throughout development, independent of genetics. Fourth (Chapter 5), to systematically assess the interplay between genetic and environmental influences in the development of adolescent psychopathology.

## Summary of chapters

*Chapter 2*

Chapter 2, entitled A meta-analysis of genetic effects on neurodevelopmental disorders and co-occurring conditions, contains a modified version of a paper published in Nature Human Behaviour. In this chapter, I synthesised the existing literature on: (1) the relative contribution of genetic and environmental factors to NDDs in childhood and adolescence, (2) the genetic and environmental overlap between different NDD categories, and (3) the co-occurrence between NDDs and DICCs. A total of 296 independent studies, with a cumulative, partly dependent sample size of 4 million, were meta-analysed using multilevel, random-effects models. This chapter provides a comprehensive account of the aetiology and sources of co-occurrence between child and adolescent developmental disorders. It covers a discussion of the uneven distribution of behaviour genetics research.

*Chapter 3*

Chapter 3 focuses on Using DNA to predict behaviour problems from preschool to adulthood and is presented as an adapted version of a paper published in the Journal of Child Psychology and Psychiatry. This chapter aims to test whether polygenic prediction of behaviour problems across development can be improved by using multiple PGSs, cross-trait, longitudinal and trans-situational approaches. The study implemented aggregation techniques that involved construction of multi-trait composites of general behaviour problems, externalizing and internalizing across developmental stages, as well as across parent, teacher, and self-reports. Polygenic prediction of cross-trait and cross-rater composites was tested using a multi-PGS framework, including PGSs of psychiatric disorders and personality. In this chapter, I discuss mechanisms underlying improved polygenic prediction and propose how aggregation techniques can facilitate developmental, multivariate, and gene-environment interplay research.

*Chapter 4*

Chapter 4— Explaining the influence of nonshared environment (NSE) on symptoms of behaviour problems from preschool to adulthood: Mind the missing NSE gap— is presented as a modified version of a paper published in the Journal of Child Psychology and Psychiatry. In this chapter, I investigated the degree to which individual differences in symptoms of behaviour problems can be accounted for by specific nonshared environmental factors,

independent of genetics and shared environment. Using multivariate longitudinal twin modelling, I explored the nonshared environmental prediction of behaviour problem measures in childhood, adolescence, and early adulthood from poly-environmental composites created from environments measured at the previous age. This chapter discusses the 'missing nonshared environment gap between variance accounted for by measured environments and total nonshared environmental variance in behaviour problem symptoms. I also assess the utility of specific environmental candidates and provide suggestions for improving the collection and efficiency of environmental measures.

*Chapter 5*

The foundational knowledge derived from Chapters 2 to 4 sets the stage for the core exploration in Chapter 5— examining the Gene-environment interplay in adolescent developmental psychopathology. The study employed PGSs of psychopathology and neurodevelopmental disorders coupled with environmental factors related to SES, parenting style, home environment and life events to investigate their collective and interactive prediction of developmental psychopathology symptoms in adolescence. The results indicated that both genetic and environmental factors play a role in development of psychopathology, though their interactions are relatively modest. The study highlights the significance of adolescents' perceptions of their environments, proposing that these interpretations impact emotional and behavioural functioning during adolescence.

*Chapter 6*

The final chapter of this thesis contains a General Discussion and offers a nuanced examination of the core findings and their implications for developmental psychopathology. By expanding the theoretical understanding, the chapter contributes valuable insights with practical applications for intervention and prevention strategies targeting developmental disorders in youth. Ethical and social considerations are highlighted, emphasising the responsibility of researchers in transparent communication, mitigating stigmatization, and addressing Eurocentric bias in genetic research. The challenges of translating research into practice, particularly in the context of PGSs, are discussed in light measurement issues, accounting for environmental factors, and navigating ethical concerns related to privacy and discrimination. The general discussion also sheds light on the research-to-practice crisis,

emphasising the need for diverse and inclusive research samples to ensure the generalizability and applicability of interventions across diverse populations.

# Chapter 2— A meta-analysis of genetic effects associated with neurodevelopmental disorders and co-occurring conditions.

This chapter is presented in a form of a published paper. It is an adapted version the following publication:

Gidziela, A., Ahmadzadeh, Y.I., Michelini, G. et al. A meta-analysis of genetic effects associated with neurodevelopmental disorders and co-occurring conditions. Nat Hum Behav 7, 642–656 (2023). https://doi.org/10.1038/s41562-023-01530-y

Supplementary Notes, Tables and Figures are included in Appendix 1.

## Abstract

A systematic understanding of the aetiology of neurodevelopmental disorders (NDDs) and their co-occurrence with other conditions during childhood and adolescence remains incomplete. In the current meta-analysis, we synthesised the literature on: (1) the contribution of genetic and environmental factors to NDDs, (2) the genetic and environmental overlap between different NDDs, and (3) the co-occurrence between NDDs and disruptive, impulse control and conduct disorders (DICCs). Searches were conducted across three platforms: Web of Science, Ovid Medline, and Ovid Embase. Studies were included only if 75% or more of the sample consisted of children and/or adolescents, and they had measured the aetiology of NDDs and DICCs using single-generation family designs or genomic methods. Studies that had selected participants based on unrelated diagnoses or injuries were excluded. We performed multilevel, random-effects meta-analyses on 296 independent studies, including over 4 million, partly overlapping, individuals. We further explored developmental trajectories and the moderating role of gender, measurement, geography, and ancestry. We found all NDDs to be substantially heritable (family-based $h^2$= 0.66 (0.03); SNP $h^2$= 0.19 (0.03)). Meta-analytic genetic correlations between NDDs were moderate (grand family based rA= 0.36 (0.12), grand SNP-based rG = 0.39 (0.19)) but differed substantially between pairs of disorders. The genetic overlap between NDDs and DICCs was strong (grand family-based rA = 0.62 (0.20)). While our work provides evidence to inform and potentially guide clinical and educational diagnostic procedures and practice, it also highlights the imbalance in the research effort that has characterized developmental genetics research.

# Introduction

Neurodevelopmental disorders (NDDs) are complex health concern, starting from childhood (Thapar et al., 2015). NDDs affect around 15% of children and adolescents worldwide and lead to impaired cognition, communication, adaptive behaviour, and psychomotor skills (Dietrich et al., 2005). The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) categorizes the following seven disorders under NDDs: intellectual disabilities, communication disorders, autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder (ADHD), specific learning disorders, motor disorders and other neurodevelopmental disorders (Association, 2015). NDDs often have lifelong trajectories: they can manifest before 12 months of age (Hyman et al., 2020) and can be diagnosed before children enter primary education (Association, 2015; Gillberg, 2010).

While some NDDs (e.g. ASD and ADHD) may persist throughout adolescence and adulthood (Faraone et al., 2006; McGovern & Sigman, 2005), others are more likely to alleviate as children get older (e.g., tic disorder (Kim et al., 2019) and communication disorders (Ellis & Thal, 2008)); nevertheless, all NDDs can lead to social and behavioural difficulties and reduced independence over the lifespan (Faraone et al., 2006; McDowell & Lesslie, 2018; McGovern & Sigman, 2005). For instance, ADHD in childhood has been associated with an increased risk of educational and occupational problems, risk-taking, and mood disorders in adulthood (Hechtman et al., 2016); and an ASD diagnosis in childhood with increased occupational difficulties and a greater risk of psychopathologies in adulthood (McCauley et al., 2020; Roux et al., 2013). Difficulties are often more salient for those children diagnosed with more than one NDD (Rasmussen & Gillberg, 2000).

A systematic understanding of the aetiology of NDDs remains incomplete. A disproportionate number of studies and systematic reviews have focused on ASD and ADHD, pointing to their substantial heritability – the extent to which observed individual differences are accounted for by underlying genetic differences. A meta-analysis of 7 twin studies of clinically diagnosed ASD in childhood and adolescent samples yielded a grand heritability estimate of 0.74 (Tick et al., 2016). Similarly sizeable heritability estimates have also been obtained from twin studies of ADHD in childhood and adolescence (Faraone & Larsson, 2019). Heritability estimates were found to differ across the two major components of ADHD, with genetic factors playing a more substantial role in the aetiology of hyperactivity

($h^2$= 0.71), if compared to inattention ($h^2$= 0.56) (Nikolas & Burt, 2010). However, other NDDs, despite showing similar prevalence rates and severity as ASD and ADHD, are less well understood and studied (Bishop, 2010).

In line with what observed for all complex traits, heritability estimates for ASD and ADHD obtained from DNA data are lower than those obtained from twin and family designs (Cheesman et al., 2017). Single nucleotide polymorphism (SNP) heritability can be calculated using large samples of individual-level genotype data (J. Yang et al., 2011) or summary statistics from genome-wide association (GWA) studies (Bulik-Sullivan et al., 2015), hypothesis-free studies aimed at discovering associations between genetic variation across the genome and individual differences in traits and disorders. The two largest studies to date that have estimated the SNP heritability of ASD and ADHD report estimates of $h^2$= 0.12 for ASD (Grove et al., 2019) and $h^2$= 0.22 for ADHD (Demontis et al., 2019).

It is now well-established that NDDs often co-occur with one another, a phenomenon known as homotypic co-occurrence, and this points to a shared underlying liability between conditions (Brimo et al., 2021; Pettersson et al., 2013). Even in this instance, most studies have focused on examining the genetic correlations —the degree to which the same genetic variants contribute to the observed covariation between pairs of traits or disorders (Knopik et al., 2017)— between ASD and ADHD, resulting in a meta-analytic genetic correlation of 0.59 (Andersson et al., 2020) across twin and family studies, and a SNP-based genetic correlation of 0.35 (Z. Yang et al., 2021). Aetiological sources of co-occurrence between all other NDDs have not been meta-analysed, but individual studies point to a moderate to strong shared liability between ASD/ADHD and other NDDs (Dworzynski et al., 2008; Lichtenstein et al., 2010; N. C. Martin, Piek, et al., 2006; Paloyelis et al., 2010a; M. J. Taylor et al., 2014).

Another category of disorders that onset and progress through childhood and adolescence are Disruptive, Impulse Control and Conduct Disorders (DICCs), which the DSM-5 describes as disorders that share the underlying features of impulsive behaviour, aggressiveness, and pathological rule breaking (APA, 2022). The DSM-5 identifies eight main DICC categories: Oppositional Defiant Disorder, Intermittent Explosive Disorder, Conduct Disorder, Antisocial Personality Disorder, Pyromania, Kleptomania, Other Specified DICC Disorder, and Unspecified DICC Disorders[3] (Figure 2. 1). Similar to NDDs, DICCs have been linked to

impaired social, emotional, and educational outcomes (Frick, 1998; Frick & Loney, 1999; Lahey & Loeber, 1994; Offord et al., 1992).

The developmental nature of DICCs makes them an ideal primary target for the investigation of how NDDs co-occur with other disorders (i.e., heterotypic co-occurrence) during childhood and adolescence. However, the distinction between NDDs and DICCs in the published literature is often blurred, particularly for disorders that include clinical features that overlap across NDD and DICC categories, such as ADHD. The most investigated example of symptom overlap between NDDs and DICCs involve ADHD and conduct disorder (Bayard et al., 2020; Thorell & Wåhlstedt, 2006), and ADHD and oppositional defiant disorder (N. C. Martin, Levy, et al., 2006). Studies highlight how these disorders are characterised by disturbances in emotion regulation, attention problems, cognitive inflexibility, and impaired inhibition (Bayard et al., 2020; Moffitt, 1993; Rubia, 2011). A shared symptomatology has also been observed between ASD and antisocial behaviour/personality disorder (that we refer to as conduct disorder in the current work since antisocial personality disorder describes adult diagnoses) (APA, 2022; Bronsard et al., 2010; Moffitt et al., 2009). However, studies on the association between NDDs and DICCs are characterized by a great deal of heterogeneity and inconsistencies across co-occurring conditions (Jones et al., 2009; O'Nions et al., 2015).-

With three core aims (Figure 2. 1) the current meta-analysis bridges gaps in our knowledge of the aetiology of NDDs and their co-occurrence with other developmental conditions in childhood and adolescence. First, we meta-analysed studies on the relative contribution of genetic and environmental influences to all NDD categories described in the DSM-5. Second, we meta-analysed estimates for the genetic and environmental overlap between different NDDs (homotypic co-occurrences). Third, given their developmental onset and progression and partly shared symptomatology, we examined the aetiology of the co-occurrence between NDDs and DICCs (heterotypic co-occurrences). In addition to addressing each disorder individually, we take a transdiagnostic approach by combining data across NDDs and including categorical (i.e., presence or absence of a disorder) and quantitative (i.e., continuously measured symptoms) measures. Clarifying the genetic and environmental aetiology of all NDDs and their homotypic and heterotypic co-occurrences will advance our knowledge of how developmental disorders cluster together, which could in turn inform educational and clinical practice (Skuse, 2007).

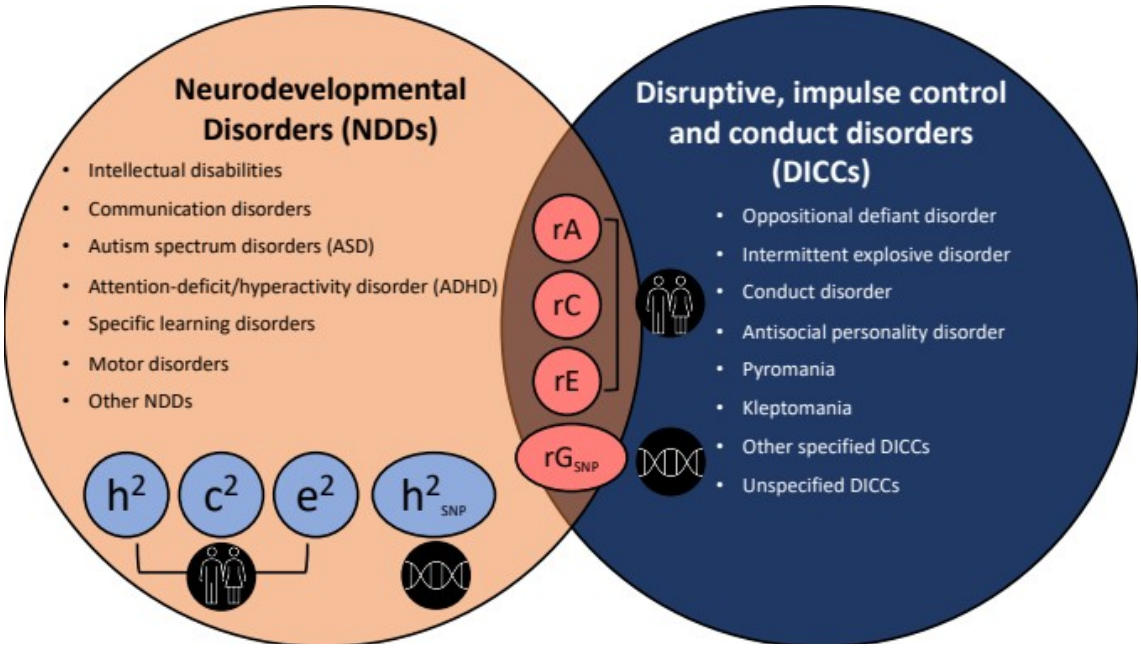



Figure 2. 1. Visual summary of the three core aims of the current meta-analysis.

Aim 1 (white & light blue): estimate family-based genetic ($h^2$), shared environmental ($c^2$) and nonshared environmental ($e^2$) influences, as well as SNP heritability ($h^2_{SNP}$) for all neurodevelopmental disorders (NDDs) identified by the DSM-5. Aim 2 (white & red): Provide grand estimates of family-based genetic (rA), shared environmental (rC) and nonshared environmental (rE) correlations and SNP-based genetic correlations ($rG_{SNP}$) between different NDDs. Aim 3 (navy blue & red): Provide grand estimates of rA, rC, rE and $rG_{SNP}$ between NDDs and disruptive, impulse control and conduct disorders (DICCs). Results for $c^2$, $e^2$, rC and rE are presented in Supplementary Note 1.

## Results

This Results section presents meta-analytic findings on genetic influences on NDDs and on their genetic overlap with other NDDs and DICCs. Meta-analytic estimates for shared and nonshared environmental factors and their overlap are presented in Supplementary Note 1. Results for all sub-categories of NDDs and DICCs are reported in Supplementary Note 2, Supplementary Figures 2 and 3 and Supplementary Tables 2, 4 and 6.

*Searches and screening*

Studies for this meta-analysis were selected during 3 screening stages including title and abstract screening, full text screening, and reference list screening (see Method for a detailed description). This selection process resulted in a total of 296 studies (292 family-based and 34 SNP-based studies) included in the current meta-analysis (Figure 2. 2). The number of family-based and SNP-based studies do not add up because some studies provided both family-based and SNP-based estimates. These studies were counted only once towards the grand total but included separately in family-based and SNP-based categories.

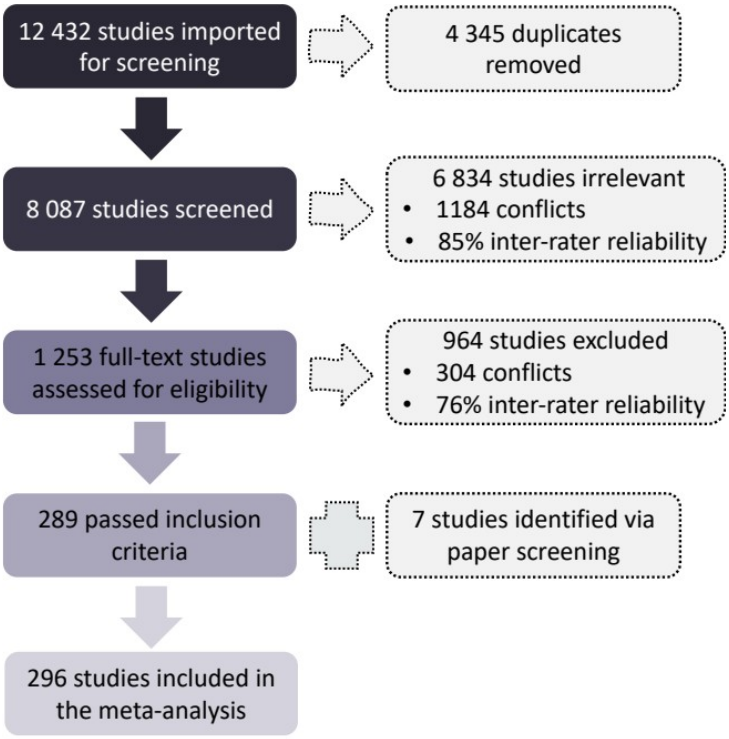



Figure 2. 2. Diagram of searches and screening.

This diagram presents an overview of the screening and selection process across primary and secondary searches, along with statistics of inter-rater reliability.

*Heritability of NDDs*

Our first aim was to obtain reliable estimates of the contribution of genetic factors to individual differences in all NDDs. We considered two broad categories of methods that allow for the estimation of heritability: family-based designs including related individuals (such as sibling comparisons and twin studies) and SNP heritability (Baselmans et al., 2021)

(see Method). Given the substantial differences in methodology and outcomes, findings across these two broad categories were meta-analysed separately.

*Family-based heritability ($h^2$)*

We identified a total of 236 family-based studies, comprising 2,792,511 partly overlapping individuals, that investigated the proportion of variance in NDDs that is accounted for by genetic factors. Out of the total, 121 studies (N= 682,340) investigated ADHD, 89 studies (N= 360,920) specific learning disorders, 36 studies (N= 1,821,970) ASD, 23 (N= 130,757) studies communication disorders, 6 studies (N= 52,278) motor disorders and 2 studies (N= 9,036) intellectual disabilities. Across all NDDs and 236 studies, the grand $h^2$ estimate was 0.66 (SE= 0.03). Grand $h^2$ estimates differed, albeit not significantly, across NDD categories, ranging from 0.86 (SE= 0.44) for intellectual disabilities to 0.62 (SE= 0.04) for specific learning disorders (see Figure 2. 3 and Supplementary Table 1). Distributions of genetic influences across studies and NDDs are presented in Supplementary Figure 1.

*SNP heritability (SNP $h^2$)*

Out of the total of 29 SNP-based studies, involving 893,896 partly overlapping individuals, the only disorders that were addressed by at least two independent studies (Viechtbauer, 2010), included ASD (15 studies; N= 637,240), ADHD (14 studies; N= 725,168), specific learning disorders (9 studies; N= 40,637) and communication disorders (4 studies; N= 14,894). SNP heritability across all NDDs was moderate (0.19, SE= 0.03) and ranged between 0.15 (SE= 0.04) for ASD to 0.30 (SE= 0.14) for communication disorders (Error: Reference source not found and Supplementary Table 1). SNP heritability estimates were not found to differ significantly across disorders, although the degree of precision in the estimates varied substantially depending on the sample size and number of individual studies included per disorder.

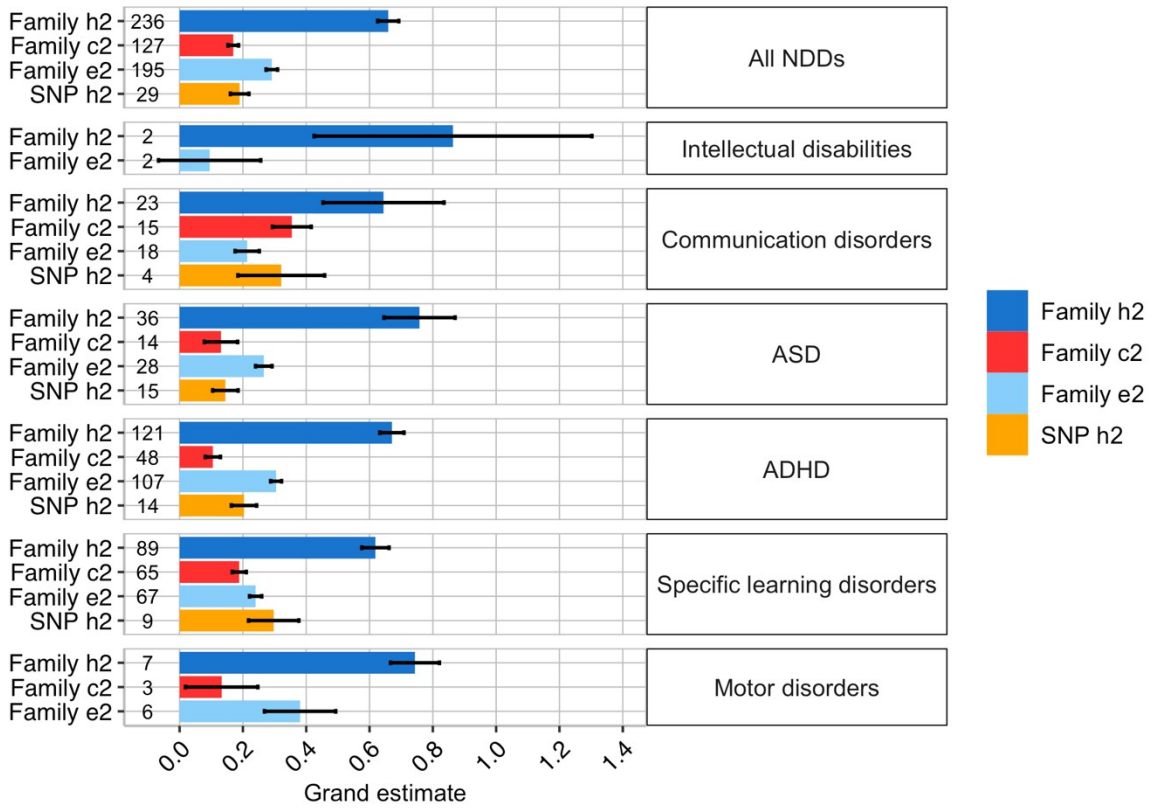



Figure 2. 3. Genetic and environmental sources of variation in neurodevelopmental disorders (NDDs).

Meta-analytic family and SNP-based heritability (h2) shared environmental influences (c2) and nonshared environmental influences (e2) on variation in NDDs. Numbers preceding bars on the y-axis denote the number of studies identified that provided estimates for specific NDDs. Error bars signify standard errors of the grand estimates of heritability and environmental influences. The results for c2 and e2 are discussed in Supplementary Note 1.

*Genetic overlap between NDDs*

When compared to the vast number of studies that had examined the aetiology of individual differences in each NDD, only a limited body of research (37 studies, N= 212,569) had investigated the co-occurrence between NDDs in childhood and adolescence. In fact, for some of the disorders, we were unable to find two independent statistics (Viechtbauer, 2010), and therefore could not provide a meta-analytic estimate.

*Family-based genetic* correlations (rA)

When considering family-based designs (see Method and Supplementary Note 3), a sufficient number of studies to allow for meta-analysis was obtained for the following NDD pairs: ADHD & specific learning disorders (15 studies; N= 67,039), ASD & ADHD (6 studies; N= 58,518), ADHD & motor disorders (2 studies; N= 8,748), communication disorders & motor disorders (2 studies; N= 3,950), and communication disorders & specific learning disorders (2 studies; N= 42,098). Only one study was identified for the following pairs of NDDs: ASD & communication disorders (N= 12,174), ASD & specific learning disorders (N= 6,858), ASD & motor disorders (N= 6,858), and specific learning disorders & motor disorders (N= 6,858), therefore these studies could only be included in the transdiagnostic meta-analysis, capturing the degree of genetic and environmental co-occurrence across all NDD pairs. In addition, 9 studies (N= 46,000) examined the co-occurrence between subtypes of specific learning disorders, such as dyslexia & dyscalculia, these studies have been included in the transdiagnostic meta-analysis and results of these finer-grained analyses are reported in Supplementary Note 2.

We first meta-analysed genetic correlations across all NDD categories (transdiagnostic genetic co-occurrence), this yielded a moderate grand estimate of rA= 0.36 (SE= 0.12). When considering NDD categories separately, the strongest genetic overlaps were found between ADHD & motor disorders (rA= 0.90, SE= 0.82), and between ASD & ADHD (rA= 0.67, SE= 0.30), while the weakest genetic correlation was found for the association between ADHD & specific learning disorders (rA= 0.07, SE= 0.12; Figure 2. 4 and Supplementary Table 3). However, given the considerable differences in sample size used to derive genetic correlations between pairs of disorders, for example between ASD & ADHD or communication disorders & motor disorders, the strength of these correlations may be difficult to compare. Low correlations could also reflect low power to detect the true overlap.

*SNP-based genetic correlations (rG)*

SNP-based designs in childhood and adolescent samples exclusively focused on the association between ASD & ADHD (5 studies; N= 242,543) and subtypes of specific learning disorders (1 study; N= 4,500). The transdiagnostic genetic correlation obtained meta-analysing SNP-based designs was 0.39 (SE= 0.19) (Supplementary Table 8), in line with the estimate obtained from family-based designs. A grand genetic correlation of 0.20 (SE= 0.14) was found for the co-occurrence between ADHD and ASD. The one remaining

study examined the co-occurrence between dyslexia & dyscalculia-related traits, specifically reading and mathematics abilities, which were strongly correlated (rG= 0.74, SE= 0.17) (O. S. P. Davis et al., 2014).

*Genetic overlap between NDDs and DICCs*

Our third aim was to obtain meta-analytic estimates of the genetic associations between NDDs and DICCs. Our search yielded only 15 eligible family-based studies (N= 42,718), and no SNP-based studies. Meta-analytic genetic correlations could only be calculated for a few NDD and DICC pairs, namely ADHD & conduct disorder (6 studies; N= 11,308), ADHD & oppositional defiant disorder (6 studies; N= 10,748) and ASD & conduct disorder (3 studies; N= 24,564). In addition, we identified 1 study (N= 360) that examined the co-occurrence between specific learning disorders & disruptive behaviour, finding a weak negative genetic correlation (rA= -0.14, SE= 0.06) (Newsome et al., 2014).

*Family-based genetic* correlations (rA)

Across all co-occurrences between NDDs and DICCs (15 studies), the grand genetic correlation was 0.62 (SE= 0.20). A similarly strong genetic correlation was observed between ADHD & conduct disorder (6 studies) and ADHD & oppositional defiant disorder (6 studies): rA= 0.66 (SE= 0.36) and rA= 0.66 (SE= 0.18), respectively; a similar level of aetiological overlap to that observed between strongly genetically correlated NDDs such as for example ADHD & ASD (Supplementary Table 5). On the other hand, the genetic overlap between ASD & conduct disorder (3 studies) was much weaker, with a meta-analytic genetic correlation of 0.35 (SE= 0.10; Figure 2. 4). The similar extent of genetic overlap between ADHD & conduct disorder or ADHD & oppositional defiant disorder and ADHD & ASD may not be free from biases introduced by an unbalanced sample size used to derive these meta-analytic estimates. In addition, large meta-analytic standard errors make assessing the significance of differences between the estimates difficult.

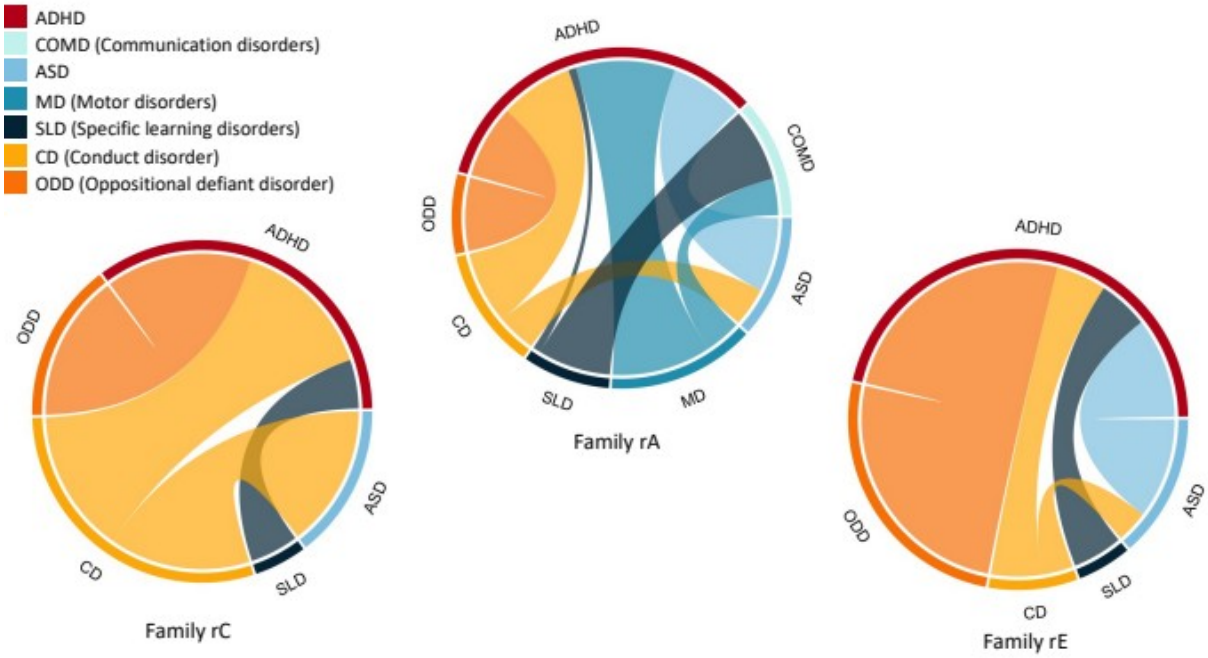



Figure 2. 4. Genetic and environmental correlations between NDDs and DICCs.

Strength of the meta-analytic genetic (rA), shared environmental (rC) and nonshared environmental (rE) correlations between neurodevelopmental disorders (NDDs) and their homotypic (other NDDs) and heterotypic (disruptive, impulse control and conduct disorders (DICCs)) co-occurrences. The outer layer of each circle shows all the different NDDs and DICCs for which meta-analytic correlation estimates could be computed. Each colored connector path indicates the strength of association between disorders, the thicker the connector path, the stronger the correlation between two disorders. The results for family rC and rE are presented in Supplementary Note 1.

*Sex differences*

Some NDDs do not affect males and females equally, for instance males are four times more likely to be diagnosed with ASD (Christensen et al., 2016; May et al., 2017) and twice as likely to be diagnosed with ADHD (Polanczyk et al., 2007). Studies have suggested that these differences in prevalence may be caused by quantitative genetic sex differences, differences in the degree to which genes influence variation in NDDs in males versus females (J. Martin et al., 2018). To provide an overview of sex differences in NDDs, we conducted separate meta-analyses including all studies that had reported sex-specific estimates.

*Family-based heritability ($h^2$)*

We identified 68 family-based studies that investigated the genetic aetiology of individual differences in NDDs in male samples and 67 studies that reported estimates for female samples. Out of all studies involving sex-stratified samples, 38 studies focused on ADHD, 21 studies on ASD, 8 studies on specific learning disorders, 4 studies on communication disorders and 2 studies on motor disorders. Across all NDDs, family-based heritability was not significantly different between males and females ($h^2$= 0.65, SE= 0.06 in males and 0.67, SE= 0.06 in females). Distributions of sex-specific family-based variance components for all NDDs, except for motor disorders for which a sufficient number of studies (>1) was not identified, are presented in Figure 2. 5 and Supplementary Table 16.

*SNP heritability (SNP $h^2$)*

Marked differences in SNP heritability were observed between males and females across all NDDs (0.19, SE= 0.07 for males and 0.09, SE= 0.10 for females). However, these estimates were based on the only two studies to date that had calculated the SNP heritability of ASD and ADHD separately by sex (Supplementary Table 16).

*Sex differences in genetic overlap between NDDs*

We identified only 4 family-based studies that had examined homotypic co-occurrences of NDDs in males and only 2 studies in females. Half of these studies considered the overlap between ASD & ADHD. The other half had considered the co-occurrence between ASD & communication disorders (1 study in both male and female) and between developmental coordination disorder & tic disorder, two subtypes of motor disorder (1 study in males only). The grand family-based genetic correlation across all NDDs was estimated at 0.86 (SE= 0.58) for males and 0.25 (SE= 0.36) for females (Supplementary Table 17).

Sex-specific grand estimates of family-based genetic correlations between specific disorders could not be calculated due to the limited number of available studies. The only exception was the co-occurrence between ASD & ADHD in males, where 2 studies were identified (rA= 0.79, SE= 0.42) (Supplementary Table 17). SNP-based genetic correlations between NDDs could not be calculated for males and females separately due to a lack of studies that examined these associations separately by sex in samples of children and adolescents.

*Sex differences in genetic overlap between NDDs and DICCs*

Sources of co-occurrence between NDDs and DICCs could only be estimated between ADHD & conduct disorder and only in in females. In fact, one out of the only two studies that examined the sex-specific co-occurrence between ADHD and conduct disorders used a female-only sample. Hence, we could only meta-analyse the co-occurrence between ADHD & conduct disorder in females. We found a meta-analytic genetic correlation of 0.75 (SE= 0.58) (Supplementary Table 18).

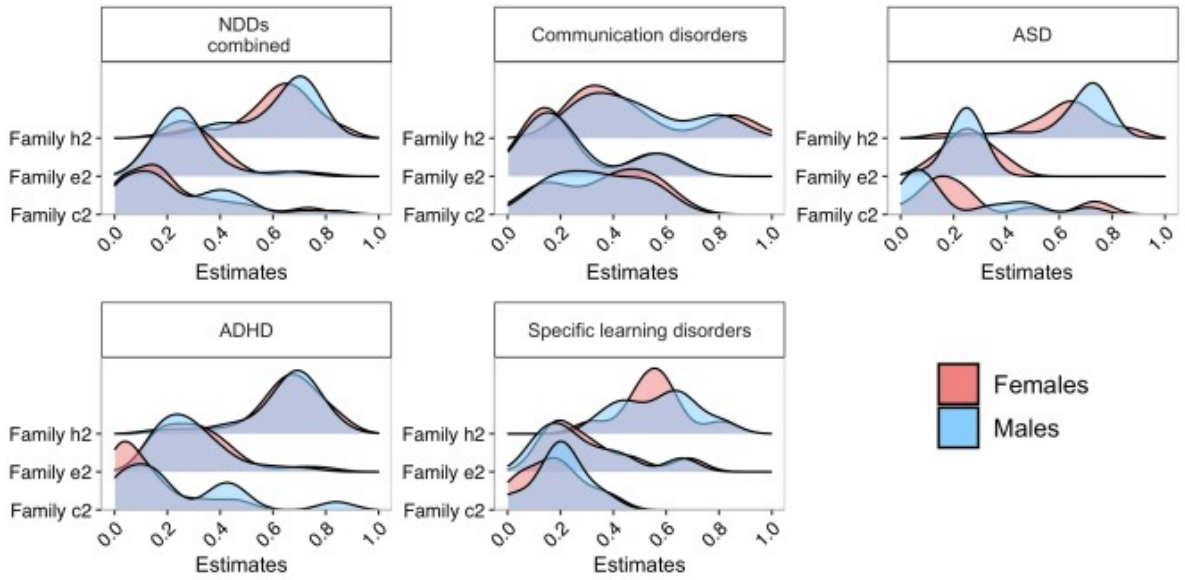



Figure 2. 5. Sex differences.

Distributions of the sex-specific meta-analytic estimates for the heritability (h2) and environmental contributions to neurodevelopmental disorders (NDDs). The top left panel shows the distributions of sex-specific estimates for the transdiagnostic meta-analysis, while the remaining panels the same estimates for specific NDDs for which a sufficient number of studies (>2) reporting sex-specific estimates was identified. The results for sex-specific $c^2$, $e^2$, rC and rE estimates are presented in Supplementary Note 1.

*Developmental trajectories*

We investigated developmental change and continuity in the relative contribution of genetic factors to NDDs by examining age-related differences in their aetiology and sources of their homotypic and heterotypic co-occurrences. We distinguished between the three following developmental stages: childhood (4-7 years), middle childhood (8-10 years) and adolescence (11-24 years). We grouped estimates in either of those three categories or across multiple

categories, for example childhood & middle childhood (4-10 years), middle childhood & adolescence (8-24 years) and childhood & adolescence (4-24 years).

*Family-based heritability ($h^2$)*

Across all NDDs, 54 family-based studies reported estimates in childhood (4-7 years), 54 studies reported estimates in middle childhood (8-10 years) and 79 studies reported estimates in adolescence (11-24 years). The remaining studies involved populations whose age range spanned across categories, i.e., childhood & middle childhood (4-10 years; 14 studies), middle childhood & adolescence (8-24 years; 50 studies) and childhood & adolescence (4-24 years; 40 studies). We investigated age-related differences in heritability including all NDD categories (Figure 2. 6A), with the exception of motor disorders for which we did not identify enough studies (>1) per age category. All estimates with standard errors, including those for age cross-categories are presented in Supplementary Table 19.

Across all NDDs, grand heritability remained relatively stable developmentally, with the estimate of 0.63 (SE= 0.03) in childhood, slight increase in middle childhood (0.68, SE= 0.04) and a subsequent drop back to 0.62 (SE= 0.08) in adolescence. This trend was consistent for some specific disorders (e.g., ASD and ADHD) but not for others (e.g., communication disorders and specific learning disorders) for which genetic influences decreased developmentally (Figure 2. 6A; Supplementary Table 19).

*SNP heritability (SNP $h^2$)*

Out of a total of 29 SNP-based studies that were identified, 13 included adolescent samples, 7 samples in middle childhood and 6 samples in childhood, while 11 studies reported estimates across childhood & adolescence. SNP heritability was stable developmentally across NDDs, and the developmental trajectory mirrored that of family-based heritability (SNP $h^2$= 0.24, SE= 0.11 in childhood; 0.26, SE= 0.08 in middle childhood and 0.23, SE= 0.07 in adolescence) (Figure 2. 6B; Supplementary Table 19). For ASD, ADHD and specific learning disorders, the specific NDDs for which grand estimates could be calculated, the developmental trends were consistent with those observed for family-based heritability (Figure 2. 6B; Supplementary Table 19).

*Developmental trajectories in genetic overlap between NDDs*

Overall, we could not explore developmental trends in genetic correlations using either method due to a lack of available studies, the only exceptions were grand estimates for adolescence and across age categories (see Supplementary Tables 20-21). Genetic correlations obtained for adolescent samples only were in line with those obtained for the total sample (for example, when considering the co-occurrence between ASD & ADHD the genetic correlation was 0.66 (0.49) in adolescent samples and 0.67 (0.30) across all age categories).

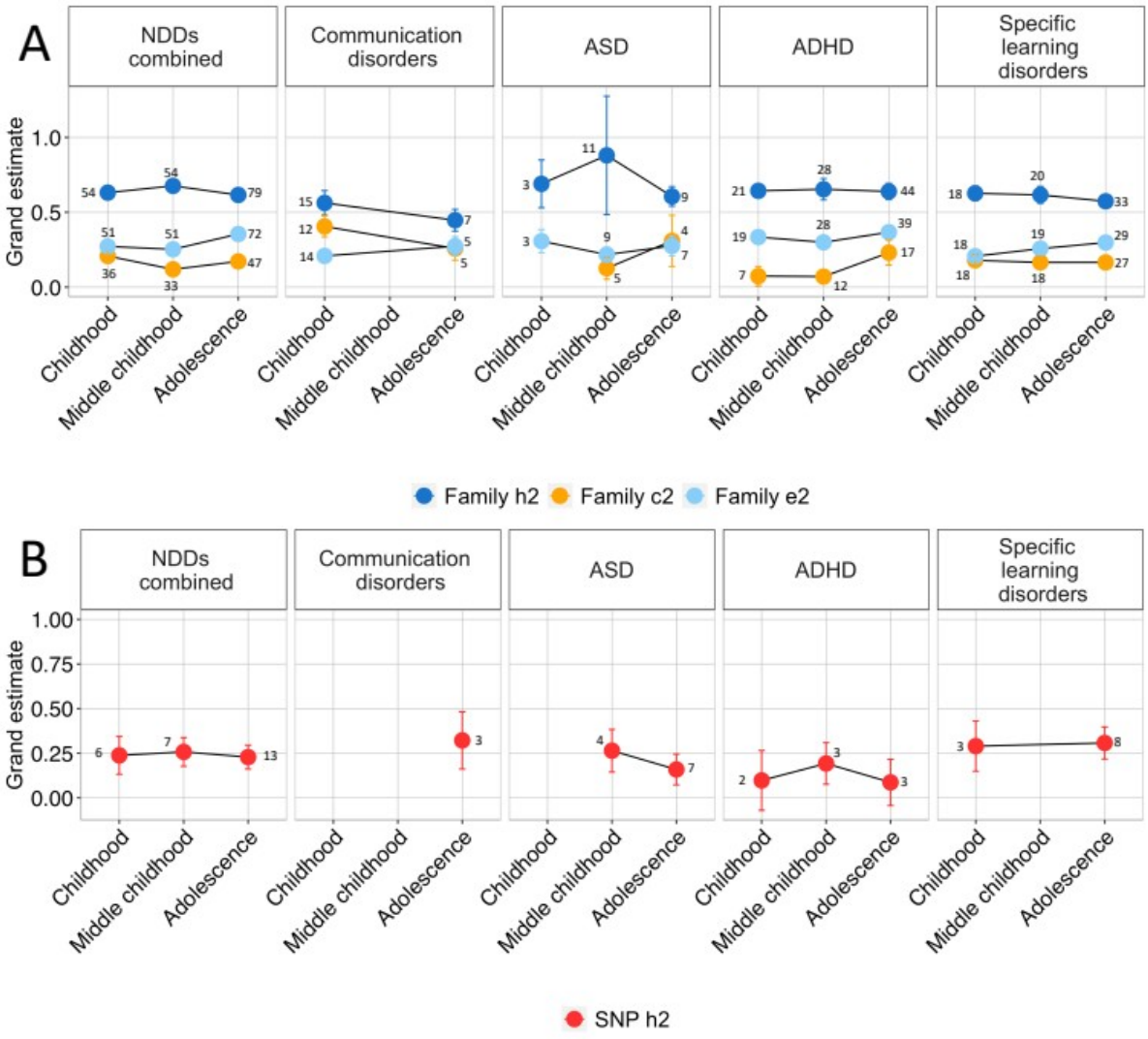



Figure 2. 6. Developmental trajectories.

Age-related differences in family-based heritability (h2), shared (c2) and nonshared (e2) environmental influences on neurodevelopmental disorders (NDDs) (panel A) and SNP heritability (panel B). Developmental stages include childhood (4-7 years), middle childhood (8-10 years) and adolescence (11-24 years). Error bars represent standard errors of grand estimates of heritability and environmental influences. Numbers located near point estimates denote the number of studies identified that provided estimates for specific developmental stages. For intellectual disabilities and motor disorders we could not identify a sufficient number of studies (>1) reporting age-dependent estimates and we were consequently unable to derive meta-analytic estimates. The results for age-stratified $c^2$, $e^2$, rC and rE are reported in Supplementary Note 1.

*Categorical versus continuous measurement*

Although we meta-analysed categorical (binary phenotypes, such as clinical diagnoses and cut-offs) and quantitative (sub-threshold symptom counts or test/questionnaire scores) measures together, we also report separate grand estimates for both measurement types. Across all NDDs, categorical measures were observed to yield significantly higher family-based heritability estimates if compared to continuous phenotypes (0.77, SE= 0.07 vs. 0.64, SE= 0.03). However, the opposite was found for SNP-based heritability (0.17, SE= 0.03 for categorical measures vs. 0.25, SE= 0.06 for quantitative assessments). Differences in sources of variation in specific NDDs, as well specific homotypic and heterotypic co-occurrences are presented in Supplementary Note 4, Supplementary Figure 26, and Supplementary Tables 28-30.

*Geography and ancestry*

Research into the genetic aetiology of NDDs and of their homotypic and heterotypic co-occurrences is largely limited to Western countries, even though, according to the Global Burden of Disease study (Institute for Health Metrics and Evaluation, 2017), the prevalence of diagnosed NDDs is not uniform across the globe. Furthermore, individuals of European ancestry represent 16% of the global population but 80% of participants in genomic (i.e., DNA-based) research ("Genetics for All," 2019). This Eurocentric bias ("Whose Genomics?," 2019) has created a major gap in our knowledge of the genetic aetiology of NDDs and their co-occurrences in non-White populations. In the following section we provide an overview of how behaviour genetics research into NDDs is distributed across countries and continents and how the estimates differ as a function of geographical location. Supplementary Note 5, Supplementary Figure 27, and Supplementary Tables 25-27 contain meta-analytic results of how heritability and genetic correlations differ at different levels of sample ancestral diversity. We created a moderator with four levels of percentage of European ancestry participants in samples: less than 50%, more than 50% but less than 75%, more than 75% but less than 100% and 100%.

*Family-based heritability ($h^2$)*

Out of the 236 studies investigating sources of individual differences in NDDs, 41% (96 studies) involved samples and cohorts based in the United Kingdom, 77 studies samples based in the United States, 24 studies Swedish samples, 19 studies Dutch samples, 11 studies Australian samples, 7 studies Canadian samples, 4 studies samples from China, and 2 studies samples from Norway. Other countries that contributed to the total grand estimate but did not have enough estimates for separate meta-analysis (i.e., only 1 study found from each country), included Finland, Japan, South Korea, and Italy. Estimates differed significantly across Countries. Considering all NDDs, the highest meta-analytic family-based heritability was estimated for Australian and Swedish samples (0.76, SE= 0.17 and 0.74 SE= 0.05, respectively), while the lowest was obtained for Canadian cohorts (0.43, SE= 0.09) (Figure 2. 7A; Supplementary Table 22).

When considering specific NDDs, these were investigated with different frequencies across countries: the aetiology of intellectual disabilities was exclusively investigated in Swedish cohorts (2 out of 2 studies), from where most studies addressing sources of variance in motor disorders also came from (4 out of a total of 7 studies). Communication disorders were mostly researched in the United Kingdom (17 out of a total of 23 studies), as were ASD (20 out of a total of 36 studies) and ADHD (42 out of a total of 121 studies). On the other hand, 47 out of a total of 89 studies investigating specific learning disorders were carried out in the United States.

*SNP heritability (SNP $h^2$)*

Studies exploring SNP heritability of NDDs focused entirely on European cohorts and were primarily conducted in the United Kingdom and the Netherlands (14 and 3 out of 29 SNP-based studies in total) (Supplementary Table 22).

*Geography and ancestry-related differences in the genetic overlap between NDDs*

Sources of homotypic co-occurrence with NDDs were investigated in 37 independent family-based studies, out of which the majority was conducted in the United Kingdom (49%) and United States (30%). The highest genetic correlation across all co-occurrences was estimated in Swedish cohorts (0.80, SE= 0.26 across 3 studies), while the lowest grand genetic overlap was estimated in Canadian samples (-0.44, SE= 0.24 across only 2 studies which investigated

the association between ADHD and specific learning disorders; Figure 2. 7B; Supplementary Table 23).

The genetic aetiology of the co-occurrence between ASD & ADHD during childhood and adolescence was exclusively researched in the United Kingdom and Sweden (3 out of a total of 6 studies each). The co-occurrence between ADHD & motor disorders was only explored by two studies, one conducted in Sweden and the other one in Australia. Most studies examining the genetic overlap between ADHD & specific learning disorders came from the United States (8 out of a total of 18 studies), whereas the overlap between communication disorders & motor disorders was only addressed by 2 studies conducted in the United Kingdom and Japan.

SNP-based studies (6 in total) addressing the co-occurrence between NDDs were exclusively conducted in combined samples from the United Kingdom and Denmark (Supplementary Table 23).

*Geography and ancestry-related differences in the genetic overlap between NDDs and DICCs*

A total of 15 family-based studies addressing the co-occurrence between NDDs and DICCs were identified, 40% of which were conducted in the United Kingdom, 20% in the United States and 20% in Sweden. Studies yielded consistently strong estimates of genetic correlations across the three regions: genetic correlations of 0.60 (SE= 0.29); 0.42 (SE= 0.15) and 0.68 (SE= 0.41), respectively (Supplementary Figure 28 and Supplementary Table 24). The remaining 20 % of studies were conducted in Australia, Finland, and South Korea, but could not be meta-analysed separately as only one estimate was available for each country.

In terms of specific co-occurrences between NDDs and DICCs, half of the studies that explored genetic overlap between ADHD & conduct disorder, and ADHD & oppositional defiant disorder were conducted in the United States (3 studies each). Three out of 4 studies examining the association between ASD & conduct disorder were conducted in the United Kingdom and 1 study in Sweden.

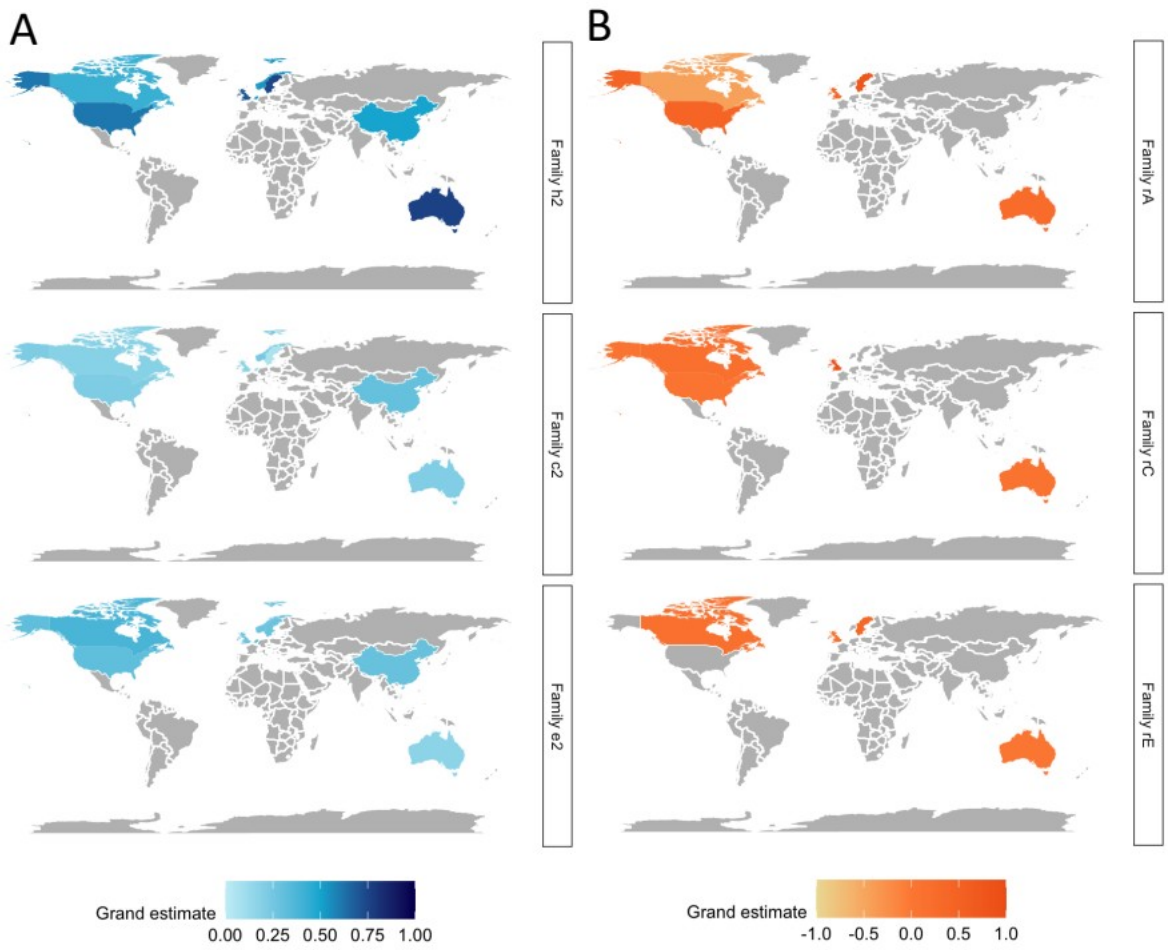



Figure 2. 7. Geographical differences.

Panel A illustrates differences in family-based heritability (h2) shared environmental (c2) and nonshared environmental (e2) influences across all neurodevelopmental disorders (NDDs). Panel B illustrates geographical differences in the genetic (rA), shared environmental (rC) and nonshared environmental (rE) overlap between NDDs. The areas shaded in grey are regions for which not enough relevant studies were identified (<2 studies). Geographical differences in rA, rC and rE between NDDs and disruptive, impulse control and conduct disorders (DICCs) are presented in Supplementary Figure 28. The results for $c^2$ and $e^2$ as well as rC and rE are discussed in Supplementary Note 1.

*Bias and heterogeneity assessment*

We applied $I^2$ statistics to assess heterogeneity in the estimates, followed by outlier and influential cases identification analyses. The results of these analyses are reported in Supplementary Note 6, Supplementary Tables 7-12, and Supplementary Figures 4-7. We applied Egger's regression and inspected funnel plots to examine the impact of publication bias on our results, the outcomes of these analyses are reported in Supplementary Note 7 and Supplementary Tables 13-15 and Supplementary Figures 8-24. Results of the risk of bias assessment are presented in Supplementary Figure 25, where 93.8% of studies showed low risk of bias across the 9 quality checklist items, and the remaining 6.2% moderate risk.

## Method

The protocol for the current meta-analysis was registered with the international prospective register of systematic reviews (PROSPERO) and can be accessed at the following link: https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=230158. This meta-analysis was conducted in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021). PRISMA 2020 Checklist and PRISMA 2020 for Abstracts Checklist (Page et al., 2021) are included in Supplementary Notes 9 and 10. Code and master extraction tables are available at https://github.com/CoDEresearchlab/Meta_analysis_NDDs_DICCs.

*Identification of relevant studies*

A total of 296 studies were included in the meta-analysis (Figure 2. 2). Studies were identified during three searches: the primary search (Supplementary Figure 29A) conducted on the 20th of January 2021, the secondary (confirmatory) search (Supplementary Figure 29B) conducted on the 15th of April 2021 and the additional search of other relevant meta-analyses and reviews finalised on the 4th of May 2021. Searches were conducted across three platforms: Web of Science, Ovid Medline, and Ovid Embase and the outputs managed with the aid of Covidence, Veritas Health Innovation, Melbourne, Australia, which is a web-based collaboration software platform that streamlines the production of systematic and other literature reviews (https://www.covidence.org/). An in-depth description of indexes, timespans, search strategy and key words is included in Supplementary Note 11. All studies included in the meta-analysis are listed in Supplementary Tables 31-36.

*Screening and inclusion criteria*

After the initial searches were conducted and duplicate studies removed, 8,087 studies met the criteria for the first stage of screening, which involved title and abstract scanning. All titles and abstracts were screened by two independent, blinded reviewers to ensure inter-rater agreement. Conflicts were resolved by a third independent reviewer and inter-rater reliability was calculated as the proportion of conflicts to the total number of studies screened (Figure 2. 2). After this initial screening phase, 6,834 studies were excluded as deemed not relevant for the purpose of the current meta-analysis.

The title and abstract screening process resulted in a total of 1,253 potentially eligible studies. The full text of each study was screened by two independent, blinded reviewers. Reviewer discrepancies were identified and resolved by a third independent reviewer. Inter-rater reliability statistic was calculated (Figure 2. 2). This resulted in 289 eligible articles. In addition, during full text screening, relevant review articles, meta-analyses, editorials, and conference abstracts were flagged to aid the potential discovery of further relevant studies by either screening the References sections or contacting the authors of conference abstracts. Through this process, 7 additional studies were identified, which resulted in a total of 296 studies included in the current meta-analysis (see Figure 2. 2). Studies were considered relevant and selected to be included at the next screening stage based on the following criteria.

First, studies were only included if 75% or more of the sample consisted of children and/or adolescents. Based on guidelines from the World Health Organization (WHO; https://www.who.int/health-topics/adolescent-health#tab=tab_1), we defined the period from childhood to end of adolescence as ranging from age 4, the earliest age for compulsory schooling, to age 24, the end of adolescence. Second, we included studies that had measured NDDs and DICCs considering either formal clinical diagnoses, clinical cut-offs, and/or quantitative measures of symptoms. Third, studies were selected only if they featured data on at least one NDD (Aim 1), at least two NDDs (Aim 2), or at least one NDD and one DICC disorder (Aim 3).

Fourth, studies using family-based designs had to have reported at least one estimate of heritability ($h^2$), shared environmental ($c^2$) or nonshared environmental influence ($e^2$), or genetic or environmental correlations. We included only single-generation family designs,

that is studies that had used twin design (Rijsdijk & Sham, 2002), sibling comparisons (Kendler et al., 2016), or extended twin designs (Posthuma & Boomsma, 2000). We excluded multiple-generation family designs (e.g., children-of-twins (Eley et al., 2015) and in-vitro fertilization (Rice et al., 2009)) due to the potential confounding in the genetic and environmental estimates that could have resulted from including parental traits in the models decomposing the covariance between family members (McAdams et al., 2018).

Fifth, studies using genomic designs were included only if they had reported at least one SNP-based heritability estimate and/or a genetic correlation (rG). Eligible SNP-based methods to quantify the proportion of phenotypic variance accounted for by common SNPs included genome-based restricted maximum likelihood (GREML, J. Yang et al. (2017)), linkage-disequilibrium score regression (LDSC, Bulik-Sullivan et al. (2015)) and SbayesS, which is a Bayesian approach to the analysis of GWA summary data (Zeng et al., 2018). Each method is described in greater detail in Supplementary Note 12. Sixth, studies that had selected participants based on other diagnoses not related to NDD or DICC categories or based on extreme vulnerability or environmental insult unrelated to NDDs or DICCs, such as alcohol abuse, were not included. Lastly, only studies published in English were included. Studies deemed eligible based on full-text scanning were also scored in terms of their scientific quality and risk of bias by two reviewers (see details on the quality scoring checklist in Supplementary Note 13).

*Data extraction*

Data extraction was conducted by the primary reviewer. Issues and uncertainties were resolved through discussion with co-authors. Missing data was requested from study authors via email or ResearchGate (for details, see Supplementary Note 14). Extracted data were compiled in a table, including information on study reference, project/cohort name, study design (e.g., classical twin study), model reported (e.g., full ACE model; when multiple models were reported, the best fitting model was selected for data synthesis), overall number of participants and number of participants in subgroups (e.g. number of monozygotic vs. dizygotic twins), average age and age range of the sample, cohort country(ies) of origin, participants ancestry (defined in terms on the percentage of participants of European ancestry in samples), broad types of NDD and DICC included (e.g., Specific Learning Disorder), sub-type of NDD and/or DICC included (e.g., dyslexia), specific phenotypes measured (e.g.,

reading fluency), measure statistics (e.g., binary (diagnosis) or continuous (symptoms continua)), measure (e.g., Conners rating scale for ADHD) and rater (e.g., parent reports), covariates included in the analyses (e.g., age and sex), statistics (e.g., family-based heritability, SNP-based genetic correlation etc.), and finally the estimated statistics and the provided index of measurement variance (e.g., standard error). Master extraction tables, 'Extraction_heritability' and 'Extraction_correlations' are available at https://github.com/CoDEresearchlab/Meta_analysis_NDDs_DICCs.

Estimates of heritability, shared and nonshared environmental influences were extracted as reported by individual studies. When studies only reported twin correlations, variance components were calculated using the Falconer's formula (Falconer, 1996), as follows:

$$h^2 = 2(r_{MZ} - r_{DZ})$$
$$c^2 = 1 - (h^2 + e^2)$$
$$e^2 = 1 - r_{MZ}$$

Where: $h^2$= family-based heritability; $r_{MZ}$= monozygotic twin correlation; $r_{DZ}$= dizygotic twin correlation; $c^2$= shared environmental influences; $e^2$= nonshared environmental influences. Genetic, shared and nonshared environmental correlations were only extracted if reported by individual studies. For studies where neither standard deviation, standard errors nor 95% confidence intervals were reported, the 95% confidence intervals were calculated using the Cir function implemented in the R package psychometric (Fletcher, 2010; R Core Team, 2022), based on the sample size of the study, and subsequently converted to standard errors via dividing the difference between upper and lower bound confidence intervals by 3.92 (Cohen et al., 2013).

*Data synthesis*

Heritability and environmental influences reported by selected studies were synthesised using a multilevel random-effects meta-analysis in metafor for R (R Core Team, 2022; Viechtbauer, 2010). We used heritability/environmental influences and genetic/environmental correlation coefficients, along with standard errors as the measures of effect size (Andersson et al., 2020). However, to avoid the risk of Type I error introduced by the distribution characteristics of the correlation coefficient (Alexander et al., 1989), we transformed all estimates using Fisher's z. Effect sizes were then weighted by their inverse

variance weight so that larger samples were given more weighting and the standard error for the common effect size resulted as a function of the allocated weights. For results presentation, Fisher's z was transformed back to variance components and correlation coefficients (Malanchini, Smith-Woolley, et al., 2019). Multilevel random-effects models enabled varying true effect sizes across studies . We introduced a 2-level structure to account for nested effects underlying heterogeneity and clustering across studies (Level 1: individual clustering; Level 2: cohort clustering). Given that some NDDs have different prevalence rates in males and females (Christensen et al., 2016; May et al., 2017; Polanczyk et al., 2007), we meta-analysed studies that provided sex-specific estimates in separate models to minimize sample heterogeneity across studies and report separate grand estimates for combined, male-only, and female-only samples.

*Data reporting*

We report transdiagnostic grand estimates across all disorders and for broad NDD categories, comprising all studies that investigated the aetiology of a disorder either using diagnoses, categorical or quantitative measures. For example, the broad ADHD phenotype includes studies that have measured ADHD using diagnoses, clinical cut-offs, and continuous measures of ADHD traits, such as checklists and questionnaires. The only exception is intellectual disability. We did not consider quantitative measures of general intelligence as indexing a continuum of intellectual disability given that intellectual disability, as described in the DSM-5 is a complex disorder, not only characterized by impairments in intellectual performance, but also in adaptive functioning and communication (APA, 2022; Moffitt et al., 2009). Finally, we considered specific manifestations of NDDs, for example, beyond ADHD, we also consider the hyperactive/impulsive and inattentive sub-types separately. Results for all sub-categories of NDDs and for their co-occurrence with other disorders are reported in Supplementary Note 2, Supplementary Figures 2 and 3 and Supplementary Tables 2, 4 and 6.

*Aggregation of non-independent effects*

Multilevel meta-analytic models allow to account for non-independence of estimates derived from partly or completely overlapping samples (i.e., estimates obtained from multiple studies that have used the same cohort of participants). To further account for the non-independence of sampling variance (i.e., when sampling errors correlate because data from partly the same individuals is used to estimate multiple effect sizes), we also aggregated multiple estimates

within each individual study (e.g., estimates at multiple timepoints derived from the same study). Aggregation of dependent effects sizes was performed at the level of each study using the R package Meta-Analysis with Mean Differences (MAd) (Del Re et al., 2022; R Core Team, 2022), applying a default correlation between estimates of 0.5. We conducted several sensitivity analyses, comparing different aggregation methods, i.e., aggregating at the level of the study, cohort, and country, and varying the assumed correlation between dependent effect sizes (0.5, 0.3 and 0.9). Results of these additional checks are presented in Supplementary Figure 30 and discussed in Supplementary Note 15. Since differences in aggregation strategy did not result in significant differences in meta-analytic effects, we report results obtained when the correlation between dependent effect sizes was set to 0.5.

*Bias and heterogeneity assessment*

The potential for publication bias was explored using funnel plots and Egger's linear regression (Sterne et al., 2005). The proportion of heterogeneity across estimates was estimated using the $I^2$ statistics, which calculates the fraction of variance across studies that can be attributed to heterogeneity, rather than chance (Borenstein et al., 2017; Higgins et al., 2003; Higgins & Thompson, 2002). The $I^2$ statistics was computed as a proportion of true variance of true effects to variance of the observed effects, in line with the following formula :

$$I^2 = \frac{V_{TRUE}}{V_{OBS}}$$

where $V_{TRUE}$ is the variation of true effects and $V_{OBS}$ is the variation due to sampling error. In other words, $I^2$ can be interpreted as the dispersion of observed effects as compared to the dispersion that would be predicted just from sampling error. The $I^2$ statistics also provides insight into the degree to which confidence intervals from individual studies are independent . We also conducted outlier cases identification analysis, followed by re-calculation of $I^2$ estimates after removing studies considered to be outliers (Viechtbauer & Cheung, 2010). Studies having a substantial impact on the grand estimates and heterogeneity were identified using influential cases identification analysis (Viechtbauer & Cheung, 2010). Heterogeneity assessment analyses were conducted using the metafor (Viechtbauer, 2010), meta (Balduzzi et al., 2019) and dmetar (Harrer et al., 2019) packages in R (R Core Team, 2022).

*Moderation analyses*

We tested for the effect of several moderators. Selection of moderator terms was determined based on available data, considering completeness of reported moderator variables. We implemented a >50% rule of thumb, i.e., if 50% or more studies reported data on the moderating variable, we included this moderator in our analyses. For example, less than 50% of studies reported the percentage of participants of Asian ancestry in the sample, hence we did not include the percentage of Asian participants in moderation analyses. We considered the following 11 moderators: age group, design, type of model, rater, measurement, percentage of individuals who identified as White, number of covariates included in the analysis, measure adopted, country, and specific phenotype measured, each moderator is described in greater detail in Supplementary Note 3. Moderation analyses were conducted using a two-step procedure. First, only studies that reported data on the level of the moderator were selected (for example, only studies reporting estimates for adolescents). Second, analyses stratified by levels of the moderator were run using a multilevel random-effects meta-analysis in metafor for R (R Core Team, 2022; Viechtbauer, 2010), i.e., a grand estimate was derived for adolescents and subsequently compared with estimates for other developmental stages (i.e., childhood and middle childhood) using the same procedure. We report unstratified estimates (Supplementary Tables 1, 3 & 5) and estimates stratified by specific phenotype measured (Supplementary Tables 2, 4 & 6), age category (Supplementary Tables 19-21), country (Supplementary Tables 22-24), and ancestry (Supplementary Tables 25-27) in the main text, whereas estimates stratified by all other moderators are reported in Supplementary tables 37-50.

*Deviations from the PROSPERO pre-registered protocol*

Although we followed the preregistered plan step-by-step, some deviations from the plan were made based on the availability of software and evidence. Below we describe our deviations from the preregistered protocol.

(1) As opposed to the first (primary) literature search which followed the procedure described in the protocol, in the second (confirmatory) literature search we included an additional set of terms to identify studies that measured Specific Learning Disorders and Communication Disorders on a quantitative scale. For details, see Supplementary Note 11.

(2) In the protocol we indicated that study screening would be documented on an excel spreadsheet. Instead, we used Covidence (https://www.covidence.org/), a software that

automatically enables the double-blinded screening of title and abstract, as well as full-text screening and study selection, without the need for external recording of decisions.
(3) Finally, while all 296 papers were assessed for publication reporting bias (see Supplementary Note 7, Supplementary Tables 13-15, and Supplementary Figures 8-24), the first 82 papers that were extracted (27.7% of the total) were also assessed for study quality using the checklist provided by Kmet et al. (2020)(see Supplementary Note 13 and Supplementary Figure 25).

*Certainty assessment*

We evaluated our confidence in the body of research included in the present meta-analysis based on a number of key factors: (a) the sample size of each study, (b) the consistency of findings across studies, (c) study quality and risk of publication bias.

(a) Because differences in sample size can introduce an imbalance in the power to estimate effects reliably across studies, in our meta-analysis we weighted each estimate by the standard errors. Estimates reported by studies conducted in larger samples had smaller standard errors and were therefore given more weight if compared to studies conducted in smaller samples.
(b) The consistency of findings across studies was assessed by visually examining forest plots. Overall, we did not find significant differences between estimates.
(c) Study quality and risk of bias were assessed in line with the framework proposed by Kmet et al. (2020)(see Supplementary Note 13 and Supplementary Figure 25). We applied Egger's regression and inspected funnel plots to examine the impact of publication bias on our results, the outcomes of these analyses are reported in Supplementary Note 7 and Supplementary Tables 13-15 and Supplementary Figures 8-24.

Based on these criteria, we place confidence in the results of the current meta-analysis that shows that: 1) NDDs in childhood and adolescence are highly heritable; 2) that the pattern of co-occurrence between NDDs is complex, and while some NDDs are closely related, others show little genetic overlap; and 3) NDDs show a moderate-to-strong genetic overlap with DICCs.

*Limitations of the review process*

The review process of the current meta-analysis does not come without limitations. A first limitations is our sole focus on childhood and adolescence. A second limitation relates to our choice of focusing on specific co-occurring conditions, DICCs, without considering other neurological disorders that have been found to co-occur with NDDs, such as epilepsy, cerebral palsy, sleep, or psychiatric disorders. The inclusion of a wider range of co-occurring conditions could have resulted in a more detailed characterization of aetiological overlaps between NDDs and other conditions. A third limitation is that the current meta-analysis only focused on single-generation studies, i.e., twin and sibling studies and excluded multi-generational family designs, such as children-of-twins and in-vitro fertilization studies. Future studies focusing on multi-generational designs could provide valuable insights into the role that parental genotypes and correlated environmental influences play in offspring's NDDs and their co-occurring conditions.

## Discussion

The findings of the present meta-analysis synthesise the current state of knowledge on NDDs and have implications that can guide future research strategies, clinical and educational practice. First, by providing estimates of the relative contribution of genetic factors to all NDDs, our work responds to the need of moving beyond the nearly exclusive research focus on ASD and ADHD. Second, by providing an account of the genetic overlap between NDDs, we highlight how genetic influences are implicated in the co-occurrence between multiple NDDs, identifying patterns of shared aetiological liability. Third, by synthesising the literature on the co-occurrence between NDDs and DICCs we highlight how disorders from these two separate groups identified by the DSM-5 share as much of their genetic aetiology as do disorders all classified as NDDs.

Our work provides meta-analytic evidence for the substantial heritability of all NDDs, particularly when considering family-based studies, which indicated that around two thirds of the variation in NDDs is accounted for by genetic differences between children and adolescents. Although males are up to four times more likely to be diagnosed with ASD and ADHD than females (Christensen et al., 2016; May et al., 2017; Polanczyk et al., 2007), we showed that, when meta-analysed, genetic effects associated with NDDs do not differ by sex. We also showed that genetic sources of variation in NDDs are remarkably stable across

developmental stages, and this developmental stability was observed across all NDDs. Genetic effects were also mostly consistent when we separated studies that had considered diagnoses and clinical cut-offs from studies that had quantified NDDs as continuous traits.

Interestingly, we found that the genetic contributions to NDDs differed substantially as a function of geography. This highlights how estimates of genetic effects associated with disorders are sensitive to different environmental contexts (Rimfeld, Krapohl, et al., 2018; Silventoinen et al., 2020). Our work on geographical differences also highlighted the major gap in our knowledge of the aetiology of NDDs in non-Western countries, a gap that is only exceeded by the lack of ancestral diversity observed across all studies of NDDs. Importantly, the current study pointed to how genetic influences on NDDs were substantially reduced in more ancestrally diverse samples, again highlighting how heritability estimates are inextricably linked to our social context (Abdellaoui et al., 2019; D. W. Belsky et al., 2019), in a sense that increased ancestral homogeneity within the sample likely entails increased environmental homogeneity, reducing environmental variability and inflating heritability in these populations.

The lack of diversity in genetic research remains its most striking limitation to date, particularly when considering DNA-based methods, limiting the extension of genetic findings to the entire population (A. R. Martin, Kanai, et al., 2019; Popejoy & Fullerton, 2016). Limited research resources in under-represented populations are likely to have profound cascading effects for future advances in clinical practice, including pharmacological and behavioural treatment. Fortunately, there are major initiatives underway to re-balance these biases (Finer et al., 2020; Ramsay & Sankoh, 2016; Wright et al., 2013).

Our second aim was to provide a clear account of how close NDDs are to one another aetiologically. We found that, while meta-analytic estimates indicated moderate genetic overlap, the degree of heterogeneity in these associations across disorders was large. We found a substantial genetic correlation between ASD and ADHD, ADHD and motor disorders, and communication disorders and specific learning disorders. On the other hand, genetic overlap was only moderate between communication disorders and motor disorders, and very weak between ADHD and specific learning disorders, which is consistent with the degree of symptom resemblance across these disorders.

Although we were able to explore general patterns of variation and co-occurrence, the aetiology of specific NDDs and of their associations could not be comprehensively characterised. The research gaps that we identified highlight an imbalance in focus across NDDs in developmental behaviour genetics research. When considering our first aim, we could only identify 2 family-based studies that investigated the genetic contributions to intellectual disabilities, if compared to 121 family-based and 14 SNP-based studies identified for ADHD, and 36 family-based and 15 SNP-based studies identified for ASD. This lack of research on intellectual disabilities, a neurodevelopmental disorder affecting 2.5% of children in the United Kingdom (Office for National Statistics [ONS], 2021), more than double the prevalence rate of ASD (Mehlmann-Wicks, 2020) is reflected in, and likely partly due to, the lack of funding bodies devoted to researching NDDs other than ASD and ADHD, as well as a lack of publicly available data repositories and resources (e.g., Autism Speaks; iPSYCH; Psychiatric Genomics Consortium).

We also identified very few studies that had examined the aetiology of motor disorders, another neurodevelopmental condition showing significant prevalence rates of 5-6% in school aged children (Zwicker et al., 2012). This unbalanced research focus, that extends far beyond genetically informative research to touch developmental and therapeutic research (Bigby, 2012; Khan et al., 2019; McGregor, 2020; Valentine et al., 2020, 2021), has led to an uneven distribution of knowledge, which could lead to limited access to interventions for children with NDDs other than ASD, ADHD, and dyslexia (Bigby, 2012).

The lack of equity in focus across NDDs was pronounced in analyses addressing our third aim. Sources of co-occurrence between NDDs and DICCs could only be investigated between ADHD & conduct disorder, ADHD & oppositional defiant disorder and between ASD & conduct disorder. Considering that in the DSM-5 the DICCs category comprises 8 distinct disruptive disorders, this highlights a major gap in our knowledge.

To conclude, this meta-analysis provides a holistic view of genetic and environmental contributions to all NDDs and commonly co-occurring developmental disorders, revealing that NDDs are just as strongly genetically correlated with other NDDs, as most of them are with DICCs. Our work identifies a lack of balance in research across different NDDs, which calls for future genetic research to focus on less investigated disorders. We provide knowledge about patterns of aetiological co-occurrence between NDDs, as well as between

NDDs and DICCs, which we hope will inform clinical and educational diagnostics and practice, resulting for example in expanded diagnostic screening.

# Chapter 3— Using DNA to predict behaviour problems from preschool to adulthood.

This chapter is presented in a form of a published paper. It is an adapted version of the following publication:

Gidziela, A., Rimfeld, K., Malanchini, M., Allegrini, A.G., McMillan, A., Selzam, S., Ronald, A., Viding, E., von Stumm, S., Eley, T.C. and Plomin, R. (2022), Using DNA to predict behaviour problems from preschool to adulthood. J Child Psychol Psychiatr, 63: 781-792. https://doi.org/10.1111/jcpp.13519

Supplementary Notes, Tables and Figures are included in Appendix 2.

## Abstract

*Background*

One goal of the DNA revolution is to predict problems in order to prevent them. We tested here if the prediction of behaviour problems from genome-wide polygenic scores (PGSs) can be improved by creating composites across ages and across raters and by using a multi-PGS approach that includes PGSs for adult psychiatric disorders as well as for childhood behaviour problems.

*Method*

Our sample included 3,065 genotyped unrelated individuals from the Twins Early Development Study who were assessed longitudinally for hyperactivity, conduct problems, emotional problems and peer problems as rated by parents, teachers and children themselves. Polygenic scores created from 15 genome-wide association studies were used separately and jointly to test the prediction of behaviour problems composites (general behaviour problems, externalizing and internalizing) across ages (from age 2 to age 21) and across raters in penalized regression models. Based on the regression weights, we created multi-trait PGSs reflecting the best prediction of behaviour problems. We compared PGS prediction to twin heritability using the same sample and measures.

*Results*

Multi-PGS prediction of behaviour problems increased from less than 2% of the variance for observed traits to up to 6% for cross-age and cross-rater composites. Twin study estimates of heritability, although to a lesser extent, mirrored patterns of multi-PGS prediction as they increased from less than 40% to up to 83%.

*Conclusions*

The ability of PGSs to predict behaviour problems can be improved by using multiple PGSs, cross-age composites and cross-rater composites, although the effect sizes remain modest, up to 6%. Our approach can be used in any genotyped sample to create multi-trait PGS predictors of behaviour problems that will be more predictive than polygenic scores based on a single age, rater or PGS.

# Introduction

Because all behaviour problems in childhood show moderate genetic influence (Cheesman et al., 2017), a next step in genetic research is to find inherited DNA variants responsible for their heritability. The ability to predict behaviour problems from DNA will facilitate research on topics such as how genetic risk unfolds developmentally, gene-environment interaction and correlation, and multivariate issues of genetic heterogeneity and co-morbidity. It will also advance clinical work by identifying problems on the basis of causes rather than symptoms, by moving away from diagnoses towards dimensions, by switching from one-size-fit-all treatments to individually tailored treatments, and by focusing on prevention rather than treatment (Plomin, 2019).

Genome-wide association (GWA) studies identify DNA variants such as single-nucleotide polymorphisms (SNPs) that are associated with complex traits and common disorders (Visscher et al., 2017). Individual SNP associations have small effect sizes, but thousands of SNP associations can be aggregated in genome-wide polygenic scores (PGSs) to predict considerably more variance (PGS heritability, aka PGS prediction) for some traits (A. R. Martin, Daly, et al., 2019). The most predictive PGSs for behavioural traits have been derived from GWA summary statistics for educational attainment (J. J. Lee et al., 2018) and general cognitive ability (Savage et al., 2018), with PGS heritabilities up to 16% and 11%, respectively (Allegrini et al., 2019). However, despite substantial twin heritability (a mean of 60%) (Cheesman et al., 2017), PGS heritabilities are modest for childhood behaviour problems such as autism spectrum disorder (2.5%) (Grove et al., 2019)and ADHD (3.3%) (Ronald et al., 2021). In a recent study, PGS prediction of childhood ADHD symptoms, internalizing and social problems was reported to be much lower for adult-based PGSs of major depression (0.2%), neuroticism (0.1%), insomnia (0.05%) and subjective wellbeing (0.06%) (Akingbuwa et al., 2020). A recent GWA study of childhood and adolescence internalizing symptoms predicted 0.4% of the variance in internalizing at age 7 and 0.03% at ages 13-18 (Jami et al., 2022). However, the predictive power of PGSs is dependent on the size of discovery samples used in GWA studies, which needs to be considered when comparing PGS prediction across cognitive and psychiatric traits. For example, for educational attainment (J. J. Lee et al., 2018), sample sizes reach up to 1.1 million individuals, whereas some of the GWA studies of psychiatric disorders had sample sizes of less than 20,000 cases (Demontis et al., 2019; Grove et al., 2019). Polygenic scores will

become more predictive as GWA sample sizes increase and as whole-genome sequencing identifies all DNA variants, rare as well as common, that contribute to heritability (Visscher et al., 2017).

Using existing PGSs, we explored ways to increase the prediction of childhood behaviour problems from DNA. Research suggests that using multiple PGSs in a multivariate framework can improve prediction (Allegrini et al., 2019; Allegrini, Karhunen, et al., 2020; Grotzinger et al., 2019; Krapohl et al., 2018; Pain et al., 2021). To test the hypothesis that the multi-PGS approach will yield greater PGS heritability than the single-PGS approach, we assessed the joint prediction of 15 PGSs in penalised regression models with hold-out evaluation of prediction accuracy (multi-PGS). In addition to PGSs for childhood behaviour problems (ADHD; autism spectrum disorder) (Demontis et al., 2019; Grove et al., 2019), we included PGSs derived from the much larger GWA studies of adult psychiatric disorders such as schizophrenia (Pardiñas et al., 2018), bipolar disorder (Stahl et al., 2019), and major depressive disorder (Wray et al., 2018) and traits such as neuroticism (Luciano et al., 2018), well-being (Okbay et al., 2016) and risk-taking (Karlsson Linnér et al., 2019) as they have been shown to predict a variety of childhood phenotypes, including general psychopathology (Allegrini, Cheesman, et al., 2020) and behaviour problems (Akingbuwa et al., 2020).

In both phenotypic and DNA-based analyses of behaviour problems, a general factor of psychopathology has been observed that is known as a ‘p-factor’ or ‘p’ (Allegrini, Cheesman, et al., 2020; Caspi et al., 2014), suggesting that diverse behaviour problems share common genetic influences. Accordingly, we created latent composites of general behaviour problems (BPp, externalizing and internalizing) and used the multi-PGS approach to test two other hypotheses to improve PGS prediction. First, because age-to-age stability is largely driven genetically (Nivard et al., 2015; Plomin, 2019), we hypothesised that longitudinal composites of behaviour problems would yield greater PGS heritability than age-specific observed variables, as suggested by previous genomic research (Cheesman et al., 2018). Second, building on the assumption that behaviour problems that emerge across situations are more heritable than situation-specific problems, we hypothesised that PGS heritability is greater for behaviour problems composites across raters such as parents, teachers and children themselves who see behaviour problems in different settings than behaviour problems assessed only by one rater (Bartels et al., 2004; Cheesman et al., 2018).

We tested these hypotheses in a sample of 3,065 unrelated individuals from the Twins Early Development Study (TEDS) (Rimfeld, Malanchini, Spargo, et al., 2019), for whom we had genotypes and ratings of behaviour problems from early childhood to early adulthood from parents, teachers and the children themselves, from age 2 to 21. Because these unrelated individuals were members of twin pairs, we included their co-twins in analyses to estimate heritability using the twin method, testing the hypotheses that cross-age and cross-rater composites increase twin heritability, mirroring the patterns of PGS heritability.

## Method

Our hypotheses and analyses were preregistered in Open Science Framework (OSF) (https://osf.io/27tpj/) prior to accessing the data. Please see Supplementary Note 1 for details. Scripts have been made available on the OSF website.

### *Participants*

Our sample consists of twins born in England and Wales between 1994 and 1996 who were enrolled in the Twins Early Development Study (TEDS; for a detailed description of the sample, please refer to the Supplementary Note 2 and Rimfeld et al., 2019). In the current study we investigated heritability of behaviour problems, using data collected when the twins were aged approximately 2, 3, 4, 7, 9, 12, 16 and 21 years old. The sample selected for construction of composites included twins who had at least half of the data on behaviour problems complete across ages and raters. Patterns of missing data were addressed using the full information maximum likelihood. This resulted in a sample of 4,778 twin pairs.

DNA has been genotyped for a subsample of 7,026 unrelated individuals from TEDS (i.e., one twin per pair), out of which 3,065 individuals were included in the present study, which provides a sample size adequate to detect a correlation of 0.10 with more than 99% power (Browner et al., 2022). For details on sample sizes per composite, please refer to Supplementary Table 1. Genotyping took place on two different genotyping platforms (AffymetrixGeneChip 6.0 and Illumina HumanOmniExpressExome-8v1.2) in two separate waves. For a detailed genotyping protocol, see Selzam et al. (2018).

*Measures*

*Polygenic* scores

Our methods for obtaining DNA, genotyping, quality control and constructing PGSs have been described previously (Selzam et al., 2018). In the present analyses, we included 15 PGSs of behaviour problems and psychopathology, derived from the most powerful GWA studies, which were used in our previous research (Allegrini et al., 2019; Allegrini, Karhunen, et al., 2020). For the list of polygenic scores, please refer to Supplementary Note 3.

*Behaviour problems*

We assessed hyperactivity, conduct problems, emotional and peer problems from early childhood to early adulthood as rated by parents, teachers and the twins themselves. The Preschool Behaviour Questionnaire (PBQ) (Behar, 1977) was used to rate hyperactivity, conduct and emotional problems at ages 2 and 3. At ages 4, 7, 9, 12, 16 and 21, the Strengths and Difficulties Questionnaire (SDQ) (Goodman, 1997)assessed peer problems in addition to hyperactivity, conduct and emotional problems. For a description of measure administration and scoring, and an illustration of the four behaviour problems domains across development, please refer to Supplementary Note 4. We also assessed mental health outcomes reported by the twins at age 21, such as mental health diagnoses and whether they have ever taken a medication for mental health.

*Composites*

Composites across ages and raters (Error: Reference source not found) were constructed using the hierarchical latent factor model, where the two first-order factors (externalizing and internalizing) loaded on a second-order factor of BPp. The hierarchical modelling was conducted using confirmatory factor analysis, based upon the results of exploratory factor analyses. For details on the exploratory and confirmatory factor analyses and composite construction, please refer to Supplementary Notes 5 and 6.

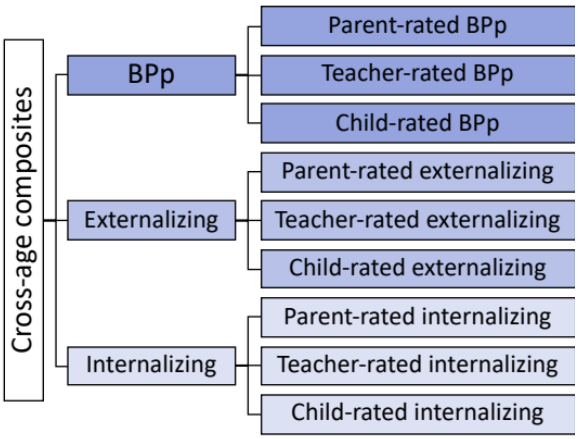
Using hierarchical confirmatory factor analysis, we constructed cross-age and cross-rater composites of BPp, externalizing and internalizing. We created cross-age composites from age 2 to 21 separately for each rater, which yielded nine cross-age composites (three rater-specific composites of BPp, three rater-specific composites of externalizing, three rater-specific composites of internalizing). Cross-rater composites were constructed separately in

childhood (ages 2-9), adolescence (ages 12 and 16) and early adulthood (age 21), which yielded nine cross-rater composites (i.e., three age-specific composites each of BPp, externalizing and internalizing). The construction of the cross-age and cross-rater composites is summarised in Supplementary Figures 1A and 1B, respectively. Phenotypic and genetic correlations between the cross-age and cross-rater composites are presented in Supplementary Note 7.

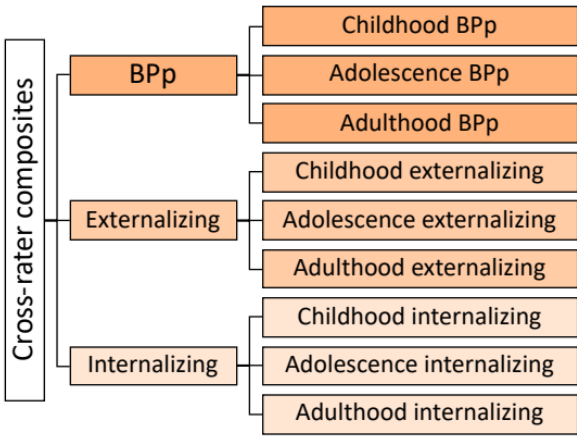
To explore whether simultaneously aggregating cross-age and cross-rater effects improves PGS heritability, we constructed cross-age-and-rater composites of BPp, externalizing and internalizing, using a three-level hierarchical model. In this model, we analysed behaviour problems at all ages (2-21) rated by parent, teacher and child (cross-age approach) to create the first-order factors of cross-age externalizing and internalizing, which were then combined across raters to create the second-order factors of cross-age-and-rater externalizing and internalizing, which subsequently gave rise to the third-order cross-age-and-rater BPp factor (Error: Reference source not foundC). We validated this approach by combining the behaviour problems scales across raters, but separately in childhood, adolescence and adulthood (cross-rater approach) on the first-order factor level, which yielded similar results.

In addition, we created single-trait composites for the four behaviour problems (hyperactivity, conduct problems, emotional problems and peer problems) in order to compare the effects of single-trait composites to BPp, externalizing and internalizing composites. Construction and results for the single-trait composites are presented in Supplementary Note 8.

A Cross-age composites.




B Cross-rater composites.




C Cross-age-and-rater composites.

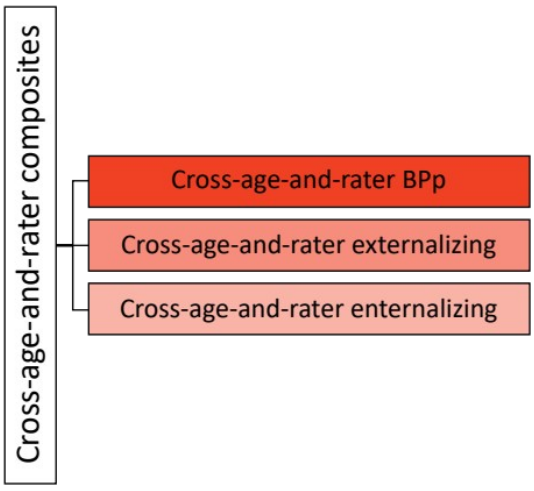



Figure 3. 1. Summary of the construction of the cross-age, cross-rater and cross-age-and-rater composites.

*Note*. This figure illustrates the components of the cross-age and cross-rater composites; it is not the hierarchical model used to create composites.

*Analyses*

All variables were regressed on 10 genetic principal components of population structure, genotyping chip, and genotyping batch (Allegrini et al., 2019). The standardized residuals from these regressions were used in all downstream analyses.

*Genome-wide polygenic scores (PGS heritability)*

Genome-wide polygenic scores are the estimated effects of thousands of genetic variants on a trait and are calculated as a weighted sum of alleles associated with the trait based on summary statistics from GWA studies (Dudbridge, 2013). The PGSs were constructed using LD-pred (Vilhjálmsson et al., 2015b), with the 1000 Genomes phase 1 sample as a reference for linkage disequilibrium structure. A detailed description of our LD-pred analytic strategy used to calculate PGSs has been published (Allegrini et al., 2019). We report results for PGSs created using a fraction of causal markers of 1.0 (i.e., assuming that all SNPs have non-zero effects), although results for PGS fractions 0.3 and 0.01 are presented in Supplementary Tables 2-5. In addition, we reported the PGS results separately for males and females (Supplementary Table 4). We estimated the joint prediction of the 15 PGSs (multi-PGS heritability) in a penalised regression elastic net model (Zou & Hastie, 2005) with hold-out evaluation of prediction accuracy. For details on the elastic net regularization analytic procedure, please refer to Supplementary Note 9 and Allegrini, Karhunen, et al. (2020).

*Multi-PGS effects*

To investigate whether a multi-PGS approach improved prediction as compared to a single-PGS approach, we compared the joint prediction of behaviour problems by the 15 PGSs (multi-PGS heritability) to individual predictions yielded by each of the 15 PGSs alone (single-PGS heritability). The multi-PGS heritability was estimated in elastic net regularization models and multiple regression models (using adjusted $R^2$). Single-PGS heritability was estimated using squared correlations ($r^2$) between each of the 15 PGSs and composites.

*Compositing effects*

We compared the multi-PGS heritability for the composites to the mean multi-PGS heritability for the individual constituent behaviour problem traits that comprise these composites (that is, the age-specific and rater-specific traits, which we will refer to as observed traits) (Supplementary Tables 2 and 5). For example, the multi-PGS heritability of

the cross-age parent-rated externalizing composite was compared to the mean of multi-PGS heritabilities of parent-rated hyperactivity and conduct scales across ages 2 to 21. Although the focus of this paper is to present a broad picture of the effect sizes, rather than formally testing for significant differences, in order to present the 95% confidence intervals of the estimates that index significance of differences, we also used a meta-analytic approach (Supplementary Note 10).

*Analysis of extremes*

In addition to continuous analyses, we investigated the ability of PGSs to predict differences in behaviour problems at the decile extremes of the multi-trait PGS, using the cross-age-and-rater composites of BPp, externalizing and internalizing as an example. We created multi-trait PGSs scores based on the individual predictor PGS coefficients from the elastic net regularization models (Supplementary Table 9), using the following formula:

$$GPSmulti_{trait\,i} = \sum_{j=1}^{k} GPS_{ij}\beta_j$$

where $GPSmulti_{trait}$ is the multi-trait PGS for individual $i$ in the full sample, $j$ {1, 2, …, 15} and denotes the PGS value for the k PGS for individual $i$ and ß indicates the elastic net coefficient of the association between the $jth$ predictor PGS and the composite that was learnt in the training set (see Supplementary Note 9 for details).

After assigning multi-trait PGS scores to each individual for BPp, externalizing and internalizing, we divided the sample into deciles and compared their mean phenotypic scores for BPp, externalizing and internalizing, as well as for other mental health outcomes.

*Twin heritability*

We compared the multi-PGS heritability results to heritability results from twin analyses (Supplementary Tables 6 and 8). The classical univariate twin design was employed to estimate broad heritability (additive and non-additive genetic variance) for individual behaviour problems as compared to composites. We performed twin analyses using OpenMx 2.0 for R (Neale et al., 2016; R Core Team, 2022). Additionally, we report the univariate twin model estimates separately for males and females (Supplementary Table 7). In order to investigate the impact of compositing on twin heritability, we contrasted twin heritability estimates for composites to the mean twin heritabilities for the observed traits. Significance of these differences was assessed using a meta-analytic approach (Supplementary Note 10).

# Results

*Multi-PGS heritability: cross-age and cross-rater composites*

Results of the multi-PGS prediction with elastic net regularization are shown in Figure 3. 2 for cross-age composites (Figure 3. 2A) and cross-rater composites (Figure 3. 2B). As shown in Supplementary Note 7, cross-age and cross-rater composites were substantially correlated phenotypically and genetically.

Compositing across ages increased multi-PGS heritability as compared to the mean multi-PGS heritability of observed traits for BPp, externalizing and internalizing (Figure 3. 2A). The greatest cross-age effect was found for parent-rated BPp, with the multi-PGS predicting 4.9% of the variance, as compared to the mean estimate of 0.6% when considering observed behaviour problems. Parent-rated multi-PGS heritabilities were 4.7% vs 0.8% for externalizing, but only 0.7% vs 0.4% for internalizing. For teacher ratings, the multi-PGS heritabilities were 3.7% vs 0.6% for BPp, 4.7% vs 0.4% for externalizing problems and 4% vs 0.8% for internalizing problems. Finally, for child ratings, the multi-PGS heritabilities were 2.7% vs 1.2% for BPp, 3.9% vs 1.4% for externalizing problems and 3.3% vs 0.9% for internalizing problems.

Compositing across raters also increased multi-PGS heritability in childhood, adolescence, and adulthood, as shown in Figure 3. 2B. For BPp, multi-PGS heritability for cross-rater composites was 2.9% as compared to the mean of 0.5% for the observed traits in childhood, 3.0% vs 0.8% in adolescence and 4.7% vs 0.8% in adulthood. For externalizing problems, multi-PGS heritabilities were 6.6% vs 0.5% in childhood, 3.6% vs 0.9% in adolescence and 2.7% vs 1.9% in adulthood. For internalizing problems, multi-PGS heritabilities were 1.8% vs 0.6% in childhood, 1.3% vs 0.7% in adolescence and 6.0% vs 0.8% in adulthood. The greatest cross-rater effect was found for externalizing problems in childhood, with the multi-PGS prediction of 6.6% as compared to 0.8% for observed traits. The analogous twin heritabilities (Figure 3. 2C and Figure 3. 2D) are discussed later.

Figure 3. 3 compares the multi-PGS approach to the single-PGS approach in prediction of cross-age and cross-rater composites. The first row of each of the six panels in Figure 3. 3 repeats the results in Figure 3. 2 showing the multi-PGS prediction using elastic net regularization for cross-age composites (Figure 3. 3A) and cross-rater composites (Figure 3.

3B). The second row shows that in most cases the elastic net regularization performed better than adjusted $R^2$ from simple multiple regressions. The rest of each panel shows the variance explained (correlation squared) by each of the 15 PGSs alone.

For BPp and externalizing problems, the ADHD PGS was the most predictive PGS for cross-age and cross-rater composites, predicting up to 2.6% of the variance in the cross-rater composite of adulthood BPp and 2.5% of the variance in the cross-age composite of teacher-rated externalizing. Other than the ADHD PGS, none of the individual PGSs predicted more than 1.5% of the variance. For internalizing problems, the most predictive PGS was the neuroticism PGS which predicted up to 1.4% of the variance in cross-age composites of child-rated internalizing and cross-rater childhood internalizing and 1.3% in cross-rater composites of childhood and adolescence internalizing.

*Twin heritability: cross-age and cross-rater composites*

Figure 3. 2C and Figure 3. 2D summarise twin heritability estimates for cross-age composites (Figure 3. 2C) and cross-rater composites (Figure 3. 2D) as compared to the mean estimates of twin heritability of the observed traits. In general, cross-age and cross-rater composites yielded greater twin heritability estimates than the observed traits.

The average heritability for cross-age composites was 61% as compared to 50% for the observed traits (Figure 3. 2C). The largest difference was found for parent-rated externalizing problems (82% vs 57%). The pattern of cross-age effects for twin heritability largely mirrored the multi-PGS heritability results, with the notable exception that twin heritability showed no increase for parent ratings of BPp, whereas this was one of the largest cross-age effects for multi-PGS heritability.

For cross-rater composites, the average heritability was 58% as compared to 51% for the observed traits (Figure 3. 2D). The average cross-rater effect across the three ages was strongest for externalizing problems (68% vs 55%), weaker for BPp (57% vs 54%) and absent for internalizing problems (51% vs 53%). The strongest cross-rater effect was observed for externalizing problems in childhood (79% vs 57%), which is consistent with the multi-PGS results. Similar to multi-PGS heritability, twin heritability for cross-rater

externalizing problems decreased from childhood (79%) to adolescence (67%) to adulthood (57%).

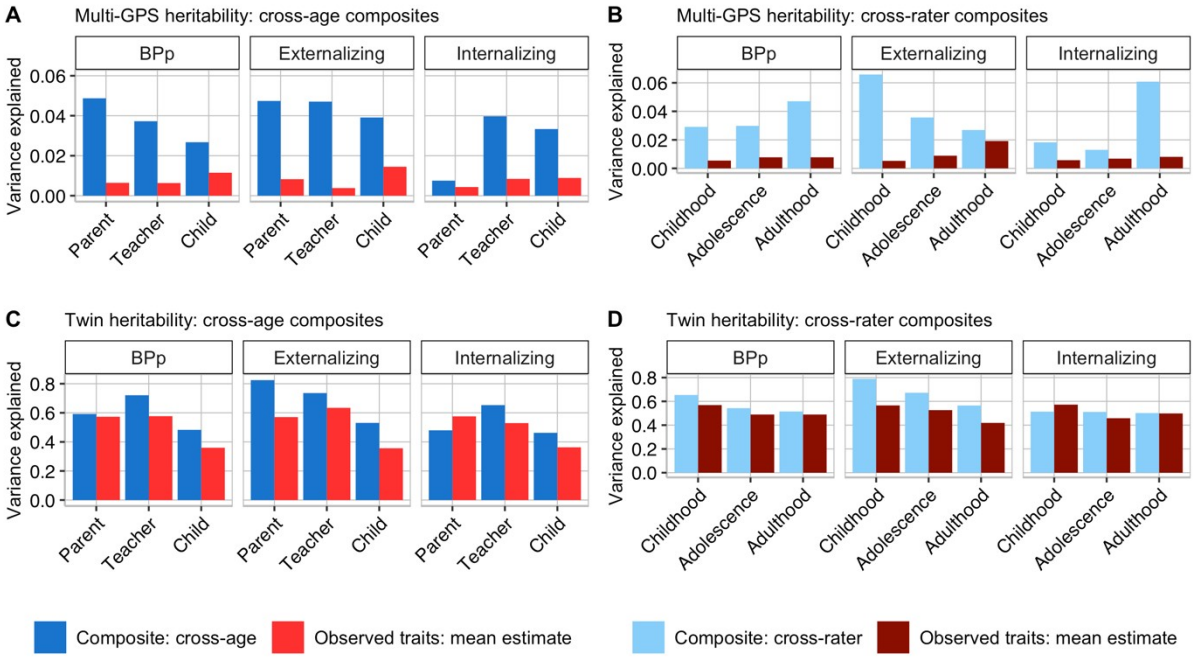



Figure 3. 2. Multi-PGS and twin heritability of cross-age composites and cross-rater composites, compared to the mean multi-PGS and twin heritability of observed traits.

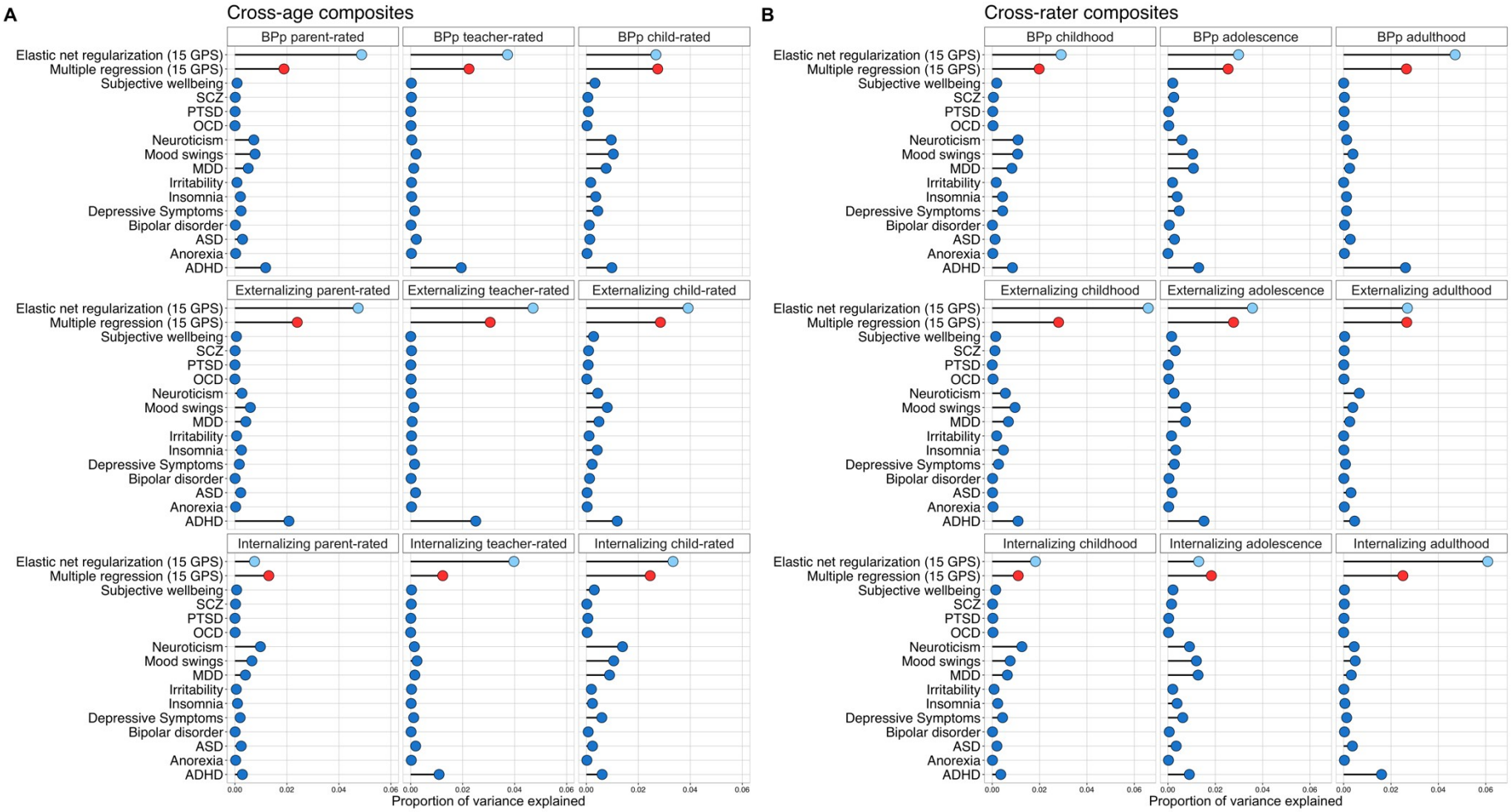



Figure 3. 3. Multi-PGS prediction as compared to single-PGS prediction of cross-age composites and cross-rater composites.

*Aggregated cross-age-and-rater effects*

Figure 3. 4 compares the multi-PGS heritability and twin heritability obtained for the combined cross-age-and-rater composites. Multi-PGS heritabilities of the cross-age-and-rater composites were similar to multi-PGS heritability of the cross-age composites (Figure 3. 4A) and cross-rater composites (Figure 3. 4B). Combining traits across ages and raters did not significantly improve PGS heritability. The variance explained by the PGSs in the combined cross-age-and-rater composites (3.3%) was similar to the average prediction yielded by cross-age and cross-rater composites (3.6%).

The twin analyses also showed that the benefits of cross-age and cross-rater compositing are not additive (Figure 3. 4C and Figure 3. 4D, respectively). The twin heritability for cross-age-and-rater composites (63%) was similar to the mean twin heritability yielded by cross-age and cross-rater composites (60%).

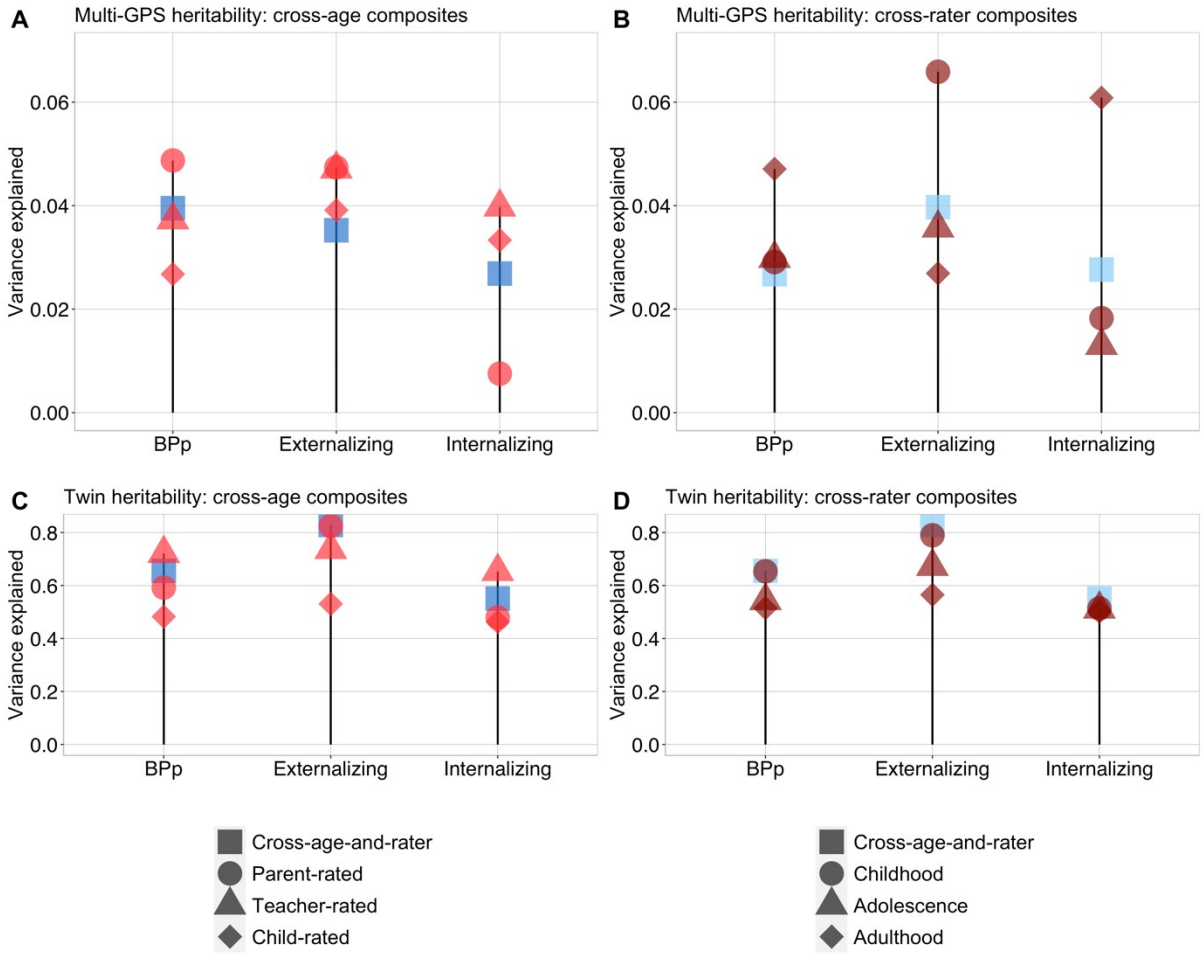



Figure 3. 4. Multi-PGS heritability and twin heritability of cross-age-and-rater composites as compared to cross-age composites and to cross-rater composites.

*Note*. Dark blue squares signifies the cross-age-and-rater composites constructed using the cross-age approach; lights blue squares signifies the cross-age-and-rater composites constructed using the cross-rater approach (see Method).

*Analysis of multi-trait PGS decile extremes*

Multi-trait PGS scores for BPp, externalizing and internalizing were created for each individual as explained earlier. We used these multi-trait PGS scores to divide the sample into deciles. Figure 3. 5 shows box plots, presenting the z-standardized scores for cross-age-and-rater BPp, externalizing and internalizing as a function of the multi-trait PGS deciles. Mean behaviour problems increase linearly from the lowest to the highest PGS deciles, with a scatterplot of scores as expected from the modest correlations between the multi-trait PGS and BPp (r= 0.19), externalizing (r= 0.20) and internalizing (r= 0.16). At the lowest and highest decile extremes, the differences are substantial: the mean standard score difference

between the lowest and highest PGS deciles is 0.61 for BPp, 0.67 for externalizing and 0.51 for internalizing.

Differences between the lowest and highest deciles were reflected in mental health outcomes. For example, 15% of individuals in the lowest multi-trait PGS decile for BPp and 15% in the lowest multi-trait PGS decile for externalizing have taken medication for mental health, compared to 20% in the highest BPp and 21% in the highest externalizing decile, although these differences are not statistically significant (odds ratio and 95% confidence intervals: 1.47 (0.84, 2.57) for BPp and 1.01 (0.58, 1.78) for externalizing). For the multi-trait internalizing PGS, 12% of individuals in the lowest decile have been diagnosed with depression, compared to 19% in the highest decile (odds ratio and 95% confidence intervals: 1.82 (1.03, 3.24)), while 7% of individuals in the lowest decile have been diagnosed with anxiety disorder, compared to 19% in the highest decile (odds ratio and 95% confidence intervals: 2.90 (1.53, 5.75)).

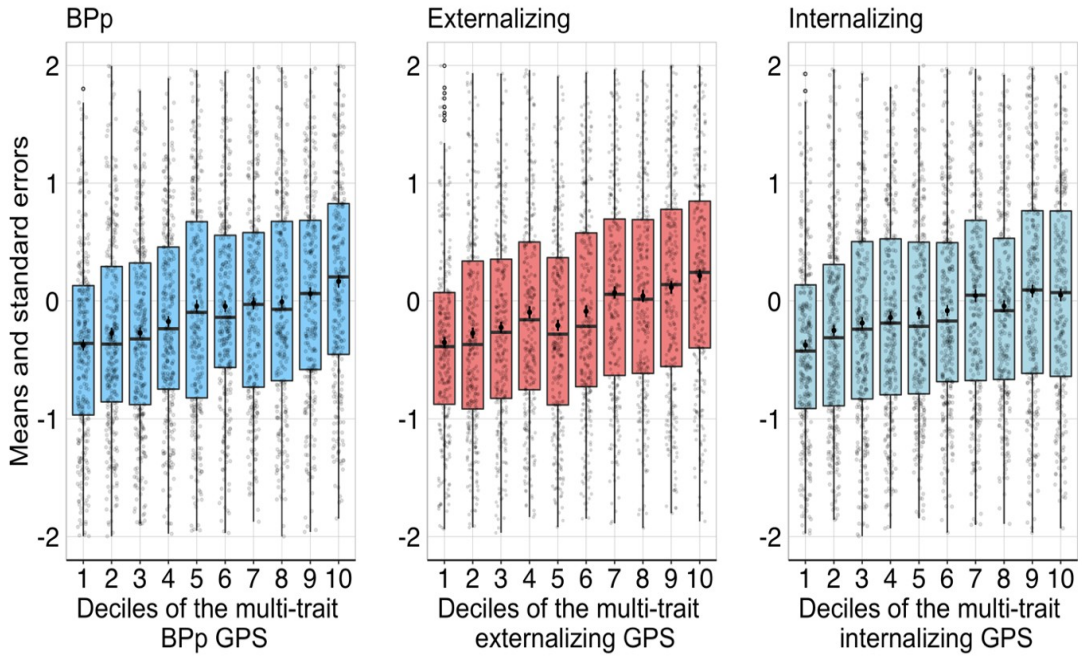



Figure 3. 5. Box plots showing z-standardized means and distributions of cross-age-and-rater multi-trait PGS scores for BPp, externalizing and internalizing.

*Note*. The boxes enclose 50% of the distribution of each PGS decile. Horizontal lines in boxes indicate the median values. Dots and error bars (vertical bars going through dots) in boxes indicate means and standard errors. Vertical lines outside the boxes indicate the normal distribution of PGS deciles. Point contours indicate outliers.

# Discussion

Our findings indicate that a multi-PGS approach using cross-age and cross-rater composites doubles the prediction estimates for general behaviour problems. These results are bolstered by twin analyses showing, although to a lesser extent, increased heritability for cross-age and cross-rater composites. The twin heritability estimates can be viewed as the prediction ceiling for PGSs because the twin design assesses the effect of all inherited DNA differences, not just SNPs shown to be associated with behaviour problems.

The multi-PGS weights for our cross-age-and-rater composites that simultaneously composite across age and across raters provide the best polygenic prediction currently available for children's BPp, externalizing and internalizing problems (Supplementary Table 9). These multi-PGS beta weights may be useful as genetic predictors of behaviour problems for other samples with DNA regardless of whether behaviour problem data is available. Just as PGSs can be created from DNA for any sample, our sets of multi-PGS weights can be used to create the strongest genetic estimates of BPp, externalizing and internalizing based on cross-age, cross-rater and cross-age-and-rater composites. These multi-trait PGSs can facilitate developmental, multivariate, and gene-environment interplay research because they are more predictive of behaviour problems than PGSs based on a single age, rater or trait. However, external validation in other samples is necessary to determine the degree to which these weights can be considered optimal.

Our goal of increasing PGS heritability led us to focus on compositing across ages, raters and traits, which should not be seen to denigrate the continued search for specific genetics effects for each age, rater or trait. Although we present results for the cross-age-and-rater multi-trait PGSs for conceptual consistency, we report weights for all the composites, which will allow researchers to construct developmental stage-specific and rater-specific multi-trait PGSs. However, it should be noted that the TEDS sample is largely of European ancestry, so are the samples involved in GWA studies from which the PGSs were derived, and the reported PGS results are likely to be less predictive in other ancestral populations (Peterson et al., 2019).

In order to condense the results, we focused on the second-order factors of externalizing and internalizing and a third-order factor representing BPp. However, we also present multi-PGS weights for the single-trait cross-age and cross-rater composites of hyperactivity, conduct

problems, emotional and peer problems (Supplementary Table 9). Although these traits generally showed increased PGS and twin heritability for cross-age and cross-rater composites, results for these trait-specific factors are subject to more measurement error, hence the results are less consistent than for the general factors representing BPp, externalizing and internalizing problems.

More research is needed to identify the mechanisms by which compositing increases PGS prediction. We had assumed that compositing across ages captures new genetic effects that come on board at later ages and that compositing across raters captures trans-situational genetic effects in the home for parent ratings and in school for teacher ratings. However, if different mechanisms are responsible for increasing PGS prediction for cross-age and cross-rater composites, we would expect that the effects of compositing across ages and across raters would be additive. Instead, we found that the combined cross-age-and-rater composites do not show increased PGS heritability, nor increased twin heritability as compared to the cross-age and cross-rater composites. Notably, we found that cross-age effects differ depending on rater, and, similarly, cross-rater effects depend on developmental stage. Furthermore, age and rater effects may correlate within, but not between developmental stages. In childhood, ratings were made mostly by parents, with teacher ratings appearing from age 7 and self-ratings appearing only at age 9. In adolescence, behaviour problems were rated equally by parents, teacher, and self-report, while in adulthood the teacher-ratings were no longer available. These interactions might explain in part why cross-age and cross-rater effects do not add up. However, going against this interaction hypothesis is the strong phenotypic overlap (~0.60) and genetic overlap (~0.65) between cross-age and cross-rater effects (Supplementary Note 7), which suggests that to a large extent the same mechanisms are responsible for increasing heritability for cross-age and cross-rater composites. A likely candidate is increased reliability, which could increase heritability for both cross-age and cross-rater composites. However, this reliability hypothesis requires the added assumption that compositing either across ages or across raters reaches a ceiling of reliability, so that there is no additional increase in heritability for cross-age-and-rater composites.

Our results are limited to existing GWA studies and will need to be updated as new GWA studies are reported. A more specific limitation is that we focused on the 15 most powerful GWA studies of psychopathology regardless of whether the GWA analysis targeted childhood disorders (autism spectrum disorder and ADHD) or disorders in adulthood (e.g.,

schizophrenia and depression). It is reasonable to expect that GWA studies targeted on childhood disorders will add disproportionately to the multi-PGS prediction of childhood behaviour problems. Supporting this expectation is our finding that the ADHD PGS was by far the strongest single PGS predictor of behaviour problems, especially for parent and teacher ratings of the BPp factor and externalizing problems (Figure 3. 3A). Nonetheless, multi-PGS predicted twice as much variance, with adult-based PGSs for neuroticism, mood swings, and major depressive disorder contributing to the prediction from the ADHD PGS, which could imply sequential comorbidity, where childhood ADHD can be predictive of both externalizing and internalizing problems in adolescence and emerging adulthood. The predictive power of ADHD PGS across developmental stages, raters and behaviour problems may also point towards overlapping longitudinal processes underlying both early risk and later externalizing and internalizing problems. Our approach is atheoretical and empirical in the sense that we would include any PGS, child-based or adult-based, that adds to the multi-PGS prediction of behaviour problems.

There is special value in focusing on PGS derived from adult-based GWA studies because they predict adult psychiatric disorders from childhood regardless of their associations with childhood behaviour problems. We chose not to do this at this time because our aim was to increase the DNA prediction of childhood behaviour problems, and we show that multi-PGS limited to extant adult-based GWA studies are weak predictors of childhood behaviour problems.

Although compositing doubles the predictive power of PGSs, the effect sizes remained modest (< 6%), suggesting that it is still a long way before we will reach levels of prediction that can be useful clinically in diagnosis, treatment, or prevention. Nonetheless, even with their current effect sizes, PGSs can be useful in clinical research. For example, we show (Figure 3. 5) that sizeable (Cohen's d ~ .5) mean differences in behaviour problems are observable at the multi-trait PGS decile extremes, such as the twofold greater risk of a depression diagnosis for individuals in the highest versus lowest decile of the internalizing PGS, although it should be noted that these results might not apply to other samples.

Increasing the power of PGSs to predict behaviour problems is the first step to exploring the biological and environmental mechanisms that mediate this prediction so that the predictive power of PGSs can be brought into more actionable space and, eventually, to prevention.

This ultimately depends on bigger GWA studies that can scoop up SNP associations of miniscule effect sizes, and whole-genome sequencing that can detect all differences in inherited DNA sequence, not just common SNPs (Wainschtein et al., 2022). Our results indicate that GWA studies can also increase their power to detect effects by conducting GWA analyses using cross-age or cross-rater composites instead of age- and rater-specific measures, to capture longitudinal and trans-situational effects, minimising the measurement error.

It seems likely that PGSs will eventually be sufficiently powerful predictors that they will affect not only clinical work but also society more generally (Plomin & von Stumm, 2022). DNA testing has already been incorporated in the national health services of Finland and Estonia and is being trialled in the UK. The next step will be DNA testing at birth. Francis Collins, the head of the US National Institutes of Health and leader of the Human Genome Project, predicted: "I am almost certain that complete genome sequencing will become part of newborn screening in the next few years.... It is likely that within a few decades people will look back on our current circumstance with a sense of disbelief that we screened for so few conditions" (Collins, 2010, p. 50). The current five-year plan of the Chinese government is to sequence the DNA of at least 50% of the 15 million babies born each year in China (Metzl, 2019a).

Medical uptake of DNA testing is driven by its potential to predict and prevent rare single-gene disorders as well as preventable common medical disorders, such as cardiovascular disease. However, the same genomic results from DNA testing can also be used to create PGSs for many other traits, including behaviour problems. Now is the time to discuss how to maximise clinical benefits and minimise risks.-

# Chapter 4— Explaining the influence of nonshared environment (NSE) on symptoms of behaviour problems from preschool to adulthood: Mind the missing NSE gap.

This chapter is presented in a form of a published paper. It is a modified version of the following publication:

Gidziela, A., Malanchini, M., Rimfeld, K., McMillan, A., Ronald, A., Viding, E., Pike, A., Asbury, K., Eley, T.C., von Stumm, S. and Plomin, R. (2023), Explaining the influence of non-shared environment (NSE) on symptoms of behaviour problems from preschool to adulthood: mind the missing NSE gap. J Child Psychol Psychiatr, 64: 747-757. https://doi.org/10.1111/jcpp.13729

Supplementary Notes, Tables and Figures are included in Appendix 3.

## Abstract

*Background*

Individual differences in symptoms of behaviour problems in childhood and adolescence are not primarily due to nature or nurture—another substantial source of variance is nonshared environment (NSE). However, few specific environmental factors have been found to account for these NSE estimates. This creates a 'missing NSE' gap analogous to the 'missing heritability' gap, which refers to the shortfall in identifying DNA differences responsible for heritability. We assessed the extent to which variance in behaviour problem symptoms during the first two decades of life can be accounted for by measured NSE effects after controlling for genetics and shared environment.

*Method*

The sample included 4,039 pairs of twins in the Twins Early Development Study whose environments and symptoms of behaviour problems were assessed in preschool, childhood, adolescence and early adulthood via parent, teacher, and self-reports. Twin-specific environments were assessed via parent-reports, including early life adversity, parental feelings, parental discipline and classroom environment. Multivariate longitudinal twin model-fitting was employed to estimate the variance in behaviour problem symptoms at each age that could be predicted by environmental measures at the previous age.

*Results*

On average across childhood, adolescence and adulthood, parent-rated NSE composite measures accounted for 3.4% of the reliable NSE variance (1.0% of the total variance) in parent-rated, symptoms of behaviour problems, 0.5% (0.1%) in teacher-rated symptoms and 0.9% (0.5%) in self-rated symptoms after controlling for genetics, shared environment and error of measurement. Cumulatively across development, our parent-rated NSE measures in preschool, childhood and adolescence predicted 4.7% of the NSE variance (2.0% of the total variance) in parent-rated and 0.3% (0.2%) in self-rated behaviour problem symptoms in adulthood.

*Conclusions*

The missing NSE gap between variance explained by measured environments and total NSE variance is large. Home and classroom environments are more likely to influence behaviour problem symptoms via genetics than via NSE.

# Introduction

Symptoms of behaviour problems are characterised by abnormalities in behavioural, cognitive and adaptive functioning that often begin in childhood and persist throughout the life course (Kessler et al., 2005; Reef, Van Meurs, et al., 2010). An important source of individual differences in symptoms of behaviour problems are nonshared environmental (NSE) effects (Plomin, 2011; Plomin et al., 2001; Plomin & Daniels, 1987). Shared environmental influences denote what is usually meant by the word nurture – environmental influences that make children growing up in the same family similar (Harris, 1998). NSE refers to residual environmental influences that do not contribute to similarity of family members. In other words, NSE effects are what makes siblings growing up in the same family environment different (Knopik et al., 2017). Examples of NSE effects include differential treatment that the twins receive from parents, as well as differences in external environment, such as classroom or peer group environment.

The finding that NSE influences behaviour problem symptoms in childhood and adolescence, while genetic and shared environmental influences are modest, is one of the most important and consistently replicated findings from genetic research (Plomin et al., 2016). The importance of NSE was first pointed out almost 50 years ago (Loehlin & Nichols, 1976), first reviewed in 1987 (Plomin & Daniels, 1987), and first popularised in 1998 (Harris, 1998). Yet, little progress has been made towards identifying specific NSE factors that predict symptoms of behaviour problems (Dunn & Plomin, 1990; Turkheimer & Waldron, 2000). In 2000, a meta-analysis of 43 papers relating sibling differences in environmental measures to sibling differences in outcomes concluded that ‘measured non-shared environmental variables do not account for a substantial portion of the non-shared variability’(Turkheimer & Waldron, 2000).

(Turkheimer & Waldron, 2000)review suggested that research into identifying the drivers of NSE influences was off to a good start. Of the variance in sibling differences in behavioural adjustment, personality and cognitive traits, 1% could be attributed to family constellation (i.e., variables related to birth order and age differences between siblings), 2% to differential parenting behaviour, 2% to differential sibling interaction and 5% to differential peer or teacher interaction (Turkheimer & Waldron, 2000). Moreover, these effects were largely independent, and together they account for 13% of the between-sibling variance (Turkheimer

& Waldron, 2000). However, estimates of NSE influence are halved in designs that controlled for genetics (Turkheimer & Waldron, 2000). Another issue is that Turkheimer and Waldron's (2000) meta-analysis focused on variance in sibling differences, not total variance in behavioural adjustment, personality, and cognitive traits. Translating the effect sizes for sibling differences to total variance estimates suggests that the estimates of NSE effects would be at least halved again when NSE variance is 0.50.

Two genetically sensitive designs have been used to disentangle genetic and environmental sources of sibling differences: The monozygotic (MZ) twin differences design and the multivariate genetic design (N. G. Martin & Eaves, 1977; Rovine, 2013). The MZ differences design involves correlating measured environmental differences within pairs of MZ twins with MZ differences in behaviour problem symptoms. This design captures NSE influence because MZ twins reared together are identical in terms of inherited DNA differences and shared environmental influences, so all their differences are due to NSE (Vitaro et al., 2009). The first MZ differences study (Pike, Hetherington, et al., 1996) was part of the Nonshared Environment and Adolescent Development (NEAD) study, a longitudinal study of 720 families including twins and adopted children aimed at exploring the NSE effects on development of adolescent behaviour and psychopathology (Neiderhiser et al., 2007; Reiss et al., 1994; Reiss & Hetherington, 2009). The MZ differences study found moderate correlations between MZ differences in parental negativity and MZ differences in adolescent depression and antisocial behaviour (Pike, Hetherington, et al., 1996).

MZ differences studies have consistently reported low-to-moderate correlations between parenting style and behaviour problem symptoms. For example, MZ twin differences in maternal negativity correlated 0.49 and 0.17 with differences in antisocial behaviour at age 5 as rated by mothers and teachers, respectively (Caspi et al., 2004). Subsequently, these findings were replicated in a sample of 7-year-olds, by correlating MZ twin differences in negative parental discipline with differences in conduct problems and callous-unemotional traits, which yielded estimates of 0.46 and 0.27 for parent ratings and 0.12 and 0.07 for teacher ratings, respectively (Viding et al., 2009).

Multivariate genetic analysis is better suited than the MZ differences analysis to answer the question of how much total variance in behaviour problem symptoms can be predicted by measured environments (Pike, McGuire, et al., 1996). Analogous to univariate genetic

analysis that decomposes variance in a trait into genetic and environmental components of variance, multivariate genetic analysis decomposes the covariance between two traits – in this case, the covariance between an environmental measure and a measure of behaviour problems – into genetic, shared environmental and NSE components of covariance (Knopik et al., 2017).

The first multivariate genetic analysis of this type investigated child-specific family environment measures and behaviour problem symptoms in 719 same-sex pairs of adolescent siblings aged 10 to 18 years (Pike, McGuire, et al., 1996). A multi-informant composite index of maternal negativity toward their child as rated by the mother, father and sibling correlated phenotypically 0.33 with a composite measure of the target child's depressive symptoms. Squaring the correlation of 0.33 indicated that 11% of the total variance in depressive symptoms could be predicted by maternal negativity.

Pike, McGuire, et al. (1996)found that NSE effects explained 1.2% of the reliable variance in depressive symptoms. Shared environment also explained 1.2% of variance, and genetic effects accounted for 17.6%.  The reason why these estimates sum to 20%, greatly exceeding the 11% of total variance explained phenotypically by the measure of maternal negativity, is that the genetic (a), shared environmental (c) and NSE (e) paths from maternal negativity explain reliable variance in depressive symptoms. Error of measurement of the total variance in depressive symptoms is included in the a, c and e residual estimates.

Another multivariate twin study conducted using a sample of 808 same-sex 11-year-old twin pairs from the Minnesota Twin Family Study reported findings consistent with those from the NEAD study (Burt et al., 2003). A multi-informant measure of parent-child conflict was found to explain 1% of the total variance in externalizing disorders via NSE, with 20% accounted for by genetics and 12% by shared environment . Modest NSE prediction was also reported in a multivariate twin study involving 1,314 adolescent twin pairs from the Twin study of CHild and Adolescent Development (TCHAD), where parental criticism predicted less than 1% of the total variance in antisocial behaviour in boys and 0.4% in girls via NSE (Narusyte et al., 2007). In contrast, genetics accounted for 12% in boys and 18% in girls.

The current research follows through on three issues raised in the NEAD reports (Pike, Hetherington, et al., 1996; Pike, McGuire, et al., 1996). First, rather than limiting the analysis to contemporaneous assessments of environment and behaviour problems symptoms, the present study uses a longitudinal twin design to systematically assess the extent to which environmental measures at one age can predict symptoms of behaviour problems at a later age via NSE after controlling for genetics and shared environment. Although this longitudinal approach embedded in a multivariate genetic design provides some purchase on causal inference, our goal here was prediction rather than addressing the complex issue of causality (Plomin & von Stumm, 2022). Second, instead of analysing individual environmental measures, our analyses assess the effect of multiple environmental measures on symptoms of behaviour problems. For that purpose, we created the multi-environment composites that included measures of early life adversity, parental feelings and discipline and classroom environment. Third, we compare results for same-rater (i.e., parent, teacher, and self-reports) and cross-rater analyses to test for rater effects in prediction of behaviour problem symptoms.

In summary, the present study tested the longitudinal NSE prediction of behaviour problem symptoms as rated by parents, teachers, and the twins themselves from parent-rated environmental measures at earlier ages. We predicted behaviour problem symptoms in childhood at ages 7 and 9 from environmental measures in preschool (ages 3 and 4), behaviour problem symptoms in adolescence (ages 12 and 16) from environmental measures in childhood, and behaviour problem symptoms in adulthood (age 21) from environmental measures in adolescence. We also investigated the extent to which symptoms of behaviour problems in adulthood are predicted cumulatively from NSE-related environmental processes in preschool, childhood, and adolescence.

# Method

Our hypotheses and analyses were preregistered with the Open Science Framework (OSF) (https://osf.io/rbv9q) prior to analysing the data. Our detailed hypotheses are listed in Supplementary Note 1. Our analysis scripts are available on the OSF page and https://github.com/CoDEresearchlab/NSE_BP.

## *Sample*

Our sampling frame consisted of twins born in England and Wales between 1994 and 1996 who have been enrolled in the Twins Early Development Study (TEDS) (Rimfeld, Malanchini, Spargo, et al., 2019).The present analyses included up to 4,039 pairs of twins with requisite environmental and behaviour problem data from infancy to early adulthood. Details of the sample and its representativeness are provided in Supplementary Note 2 and Supplementary Table 1.

## *Measures*

### *Environmental measures*

We selected parent-reported environmental measures for which twins in the same family could have different scores such as twin-specific parenting, in contrast to family-general measures such as parental education for which both twins have the same score, and which cannot be used in analyses of NSE. However, such 'twin-specific' environmental measures do not assess completely different experiences of twins in a family. That is, twin correlations for such measures are often substantial, this covariance is included in the shared environment component in multivariate genetic analysis so that only the twin-specific component is ascribed to NSE. Initially, measures included virtually all environmental items and scales available in TEDS data dictionary (https://www.teds.ac.uk/datadictionary/home.htm). We grouped the environmental measures in three age groups: preschool (ages 3 and 4), childhood (ages 7 and 9) and adolescence (ages 12 and 16).

As explained in Supplementary Note 3, we reduced the hundreds of twin-specific environmental items available in the TEDS data dictionary at each age to a single 'poly-E' composite after excluding measures with low correlations with behaviour problem symptoms at the subsequent developmental stage (cut-off= 0.20, determined based on the distribution of correlations as illustrated in Supplementary Figure 1). We also excluded highly correlated

environmental measures. This criterion was applied as we created a 'poly-E' composite at each age using a penalized regression elastic net regularization with hold-out sample tests of prediction accuracy. This procedure overcomes problems of multicollinearity as well as overfitting (Allegrini, Karhunen, et al., 2020; Gidziela et al., 2022; Zou & Hastie, 2005). The poly-E composites included measures of early life adversity (aka environmental risk) (Cox et al., 1987; Matheny et al., 1995), parental feelings and discipline (Deater-Deckard, 2000; Deater-Deckard et al., 1998), and classroom environment (Ainley & Bourke, 1992). For details of the construction of the poly-E composites, see Supplementary Note 4. Environmental variables surviving the selection process are listed and described in Supplementary Table 2.

*Behaviour problem measures*

Hyperactivity-inattention, conduct problems, emotional problems and peer relationship problems were assessed using the Preschool Behaviour Questionnaire (PBQ) (Behar, 1977) at age 3 and Strengths and Difficulties Questionnaire (SDQ) (Goodman, 1997)from age 4 to age 21. The four scales were combined in preschool (ages 3 and 4), childhood (ages 7 and 9), adolescence (ages 12 and 16) and adulthood (age 21) as rated by parents (ages 3-21), by teachers (ages 7-12) and by the twins (ages 9-21). For each of the four scales and three raters, mean scores were calculated across ages in childhood and in adolescence or set to missing if more than half of the data was missing. This data reduction resulted in 36 behaviour problem symptoms variables for the four scales, three ages and three raters, as summarised in Supplementary Figure 2.

*Analyses*

We used univariate twin model-fitting analyses to estimate components of variance for the 36 behaviour problem symptoms variables. Bivariate twin model-fitting (Cholesky decomposition) analysis (see Supplementary Note 5 and Supplementary Figure 3) was used to estimate the variance in behaviour problem symptoms variables at one developmental stage (e.g., childhood) predicted by the poly-E composite at the previous stage (e.g., preschool). Analyses were conducted for same-rater comparisons (i.e., predicting parent-rated behaviour problem symptoms from parent-rated poly-E composites), as well as for cross-rater comparisons (i.e., predicting teacher and self-rated behaviour problem symptoms from parent-rated poly-E composites). Multivariate twin model-fitting analysis was also used to

estimate the variance in parent and self-rated behaviour problem symptoms at age 21 predicted cumulatively by parent-rated poly-E composites from preschool, childhood and adolescence (Supplementary Figure 3). For details of these twin analyses, see Supplementary Note 5.

We compared the bivariate twin model-fitting results to results from analyses using the MZ differences design. As explained in Supplementary Note 6, we created relative difference scores for MZ twins for the poly-E variables and correlated them with MZ difference scores for the behaviour problem symptoms variables. As an alternative to MZ difference scores, we also created indices of within-pair differences for the poly-E and behaviour problem variables from the standardized residuals after regressing Twin 1's scores on Twin 2's scores. We correlated these residualised scores and simple MZ difference scores with behaviour problem symptoms of individuals to estimate the NSE effect on variation in behaviour problem symptoms.

## Results

We present results in four sections. The first section summarises estimates of the NSE, genetic and shared environmental variance for behaviour problem symptoms and poly-E composites over development. The second section describes contemporaneous as well as longitudinal phenotypic correlations between poly-E measures and behaviour problem symptoms. The third section describes the prediction of behaviour problem symptoms at each age from environmental measures at the previous age. The fourth section addresses the cumulative prediction of behaviour problem symptoms in adulthood from environmental measures in preschool, childhood, and adolescence. The fifth section outlines results of MZ differences and residualised scores analyses.

### *Univariate twin analyses*

Figure 4. 1 illustrates the NSE, genetic and shared environmental components of variance from the univariate twin model fitting of behaviour problem symptoms (panel A) and poly-E composites (panel B). These estimates, along with 95% confidence intervals are presented in Supplementary Table 3 for the total sample. Supplementary Tables 4 and 5 show that results are not significantly different between males and females, as shown by the overlapping 95% confidence intervals.

*Behaviour problem symptoms*

For parent-rated behaviour problem symptoms, NSE influences plus error of measurement on average accounted for about a third (37%) of the variance (43% for hyperactivity, 30% for conduct problems, 41% for emotional problems and 33% for peer problems), with three quarters accounted for by genetic influences (60%) and with little to no shared environmental contribution (3%) (Figure 4. 1A). For teacher-rated behaviour problem symptoms, the mean NSE estimate was 40% and ranged from 33% for hyperactivity to 53% for emotional problems, while the rest of the variance was accounted for by genetic influences (60%). The largest average NSE estimates across developmental stages were observed for self-rated symptoms of behaviour problems, 59% on average, ranging from 56% for peer problems to 61% for emotional problems, with genetics being the second largest contributing factor (39%) and with little shared environmental influences (2%). Across all four behaviour problems measures, NSE accounted for more variance in adulthood (54%) compared to preschool (42%), childhood (41%) and adolescence (42%).

*Poly-E composites*

As seen in Figure 4. 1B, across ages, NSE accounted for much less of the variance in the poly-E composites as compared to behaviour problem symptoms (Figure 4. 1A). In the preschool years, NSE accounted for only 8% of the variance in poly-E composites, with most of the variance explained by shared environmental influences (71%) and with a moderate contribution of genetics (22%). In childhood, NSE influences explained 23% of the variance, with genetic influences accounting for 58% and shared environment for 19%. In adolescence, NSE accounted for 14% of the variance, with similar contributions from genetics (45%) and shared environment (41%).

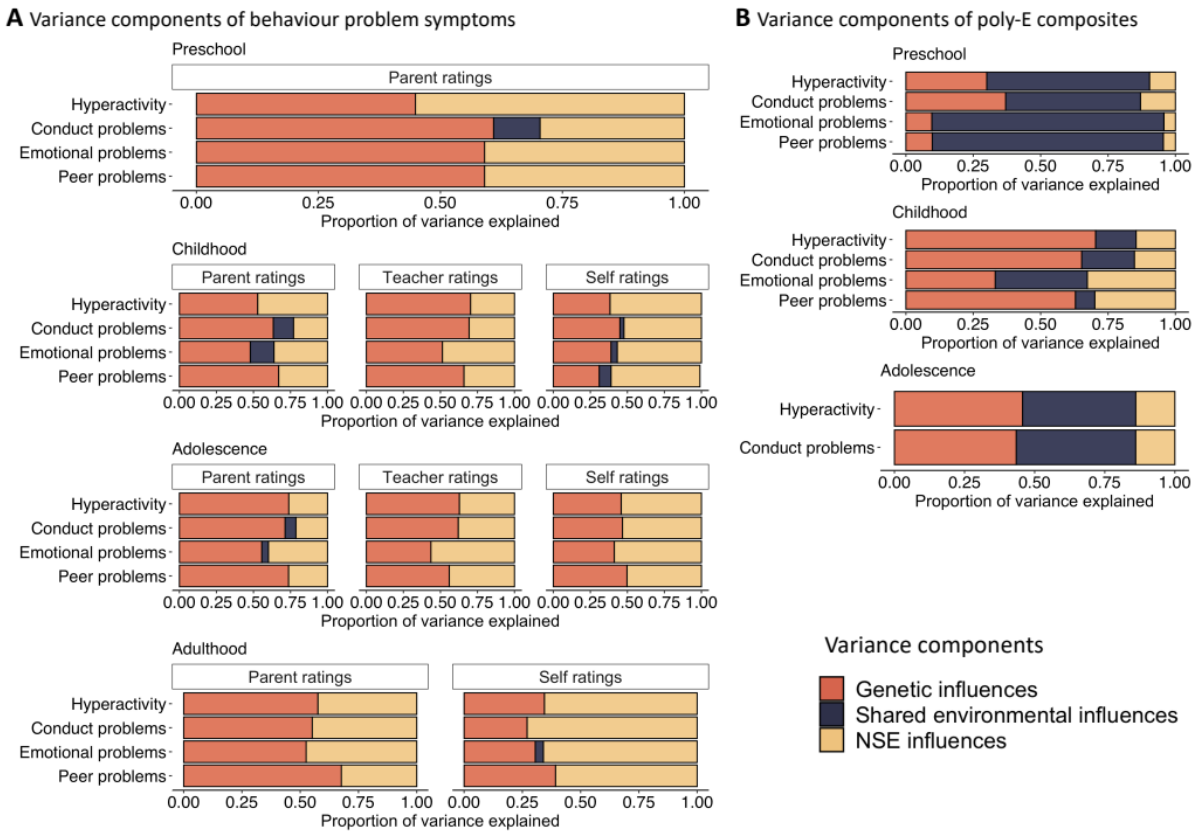



Figure 4. 1. Genetic, shared environmental and nonshared environmental (NSE) components of variance in behaviour problem symptoms (panel A) and poly-E composites (i.e., environmental measures) (panel B) across development, rated by parents, teacher and the twins themselves.

*Note*. Different poly-E composites were created for each behaviour problem measure, i.e., hyperactivity, conduct problems, emotional problems and peer problems. Results for poly-E composites for emotional problems and peer problems in adolescence are not included due to weak correlations with E measures ($r < 0.20$), meaning that they fell below our criterion for inclusion in poly-E composites.

*Phenotypic correlations*

Although we focus on the longitudinal prediction of behaviour problem symptoms from earlier environmental measures, contemporaneous correlations between poly-E composites and symptoms of behaviour problems (i.e., correlations between poly-E composites in preschool, childhood and adolescence and behaviour problem symptoms at the same age) are shown in Supplementary Figure 5. As expected, these contemporaneous correlations are greater than the longitudinal correlations between behaviour problem symptoms and earlier environmental measures.

The average contemporaneous correlations between poly-E composites and parent-rated behaviour problem symptoms were 0.38 in preschool, 0.55 in childhood and 0.43 in adolescence. In contrast, the mean longitudinal correlations between preschool, childhood and adolescence poly-E measures and parent-rated behaviour problem symptoms at subsequent developmental stages (i.e., childhood, adolescence and adulthood) were 0.31, 0.41 and 0.25, respectively.

*Bivariate twin analyses*

Table 4. 1 presents the proportions of variance in behaviour problem symptoms in childhood, adolescence and adulthood predicted by environmental measures (poly-E composites) at the previous age. Supplementary Figure 4 shows the NSE path analytic results underlying Table 4. 1. Supplementary Table 6 presents the full model-fitting results for genetic, shared environmental and NSE components of covariance, as well as 95% confidence intervals for path estimates for the total sample. Supplementary Tables 7 and 8 contain results separately for males and females, which are highly similar.

| Behaviour problem measure | Rater | Developmental stage | % of variance explained via NSE | | % of variance explained via genetics | | % of variance explained via shared environment | |
|---|---|---|---|---|---|---|---|---|
| | | | % of NSE variance | % of total variance | % of genetic variance | % of total variance | % of shared environmental variance | % of total variance |
| | | | | | | | | |
| Hyperactivity | Parent | Childhood | 2.22% | 1.06% | 32.45% | 16.05% | 100.00% | 1.33% |
| Conduct problems | | | 2.34% | 0.54% | 34.15% | 21.45% | 19.67% | 2.70% |
| Emotional problems | | | 0.46% | 0.17% | 1.10% | 0.53% | 52.79% | 8.32% |
| Peer problems | | | 0.96% | 0.32% | 0.55% | 0.33% | 100.00% | 4.57% |
| | | | | | | | | |
| Hyperactivity | Teacher | Childhood | 0.12% | 0.04% | 12.24% | 8.46% | 100.00% | 0.09% |
| Conduct problems | | | 0.01% | 0.00% | 12.24% | 8.40% | 100.00% | 0.02% |
| Emotional problems | | | 0.46% | 0.22% | 0.19% | 0.10% | 100.00% | 0.53% |
| Peer problems | | | 0.20% | 0.07% | 1.03% | 0.66% | 100.00% | 0.52% |
| | | | | | | | | |
| Hyperactivity | Self | Childhood | 0.46% | 0.28% | 17.77% | 6.78% | 100.00% | 0.06% |
| Conduct problems | | | 0.48% | 0.25% | 16.32% | 7.36% | 62.26% | 1.63% |
| Emotional problems | | | 0.07% | 0.04% | 2.82% | 1.09% | 94.37% | 4.15% |
| Peer problems | | | 0.08% | 0.05% | 1.94% | 0.60% | 30.10% | 2.61% |
| | | | | | | | | |
| Hyperactivity | Parent | Adolescence | 9.11% | 2.30% | 35.67% | 25.13% | 100.00% | 0.12% |
| Conduct problems | | | 6.02% | 1.27% | 29.61% | 20.87% | 7.56% | 0.54% |
| Emotional problems | | | 4.33% | 1.72% | 18.97% | 10.51% | 34.13% | 1.60% |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Peer problems | | | 7.71% | 1.98% | 32.94% | 23.76% | 100.00% | 0.14% |
| | | | | | | | | |
| Hyperactivity | Teacher | Adolescence | 2.04% | 0.75% | 13.62% | 8.49% | 99.99% | 0.00% |
| Conduct problems | | | 0.74% | 0.28% | 4.52% | 2.78% | 100.00% | 0.22% |
| Emotional problems | | | 0.05% | 0.03% | 7.83% | 3.35% | 100.00% | 0.51% |
| Peer problems | | | 0.19% | 0.08% | 17.56% | 9.74% | 100.00% | 0.00% |
| | | | | | | | | |
| Hyperactivity | Self | Adolescence | 2.28% | 1.23% | 19.33% | 8.76% | 100.00% | 0.14% |
| Conduct problems | | | 2.96% | 1.59% | 12.10% | 5.38% | 100.00% | 1.45% |
| Emotional problems | | | 1.60% | 0.94% | 5.37% | 2.12% | 100.00% | 1.33% |
| Peer problems | | | 0.39% | 0.19% | 24.61% | 12.17% | 100.00% | 0.07% |
| | | | | | | | | |
| Hyperactivity | Parent | Adulthood | 0.77% | 0.32% | 13.52% | 7.59% | 100.00% | 0.11% |
| Conduct problems | | | 0.32% | 0.14% | 20.27% | 11.07% | 100.00% | 0.31% |
| | | | | | | | | |
| Hyperactivity | Self | Adulthood | 0.08% | 0.05% | 3.24% | 1.11% | 100.00% | 0.33% |
| Conduct problems | | | 0.07% | 0.05% | 14.36% | 3.88% | 100.00% | 0.03% |

Table 4. 1. Nonshared environmental (NSE), genetic and shared environmental results of the bivariate Cholesky model of poly-E composites (i.e., environmental measures) in preschool, childhood and adolescence predicting variance in measures of behaviour problem symptoms in subsequent developmental stages.

Prediction of behaviour problem symptoms from poly-E composites via NSE

Table 4. 1 summarises the NSE results of Cholesky decomposition analysis of parent-rated poly-E composites and behaviour problem symptoms (parent, teacher and self-rated). As shown in Supplementary Figure 3, the Cholesky model decomposes the variance in behaviour problem symptoms into variance explained by the environmental measure and the rest of the variance independent of the environmental measure. For example, the NSE estimate for parent-rated hyperactivity in childhood (i.e., the sum of squared paths e12 and e22) is 48%. The preschool poly-E composite explains 2.2% of this NSE variance, or 1.1% of the total variance. In other words, more than 98% of the total variance in childhood hyperactivity is not explained by NSE processes related to the poly-E composite.

On average, poly-E composites predicted 3.4% of the reliable NSE variance (1.0% of the total variance) in parent-rated symptoms of behaviour problems, 0.5% (0.2%) in teacher-rated symptoms and 0.9% (0.5%) in self-rated symptoms. Poly-E composites accounted for more variance in behaviour problem symptoms in adolescence (3.1% of the NSE variance or 1.0% of the total variance), than in childhood (0.7% or 0.3%) and in adulthood (0.3% or 0.1%). Similar proportions of NSE variance (or total variance) were accounted for in hyperactivity (2.1% or 0.8%), conduct problems (1.6% or 0.5%), emotional problems (1.2% or 0.5%) and peer problems (1.6% or 0.5%).

Prediction of behaviour problem symptoms from poly-E composites via genetics

As presented in Table 4. 1, genetics accounted for much more of the poly-E prediction of behaviour problem symptoms. On average, genetic processes explained 13.7% of the total variance in parent ratings of symptoms of behaviour problems, 5.3% in teacher and 4.9% in self reports. Consistently higher prediction across developmental stages emerged for hyperactivity (10.3%) and conduct problems (10.2%) as compared to emotional (3.0%) and peer problems (7.9%). The mean proportion of total variance explained via genetics was higher in adolescence (11.1%) than in childhood (6.0%) and adulthood (5.9%).

Prediction of behaviour problem symptoms from poly-E composites via shared environment

Table 4. 1 also presents Cholesky results for parent, teacher, and self-rated behaviour problem symptoms as predicted by poly-E composites via shared environment. In childhood and adolescence, the variance explained by poly-E composites via shared environment was

modest (2.2% and 0.5%, respectively). Shared environmental influences were not present in behaviour problem symptoms in adulthood.

*Multivariate twin analyses*

Table 4. 2 summarises results of Cholesky decomposition analysis predicting parent- and self-rated hyperactivity and conduct problems in adulthood cumulatively from parent-rated poly-E composites in preschool, childhood, and adolescence, via NSE, genetics and shared environment. Supplementary Figure 6 shows the NSE path models summarised in Table 2. Supplementary Table 9 includes the full model-fitting results and confidence intervals. Results for emotional problems and peer problems are not included due to weak correlations with environmental measures ($r < 0.20$) that they fell below our criterion for inclusion in poly-E composites.

| Behaviour problem measure | Rater | Developmental stage | % of variance explained via NSE | | % of variance explained via genetics | | % of variance explained via shared environment | |
|---|---|---|---|---|---|---|---|---|
| | | | % of NSE variance | % of total variance | % of genetic variance | % of total variance | % of shared environmental variance | % of total variance |
| Hyperactivity | Parent | Adulthood | 4.57% | 1.91% | 20.75% | 11.00% | - | 1.00% |
| Conduct problems | Parent | Adulthood | 4.85% | 2.17% | 20.75% | 11.00% | - | 1.00% |
| Hyperactivity | Self | Adulthood | 0.52% | 0.34% | 12.50% | 4.00% | - | 1.00% |
| Conduct problems | Self | Adulthood | 0.13% | 0.10% | 25.00% | 6.00% | - | 2.00% |

Table 4. 2. Nonshared environmental (NSE), genetic and shared environmental results of the multivariate Cholesky model of poly-E composites (i.e., environmental measures) in preschool, childhood and adolescence cumulatively predicting variance in hyperactivity and conduct problems in adulthood.

*Cumulative (longitudinal) prediction via NSE*

The NSE variance in parent-rated hyperactivity in adulthood is 42%. Cumulatively, the poly-E measures in preschool, childhood and adolescence predict 4.6% of this NSE variance, or 1.9% of the total variance in hyperactivity. On average, poly-E composites cumulatively across development predicted 4.7% of the NSE variance (2.0% of the total variance) in parent-rated and 0.3% (0.2%) in self-rated symptoms of behaviour problems in adulthood. Similar proportions of the NSE variance were accounted for in conduct problems (2.5% or 1.1% of the total variance) and hyperactivity (2.5% or 110%).

*Cumulative (longitudinal) prediction via genetics*

Poly-E composites cumulatively across development predicted 11.0% of the total variance in parent-rated and 5.0% in self-rated symptoms of behaviour problems in adulthood via genetics (Table 4. 2). The poly-E composites accounted for a similar proportion of variance in hyperactivity (7.5%) and conduct problems (8.5%).

*Cumulative (longitudinal) prediction via shared environment*

Table 4. 2 also presents shared environmental results of the longitudinal multivariate Cholesky decomposition. Because no shared environmental variance was found for symptoms of behaviour problems in adulthood, shared environmental processes did not contribute to the prediction of behaviour problem symptoms in adulthood from poly-E composites at earlier ages.

*Comparing results from MZ differences design and residualised scores*

We compared our Cholesky results to those using the MZ differences design rather than the full twin model. In general, correlations between MZ poly-E differences and MZ behaviour problem symptom differences (Supplementary Figure 7) yielded similar NSE estimates as Cholesky decomposition, as illustrated in Supplementary Figure 8. Results of the MZ differences analysis are described in Supplementary Note 7. Supplementary Figure 8 shows that NSE results obtained using the residualised scores approach are also similar to those obtained from MZ differences and Cholesky analyses. Supplementary Figure 9 presents correlations between these residualised poly-E and behaviour problem measures.

# Discussion

Our attempt to assess the extent to which parent-rated environmental measures taken together predict NSE effects on behaviour problem symptoms during the first two decades of life revealed the large 'missing NSE' gap between the variance explained by measured environments and the NSE variance of behaviour problem symptoms estimated from twin studies (Turkheimer, 2011).

We were especially interested in the long-term ability of parent ratings of earlier environments to predict NSE variance in adult self-reports of behaviour problem symptoms because many studies focus on predicting adult self-reports of behaviour from parents' ratings of early environments. Cumulatively across development, our parent-rated poly-E measures in preschool, childhood and adolescence predicted only 0.3% of the reliable NSE variance in self-rated symptoms of behaviour problems in adulthood. In contrast, parent-rated poly-E measures cumulatively accounted for 4.7% of the NSE variance in parent-rated symptoms of behaviour problems in adulthood. These predictions of parent-rated symptoms are much greater than predictions of self-rated symptoms presumably because the same rater (the parent) rated both the poly-E measures and the symptoms. All of these predictions are weaker when they are converted to the total variance accounted for, rather than the reliable NSE variance: 0.2% instead of 0.3% and 2.0% instead of 4.7%. Genetics accounted for much more of the total variance: 5.0% for self-rated symptoms and 11.0% for parent-rated symptoms.

We found similar patterns of results for predictions from preschool to childhood and from childhood to adolescence for NSE, genetic and shared environmental processes. On average, parent-rated poly-E measures accounted for 1.5% of the reliable NSE variance in parent ratings of symptoms of behaviour problems in childhood, 0.2% in teacher ratings and 0.3% in self ratings, after controlling for genetics, shared environment and error of measurement. In adolescence, the NSE predictions were 6.8% for parent-rated, 0.8% for teacher-rated and 1.8% for self-rated behaviour problem symptoms. Results for adolescence-to-adulthood analyses were consistently weaker, but this is most likely due to our weaker assessment of the environment in adolescence.

For the specific measures used in our study, we conclude that preschool, primary and secondary school environments do not have a major environmental impact, whether NSE or shared environment, on behaviour problem outcomes in adulthood. The strongest predictive processes are genetic. Similar results have been found in previous research, for example, predicting depressive symptoms (Pike, McGuire, et al., 1996), externalizing disorders (Burt et al., 2003) and antisocial behaviour (Narusyte et al., 2007; Pike, McGuire, et al., 1996).

These results are limited to the normal range of environmental variation and cannot be assumed to generalise to environmental extremes of neglect, abuse or catastrophic events. Some research supports the possibility that NSE effects are greater in higher risk environments (Asbury et al., 2003). Another limitation is that the measures of behaviour problems used in the present study, although standard measures often used in other research, are limited to questionnaire ratings by parents, teachers and the twins. Moreover, our measures of the environment are limited to ratings by parents. There is some evidence that observational measures yield stronger NSE results than questionnaires (Pike, McGuire, et al., 1996; Turkheimer & Waldron, 2000). On the other hand, self-report questionnaires tap into perceptions, which is how the environment is experienced (Plomin, 1994) and aggregate information over time, as opposed to a few observed instances.

A general limitation for research on NSE is that measures of the family environment have traditionally focused on between-family rather than within-family environments specific to each child (Asbury et al., 2017; Daniels & Plomin, 1985). More measures of the within-family environment are needed that are specific to each child in a family because there is no necessary relationship between the environmental causes of differences between families and the environmental causes of differences within families (Plomin & Daniels, 1987). One example of the within-family NSE factor includes unequal distribution of affection from parents, measured based on siblings' perceptions (Plomin & Daniels, 1987).

At the least, our results can be seen as a challenge to researchers to account for more of the NSE variance in behaviour problem symptoms after controlling for genetics. This is an important goal because NSE is the way the environment works to affect symptoms of behaviour problems, not just for siblings but for all children. These results underline the need to control for the effects of genes because correlations between environmental measures and symptoms of behaviour problems are substantially (about 50%) mediated by genetic factors.

More generally, these findings remind us that correlations between environmental measures and behaviour problem symptoms cannot be assumed to be environmentally causal.

The major question raised by this research is how we can narrow the large 'missing NSE' gap between variance in behaviour problem symptoms explained by measured NSE and the NSE component of variance, especially if specific NSE factors, as we currently measure them, have miniscule effect sizes. One possibility has been called the gloomy prospect: 'that the salient environment might be unsystematic, idiosyncratic, or serendipitous events such as accidents, illnesses, and other traumas' (Plomin & Daniels, 1987, p. 8), which could include 'intrinsic stochasticity of molecular processes' (Tikhodeyev & Shcherbakova, 2019). We should not accept this null hypothesis of the gloomy prospect until we have exhausted attempts to prove it wrong, because NSE effects are real and the 'missing NSE' gap might reflect our current inability to measure and detect systematic effects.

An instructive comparison is the 'missing heritability' gap (Manolio et al., 2009; Turkheimer, 2012), which refers to the disparity between variance in behaviour problem symptoms explained by measured DNA variants (about 4%) and their heritability (about 40%) (Cheesman et al., 2017; Gidziela, Rimfeld, et al., 2022). The first wave of DNA research investigated candidate genes, which were assumed to have large effects, but this candidate gene research failed to yield replicable associations (L. E. Duncan & Keller, 2011). Most NSE research is at an analogous 'candidate NSE' stage, testing for large effects of the usual suspects such as parenting and peers.

One possibility to narrow the 'missing heritability' gap came with a technological advance, the DNA chip, which enabled the systematic strategy of genome-wide association (GWA) studies (Plomin, 2019). GWA analyses revealed that the largest associations were much smaller than anyone imagined (Visscher et al., 2017). A technological advance comparable to the DNA chip that could create a similar breakthrough for NSE research is the RNA chip, which makes it possible to adopt a systematic approach analogous to the DNA chip and GWA analysis by assessing the expression levels of all 30,000 genes in the genome (von Stumm & d'Apice, 2022). Crucially, gene expression is responsive to the endogenous and exogenous environment (Feil & Fraga, 2012). In this way, RNA chips can provide a genome-wide snapshot of environmental effects. However, gene expression reflects a momentary state because RNA transcripts degrade quickly, the better to reflect changes in the environment. A

more focused starting point is the slow-motion gene expression changes involving epigenetic mechanisms, which can be assessed via DNA methylation marks and which are substantially due to NSE (Bell & Spector, 2011; C. C. Y. Wong et al., 2014). A major limitation is that both transcriptomics and epigenomics are tissue specific, and the tissue that most interests psychologists is the brain, which is not accessible except post mortem.

Another solution to the 'missing NSE' gap could come from technological advances in remote real-time biological and behavioural monitoring using wearable devices and smartphones and in digital footprints left in social media (Adjerid & Kelley, 2018). New analytic approaches such as machine learning can make sense of these massive datasets, especially in relation to prediction rather than explanation (Yarkoni & Westfall, 2017).

A limitation of any attempt to identify NSE causes of behaviour problem symptoms is that it is difficult to establish causality (Turkheimer & Waldron, 2000). For this reason, we have refrained from interpreting NSE-mediated correlations between environmental measures and behaviour problem symptoms as causal, even though we correlated environmental measures at one age with behaviour problem symptoms at a later age. Our goal is to identify NSE factors that predict symptoms of behaviour problems, which is a prerequisite for explaining these associations. Moreover, in our view, prediction is a more tractable and practical goal than explanation for understanding the major source of variance in symptoms of children's behaviour problems— nonshared environment.

# Chapter 5— Gene-environment interplay in adolescent developmental psychopathology.

This chapter is presented as an adapted version of a manuscript in preparation for peer-review.

Supplementary Notes, Tables and Figures are included in Appendix 4.

## Abstract

A combination of genetic (G) and environmental (E) influences working in complex interplay are thought to underlie differences in symptoms of psychopathology between adolescents. However, studies that have investigated gene-environment interaction (G×E) in isolated aspects of developmental psychopathology are characterized by a lack of robust effects, suggesting the need for a more comprehensive approach. We adopted a multivariable approach to investigate G×E in developmental psychopathology. Our sample included 4,000 16-year-olds enrolled in the Twins Early Development Study. Adolescents and their parents provided data on externalizing and internalizing symptoms of psychopathology. We estimated G by combining polygenic scores for neurodevelopmental disorders and psychopathology. We measured E by combining environmental exposures, including home environments and life events, assessed during childhood and adolescence. We used elastic net regularization to examine the main effects of G and E on symptoms of psychopathology, their joint effects (G+E) and their interaction (G×E). Polygenic scores jointly accounted for less than 3% of the variance in developmental psychopathology. The prediction was stronger for externalizing symptoms, compared to internalizing. Parent-rated psychopathology symptoms at age 16 were best predicted by parent-rated environments measured during childhood and early adolescence (accounting for 10.4% of the variance on average), while self-rated symptoms at age 16 were best predicted by self-reported contemporaneous environmental experiences ($R^2$= 11%). We observed small and isolated G×E effects accounting for <1% of the variance and weak correlations between G and E. The findings point to the challenges of investigating G×E in developmental psychopathology and highlight the role of specific family environments.

# Introduction

Symptoms of developmental psychopathology, affecting behavioural, cognitive, and adaptive functioning frequently onsets between ages 6 and 21 and affects up to 6.5% of children and adolescents worldwide (Colman et al., 2009; Kessler et al., 2005; Polanczyk et al., 2015; Woodward & Fergusson, 2001). Childhood psychopathology can include symptoms of anxiety, mood disorders, as well as behaviour problems and impulse-control disorders such as attention-deficit hyperactivity disorder (ADHD) and conduct disorder. Symptoms of these disorders are likely to persist throughout the life course and have been found to predict adult mental illness over two decades later (Reef et al., 2010).

Twin-and adoption studies have found evidence for genetic effects on developmental psychopathology, with heritability estimates ranging between 26% and 67% for mood disorders, between 41% and 78% for symptoms of ADHD and between 36% and 62% for conduct problems, depending on whether symptoms were reported by children, parents or teachers (Anckarsäter et al., 2011; Cheesman et al., 2017; Faraone & Larsson, 2019). A meta-analysis of 236 studies found that genetic influences accounted for 66% of the variation across all neurodevelopmental disorders (Gidziela, Ahmadzadeh, et al., 2023). DNA-based approaches to estimating single nucleotide polymorphism (SNP) heritability– i.e., the proportion of phenotypic variation accounted for by variation in single nucleotide polymorphisms (SNPs), provide lower heritability estimates than those reported by twin studies across all measures of developmental psychopathology. Single nucleotide polymorphism heritability has been estimated at 0%-6% for mood disorders (Cheesman et al., 2017), 0%-22% for ADHD (Cheesman et al., 2017; Demontis et al., 2023) and 1%-13% for conduct problems (also called antisocial behaviour in adulthood) in adolescent and adult samples (Cheesman et al., 2017; Tielbeek et al., 2022). Meta-analytic estimates of SNP heritability across 29 studies of several developmental disorders in children and adolescents have been reported at 19% (Gidziela, Ahmadzadeh, et al., 2023). A further way of estimating genetic effects on a trait from DNA data is to calculate a genome-wide polygenic score (PGS), which aggregates hundreds of SNP associations into a single composite index (Belsky & Harden, 2019; Dudbridge, 2013). Polygenic scores for neurodevelopmental disorders and psychopathology have been found to explain up to 5% of the variance in childhood and adolescent behavioural and emotional problems (Gidziela et al., 2022; Plomin et al., 2022).

In addition to genetic effects, environmental factors that are not shared by siblings raised in the same family have been linked to developmental psychopathology (Knopik et al., 2017; Plomin, 2011; Plomin & Daniels, 1987). Twin studies of children and adolescents have estimated that these nonshared environmental factors account for 40-50% of the variance in mood disorders (Eley et al., 2003; Gidziela, Malanchini, et al., 2023; Lau & Eley, 2006), ~30% in ADHD (Burt, 2009) and ~37% in conduct disorder (Anckarsäter et al., 2011). A meta-analysis of 195 studies estimated that nonshared environmental influences accounted for 29% of individual differences across all child and adolescent neurodevelopmental disorders (Gidziela, Ahmadzadeh, et al., 2023). Despite the substantial contribution of nonshared environmental effects to variation in developmental psychopathology, studies have struggled to identify the specific environments that act as the nonshared environmental influences. In the hope of bridging this *missing nonshared environment gap* (Turkheimer, 2011), studies have brought together multiple environmental measures, like home setting, parenting and classroom environment, into poly-environmental composites (Gidziela, Malanchini, et al., 2023). These poly-environmental scores were found to account for up to 4.7% of the nonshared environmental variance in symptoms of behaviour problems in adulthood (Gidziela, Malanchini, et al., 2023).

Beyond the relative contribution of genetic and environmental factors, the interplay between them (GE interplay) has been proposed as a key contributor to developmental psychopathology (Rutter & Silberg, 2002). Two main forms of interplay between genetic and environmental influences have been described: gene-environment correlation (rGE) and gene-environment interaction (G×E) (Moffitt, 2005; Plomin et al., 1977; Viding et al., 2008; Viding & McCrory, 2020). Gene-environment correlation refers to how individuals experience environments that are in line with their genetic dispositions, which statistically is reflected in the covariance between an individual's genotype and environmental factors (Plomin et al., 1977). For example, children with higher genetic risk for antisocial behaviour were found to elicit harsher punishment from their parents, if compared to children with a lower genetic risk (O'Connor et al., 1998). Gene-environment interaction occurs when individuals' responses to the environment vary depending on their genetic dispositions (Domingue et al., 2022). Early twin research into G×E found that children responded differently to adverse environments, such as childhood maltreatment, based in part on their genetic disposition towards conduct disorder (Jaffee et al., 2005).

Recent developments led the G×E research in developmental psychopathology to employ PGSs as measures of genetic influences (Plomin et al., 2022; Plomin & Viding, 2022). However, because PGSs in child and adolescent samples are either unavailable or based on underpowered gene discovery studies (i.e., genome-wide association (GWA) studies), studies have used PGSs of adult psychiatric disorders as predictors (Plomin et al., 2022). A recent investigation found that genetic susceptibility to major depressive disorder increased the risk of depressive symptoms in adolescents who were exposed to higher levels of criticism from their parents (Nelemans et al., 2021). Another study found that a genetic disposition to alcohol dependence was more predictive of conduct problems in individuals who experienced adverse environmental conditions (Bares et al., 2020). A further study found that early environmental risk moderated the association between genetic disposition towards ADHD and externalizing behaviour problems in adolescence, as well as the association between genetic disposition towards neuroticism and internalizing symptoms; nonetheless, these interaction effects only accounted for up to 0.4% of the variance (Plomin et al., 2022). Other studies of G×E in developmental psychopathology obtained negative results. For example, the PGS for ADHD was not found to interact with childhood maltreatment in predicting symptoms of ADHD in adolescence (He & Li, 2022). Similarly, childhood maltreatment was not found to moderate the polygenic prediction of adolescent externalizing problems (Ksinan et al., 2022).

This observed lack of significant and robust interaction effects points to the need for a shift in the methodology adopted to investigate G×E in developmental psychopathology. Potential gains in prediction might be achieved by employing a multi-PGS framework– combining multiple PGSs for psychiatric disorders (Gidziela et al., 2022; Krapohl et al., 2018). Further gains might be achieved by combining multiple environmental measures and estimating their joint role in predicting symptoms of developmental psychopathology (Allegrini, Karhunen, et al., 2020; Gidziela, Malanchini, et al., 2023). This multivariable approach, including an array of genetic instruments (G), environmental measures (E) and their interaction (G×E) was found to improve the prediction accuracy of academic achievement in adolescence (Allegrini, Karhunen, et al., 2020). Therefore, building on our previous work (Gidziela et al., 2022; Gidziela, Malanchini, et al., 2023; Plomin et al., 2022), the current study aims to leverage a multivariable approach to comprehensively investigate how G and E effects combine and interact in predicting individual differences in symptoms of hyperactivity/inattention, conduct problems, anxiety, and mood disorders, rated by adolescents and their parents at age 16. We

will measure genetic disposition towards developmental psychopathology by combining well-powered PGSs of neurodevelopmental disorders and psychopathology. In parallel, we will combine multiple measures of E effects including SES, home environment and life events at ages 9, 12 and 16. We will examine the main effects of G and E, as well as their joint effects (G+E) and their interaction (G×E).

Recognising and accounting for rGE alongside G×E is essential because it reveals that individuals, based on their genetic predispositions, may actively seek or create environments that align with their genetic propensities (Plomin & Viding, 2022). This introduces a layer of complexity in interpreting G×E effects, as ignoring rGE can lead to misinterpretations and may hinder the identification of genuine G×E effects. Therefore, in addition to analyses of G×E, we will test for rGE to establish the degree of overlapping information between genetic and environmental effects and their mediating role in prediction of behavioural and emotional problems in adolescence. Considering the interplay between genes and environment in developmental psychopathology provides the advantage of looking at how nature and nurture interact and enhances the understanding of individual differences in behavioural and emotional outcomes of adolescents, based on how their reactions to environmental settings vary depending on genetic propensities.

## Method

Analyses for this project were preregistered with the Open Science Framework (OSF) (https://osf.io/dzqnu/). The hypotheses are listed in Supplementary Note 1. Analytic scripts are available on the OSF page and https://github.com/CoDEresearchlab/GE_interplay_devpp.

### *Sample*

Our sample included twins born in England and Wales between 1994 and 1996 enrolled in the Twins Early Development Study (TEDS). For a detailed description of the sample and its representativeness, see Supplementary Note 2, Supplementary Table 1 and (Lockhart et al., 2023).

In the present study we investigated the prediction of symptoms of developmental psychology at age 16, using the PGSs and measures of the environment collected when the twins were approximately 9, 12 and 16 years old. DNA was collected from a subsample of

7,026 unrelated twins and 3,320 dizygotic twin pairs. The genotyping procedure involved two different platforms (AffymetrixGeneChip 6.0 and Illumina HumanOmniExpressExome-8v1.2) and was conducted in two separate waves. For details on genotyping, imputation and quality control, see Selzam et al. (2018). Our models were tested using data from unrelated twins, which was achieved by randomly selecting one dizygotic twin per each genotyped pair. The resulting sample size ranged from 4013 to 897 individuals with developmentally complete phenotype data for G models and from 1513 to 613 for E models. The sample size of more than 600 individuals provides adequate power to detect G and E effects accounting for 1% of the variance with 80% power (Duncan & Keller, 2011). We also conducted sensitivity analyses using the total genotyped sample, i.e., including the dizygotic co-twins.

*Measures*

Variables in the current study included polygenic scores (PGSs, aka G), parent and self-rated measures of the environment at age 9, 12 and 16 (aka E), as well as parent and self-rated symptoms of developmental psychopathology measured at age 16. For a visual illustration of G, E and developmental psychopathology variables used in analyses please refer to Figure 5. 1.

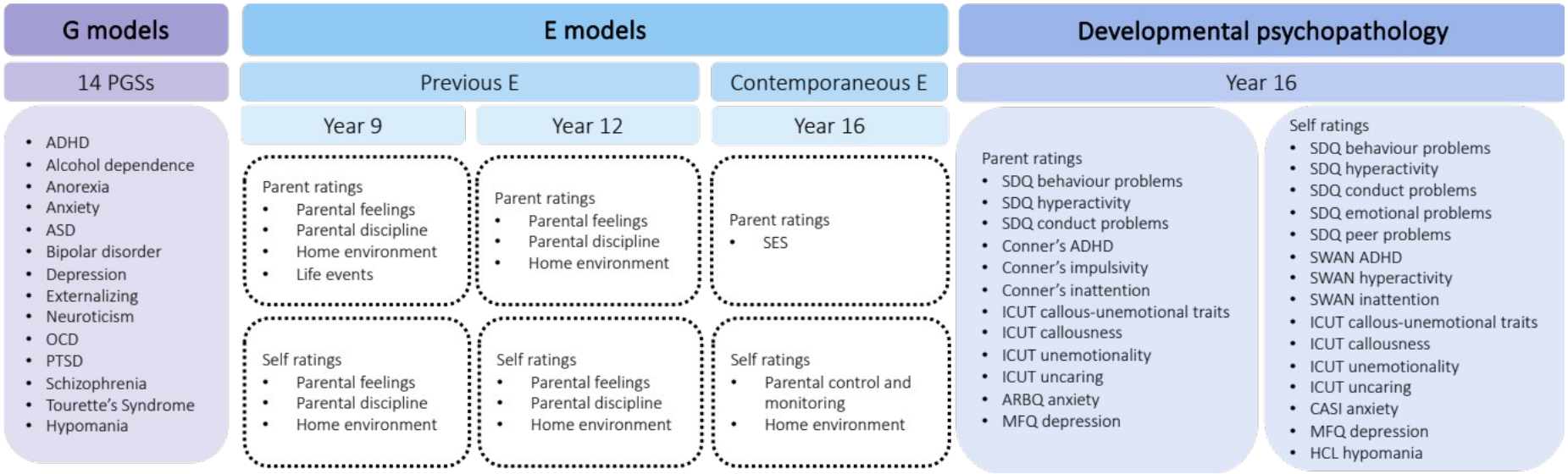



Figure 5. 1. A visual representation of genetic, environmental and developmental psychopathology measures used in the study. G models refer to predicting symptoms of developmental psychopathology using polygenic scores (PGSs). E models refer to predicting symptoms of developmental psychopathology using environment data collected at ages 9, 12 and 16.

*Polygenic scores (PGSs)*

We used PGSs derived from 11 most powerful GWA studies of neurodevelopmental disorders and broadly defined psychopathology from Grotzinger et al. (2022). In addition, we used PGSs derived from the GWA studies of neuroticism (Luciano et al., 2018) due to its predictive power for emotional symptoms and peer relationship problems (Gidziela et al., 2022), externalizing behaviour (Karlsson Linnér et al., 2021), and hypomania (Gidziela et al., in preparation). All PGSs are listed in Supplementary Table 2. Polygenic scores for the TEDS sample were constructed in LDpred and LDpred2 (Privé et al., 2020; Vilhjálmsson et al., 2015), using all available SNPs (for details, refer to Supplementary Note 3 and Allegrini et al., 2020).

*Environmental measures*

The predictor variables included item-level parent and self-rated measures of the environment assessed at age 9, 12 and 16, previously found to be predictive of behavioural and emotional problems (see Gidziela, Malanchini, et al. (2023)). Item-level data was selected to increase precision of variable selection and identification of nuanced G×E effects between specific aspects of environment and PGSs. We incorporated measures of the SES, parental feelings (Deater-Deckard, 2000), discipline (Deater-Deckard et al., 1998), control and monitoring ("Child Care and Child Development: Results from the NICHD Study of Early Child Care and Youth Development," 2005), home environment (Matheny et al., 1995) and life events. These environmental variables are presented in Supplementary Table 3.

*Developmental psychopathology*

We investigated the prediction of developmental psychopathology phenotypes, such as hyperactivity/inattention, conduct problems, emotional problems and peer relationship problems at age 16, measured using the Strengths and Difficulties Questionnaire (SDQ) (Goodman, 2001). Additional measures of developmental psychopathology included assessment tools of ADHD, such as the Conners Rating Scale (Keith Conners et al., 1998) and the Strengths and Weaknesses of Attention-Deficit/Hyperactivity Symptoms and Normal Behaviors (SWAN; Swanson et al. (2012)), the Inventory of Callous-Unemotional Traits (ICUT; Frick (2004)), the Anxiety-Related Behaviours Questionnaire (ARBQ; Eley et al. (2003)), Childhood Anxiety Sensitivity Index (CASI; Silverman et al. (1999)) and measures of mood disorders, such as the Mood and Feelings Questionnaire to assess depressive

symptomatology (MFQ; Messer et al. (1995)) and Hypomania Checklist (HCL-16; Forty et al. (2010)).

## *Analyses*

### *Data pre-processing*

All environmental variables were residualised on age and sex. Polygenic scores were additionally regressed on 10 genetic principal components and genotyping chip. The obtained standardized residuals were used in all downstream analyses. Environmental variables and measures of developmental psychopathology were assessed for normality and square root or inverse transformations were applied for variables with skewedness larger than 1 or lower than -1. For details on transformation methods used, distributions and correlations between transformed and raw variables, see Supplementary Note 4, Supplementary Table 4 and Supplementary Figures 1-3.

### *Gene and environment (GE) prediction*

We estimated the independent effects of G and E using elastic net regularization (Allegrini et al., 2020; Hastie et al., 2023; Zou & Hastie, 2005) with hold-out sample tests of prediction accuracy, using the R package glmnet (Hastie et al., 2023) implemented in caret (Kuhn, 2008; R Core Team, 2022). Elastic net regularization overcomes issues of multicollinearity and overfitting by combining the strengths of both Lasso and Ridge regression techniques, penalizing large coefficients while simultaneously encouraging grouping of correlated predictors, thus providing a more parsimonious model (Allegrini et al., 2020; Zou & Hastie, 2005). For a detailed description of the method, see Supplementary Note 5 and Allegrini et al. (2020). We fitted all PGSs and all environmental measures in separate sets of elastic net models for each developmental psychopathology phenotype (see Figure 5. 1).

### *Gene-environment interaction (G×E)*

To identify two-way interactions between the PGSs and environmental measures (G×E), we employed a hierarchical lasso procedure implemented in the R package glinternet (group-lasso interaction network) (Lim & Hastie, 2015; R Core Team, 2022). This procedure helps minimize the impact of multiple testing and low power to detect small G×E effects. To select interactions, glinternet uses a group lasso and performs variable selection on groups of variables, simultaneously eliminating or maintaining them in the model. For an interaction

between two variables to be selected, main effects of both these variables need to be detected based on non-zero model coefficients. The selected 2x2 interactions between the PGSs and environments were reintroduced to the joint G+E models to explore a change in prediction accuracy.

*Sex differences*

We fitted the G+E models for males and females separately in order to investigate differences in proportion of variance explained by the PGSs and environmental measures. In addition, we performed hierarchical lasso procedure for sex-specific samples and compared changes in prediction after adding G×E terms to the joint G+E models, separately for males and females.

*Gene-environment correlation (rGE)*

In addition to tests of G×E, we also performed a set of exploratory analyses to explore rGE in developmental psychopathology to ensure that the correlations between genetic and environmental factors are not partly responsible for the discovered G×E effects (Plomin & Viding, 2022). We modelled rGE effects in two ways. First, by correlating the predicted values from G and E elastic net models we estimated the overlap between G and E effects on developmental psychopathology (Allegrini, Karhunen, et al., 2020). Second, by using mediation models (Supplementary Note 6 and Supplementary Figure 4), we tested for the effects of G on symptoms of developmental psychopathology mediated by E and vice versa, the effects of E mediated by G (Allegrini, Karhunen, et al., 2020). The mediation analyses were performed using lavaan for R (R Core Team, 2022; Rosseel, 2012).

## Results

*G models*

Figure 5. 2 presents the variance in developmental psychopathology predicted jointly by the 14 selected PGSs and regression coefficients of specific PGSs for parent and self-rated data. Full results and fit parameters of the G models are presented in Supplementary Table 5. The PGSs jointly predicted about 2.4% in parent-rated and 2.7% in self-rated symptoms of developmental psychopathology. For parent-rated data, the prediction ranged from 3.1% for SDQ conduct problems to 1.5% for ICUT callous traits, while for child-rated data the variance explained ranged from 4.4% for SWAN inattention to 0.6% for SDQ peer problems. On average, the PGSs explained more variance in externalizing, than in internalizing

psychopathology (3.0% vs 1.7%). As presented in Figure 5. 2, the PGSs with the most predictive power for almost all developmental psychopathology phenotypes, especially behaviour problems, included the PGSs for externalizing and ADHD, whereas the neuroticism PGS was the strongest predictor of anxiety and depression.

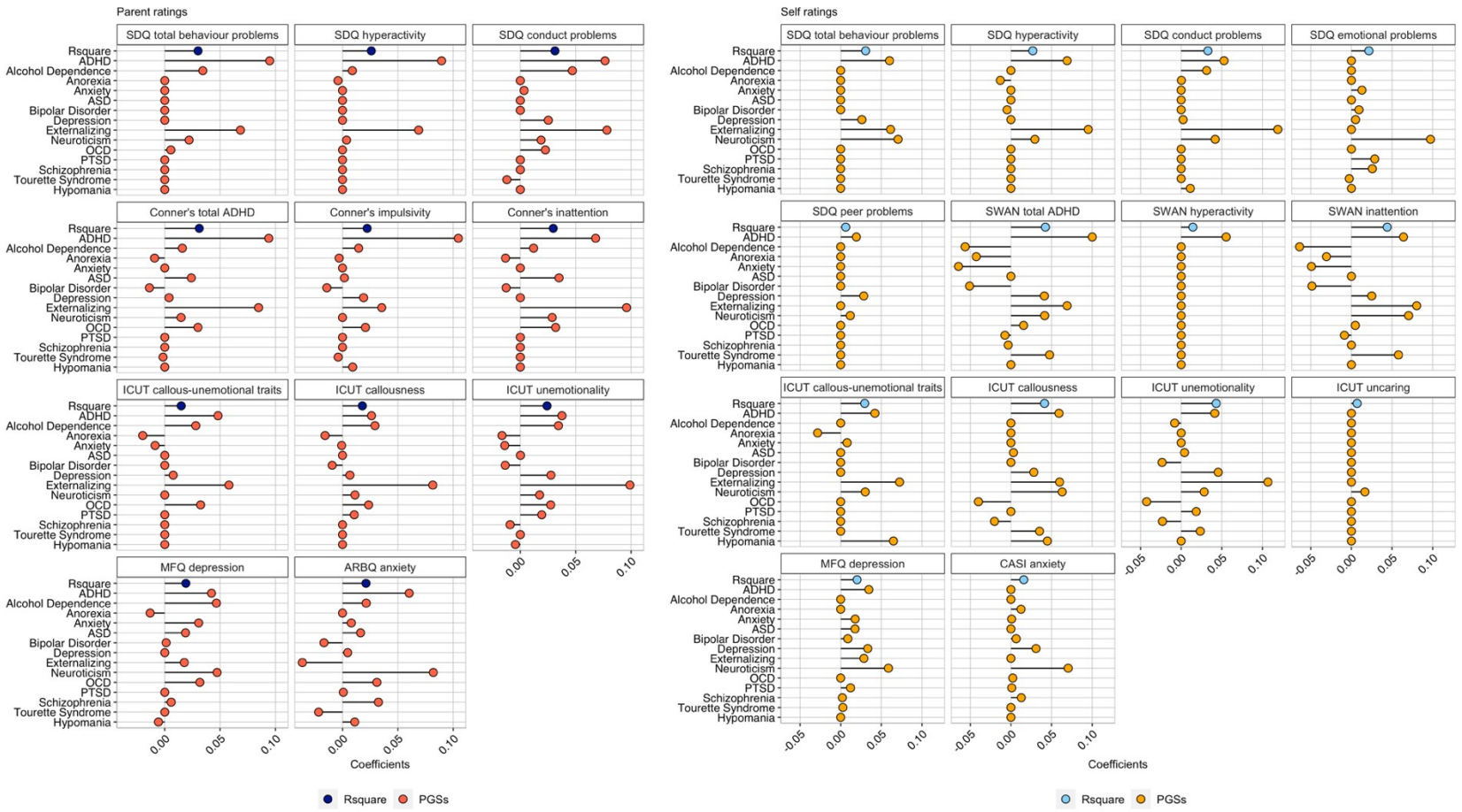



Figure 5. 2. Results of the G models predicting symptoms of developmental psychopathology using genome-wide polygenic scores (PGSs.) The first row of each panel represents the proportion of variance explained in developmental psychopathology. The remaining rows represent elastic net coefficients of the association between PGSs and developmental psychopathology measures.

*Note*. Parent-rated ICUT uncaring and self-rated HCL hypomania scales are not included in the figure due to all coefficients being shrunk to 0 within the models.

*E models*

Predictive power of the environmental factors at ages 9, 12 and 16 is illustrated in Figure 5. 3. Full results and fit parameters of the E models are presented in Supplementary Table 6. Similar proportion of variance was explained by measured environmental factors in parent and self-rated symptoms of developmental psychopathology (8.0% and 7.0%, respectively). For parent-rated developmental psychopathology, more variance was accounted for by the parent-rated environments measured at age 12 and 9 (9.3% and 11.5%), than at age 16 (2.8%). The opposite was observed for self-rated developmental psychopathology, where the variance predicted by self-rated environment data collected at age 16 was twice that of ages 9 and 12 (11.0% vs 4.1% and 5.6%, respectively). Parent-rated environmental factors were more predictive of SDQ behaviour problems and Conners ADHD traits (10.6% and 8.6%) than ICUT callous-unemotional traits and anxiety & mood disorders (6.8% and 5.1%). Self-rated environments were more predictive of SDQ behaviour problems and ICUT callous-unemotional traits (7.5% and 8.7%), than SWAN ADHD traits and anxiety & mood disorders (6.5% and 4.5%).

The most important environmental factors in prediction of parent-rated symptoms of developmental psychopathology at age 9 included parental feelings and home chaos scales, as well as important life events, such as financial difficulties or birth of a new sibling (Supplementary Figure 5). At the age of 12, the strongest predictors of parent-rated developmental psychopathology included the parental feelings, especially frustration and impatience, as well as home chaos, whereas at age 16 the strongest predictors involved measures related for family SES and household income. In case of self-rated environmental measures and developmental psychopathology, parental feelings and home chaos were the most relevant predictors throughout adolescence (Supplementary Figure 6).

*G+E models*

Figure 5. 3 shows the proportion of variance in parent and self-rated developmental psychopathology jointly accounted for by the PGSs environmental measures at ages 9, 12 and 16. Full results and fit parameters of the E models are presented in Supplementary Table 7. Results of the sensitivity G+E models that were conducted using the total genotyped sample, including DZ co-twins are presented in Supplementary Table 8. Additionally, Supplementary Tables 9, 10 and 11 show results of G+E models for cross-rater and sex-specific prediction,

respectively. Comparison of the proportion of variance explained by sensitivity models is presented in Supplementary Figure 7. The proportion of variance in developmental psychopathology jointly accounted for by the PGSs and parent-rated environmental factors was on average 11.0% for age 9 environments, 13.0% for age 12 environments and 4.7% for age 16 environments. For self-rated environmental measures, the variance explained jointly with the PGSs was 6.8% for age 9 environments, 8.6% for age 12 environments and 13.4% for age 16 environments.

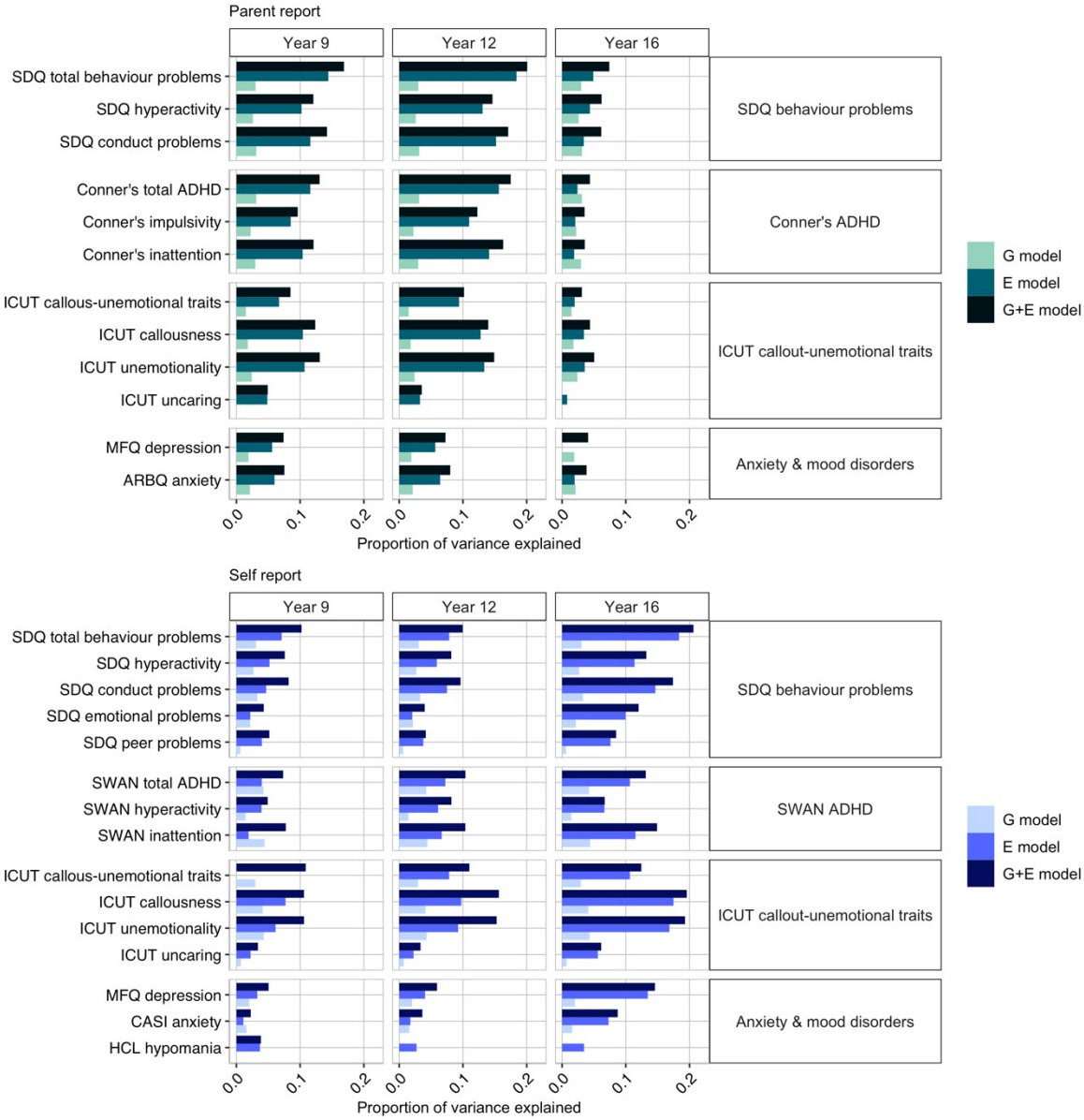



Figure 5. 3. Variance in symptoms of developmental psychopathology jointly accounted for by the genome-wide polygenic scores (PGSs) and environments measured at ages 9, 12 and 16, compared to the variance explained by G and E models.

*G×E models*

Figure 5. 4 presents results for the only phenotype for which significant G×E was detected—self-rated SDQ total behaviour problems. Significant interactions were observed between ADHD, anxiety, neuroticism and schizophrenia PGSs and self-rated items from the chaos and parental feelings scales measured at age 12. Adding interaction terms to the G+E model increased the proportion of variance explained by 0.7%. Among 7 of the detected interactions, the ones with most predictive power included the interactions between anxiety PGS and *a real zoo* item from the chaos scale, as well as between schizophrenia PGSs and *I make parent angry* item from the parent feelings scale.

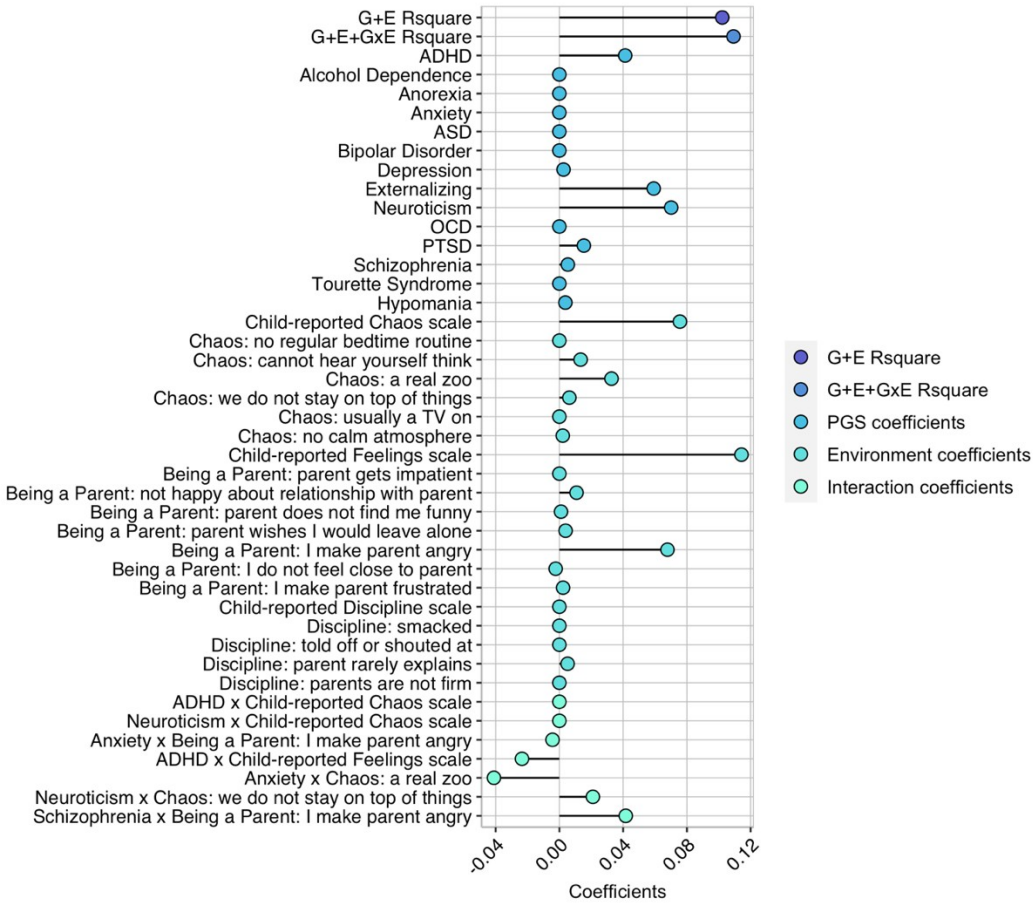



Figure 5. 4. Results of the joint G+E+G×E models predicting self-rated SDQ total behaviour problems using genome-wide polygenic scores (PGSs, aka G), environmental data collected at age 12 (E) and interactions between the PGSs and environments (G×E). The first two rows represent the proportion of variance explained jointly by G+E and G+E+G×E. The remaining rows represent elastic net coefficients of the association between G, E, G×E and self-rated SDQ total behaviour problems.

*Tests of rGE*

Correlations between values predicted from G and E models are presented in Supplementary Figure 8 for parent and self-rated data. Based on these correlations being generally less than 0.18 for parent-rated environmental data and less than 0.14 for self-rated data, we did not observe substantial evidence for rGE in developmental psychopathology. Based on mediation models of rGE, significant indirect effect was observed for the mediation role of ADHD PGS and chaos scale, neuroticism PGS and chaos scale and ADHD PGS and *I make parent angry* item from parental feelings scale (Supplementary Table 12).

# Discussion

The present study utilized the PGSs derived from GWA studies of neurodevelopmental disorders and psychopathology, combined with environmental indices of the family environment and life events to examine their joint and interactive effects in predicting symptoms of developmental psychopathology during adolescence. The results demonstrated that while both genetic and environmental factors play a role in the development of psychopathology, their interactions in predicting individual differences in behavioural and emotional outcomes are relatively small. Several factors contribute to these observations. Firstly, the limited predictive capacity of psychiatric PGSs fails to encompass the full intricacy of genetic influences on developmental psychopathology (Plomin et al., 2022). Further, our study's statistical power, although adequate for detecting substantial G×E effects exceeding 1% of the variance, is insufficient to pinpoint more subtle effects (Duncan & Keller, 2011; Plomin et al., 2022). The inherent complexity of rGE in psychopathology outcomes adds an additional layer of challenge. Recognizing the role of rGE is crucial, revealing that individuals, influenced by their genetic predispositions, may actively seek or shape environments in alignment with their inherent propensities (Plomin & Viding, 2022).

Our findings indicated that the PGSs collectively accounted for about 2.4% to 2.7% of the variance in parent and self-rated symptoms of developmental psychopathology. The strongest predictors of most developmental psychopathology phenotypes were PGSs for externalizing behaviour and ADHD, while neuroticism PGS showed greater predictive power for anxiety and depression. These results are consistent with previous research showing that PGSs contribute to the prediction of behavioural and emotional problems, especially externalizing symptoms (Akingbuwa et al., 2020; Allegrini, Cheesman, et al., 2020; Gidziela et al., 2022; Plomin et al., 2022).

Measured environmental factors accounted for approximately 7.0% to 8.0% of the variance in parent and self-rated symptoms of developmental psychopathology. Notably, parent-rated environments at age 9 and 12 were more predictive of parent-rated symptoms, while self-rated environments at age 16 were more predictive of self-rated symptoms. This finding suggests that adolescents' own perceptions of their environments at a later stage of development may have a stronger impact on their emotional and behavioural functioning during this critical developmental period. Adolescence is a time of increased autonomy and

identity formation, and the results highlight the importance of considering how adolescents' perceptions of their environments contribute to their developmental outcomes. Therefore, a comprehensive evaluation of developmental psychopathology necessitates moving beyond conventional measurement scales. It calls for a more nuanced approach, involving symptom-level analyses and assessments of daily functioning (Markon, 2010; Russell & Gajos, 2020). Daily functioning measures gauge the practical impact of symptoms on an individual's ability to navigate various life domains, placing emphasis on adaptive functioning and independence (Russell & Gajos, 2020). Moreover, the incorporation of sleep patterns and biological markers, such as cortisol levels, provides a deeper understanding of the intricate interplay between psychological and physiological factors (Malanchini et al., 2021; Meltzer, 2017; Sadeh, 2015). This multimodal assessment, rooted in real-world contexts and ecological validity, aims to capture the complexity of developmental psychopathology. It enables more precise evaluations and facilitates research on G×E.

Among the measured environmental factors, parental feelings and home chaos were identified as the most important predictors of developmental psychopathology. The fact that parental feelings, particularly feelings of frustration and impatience, emerged as important factors associated with the development of behavioural and emotional problems in adolescents highlights the significance of parental emotional regulation and communication styles in shaping adolescents' emotional well-being. Home chaos, which encompasses disorganization, lack of routine, and unpredictability in the household environment, also played a critical role in predicting psychopathology during adolescence. A chaotic home environment can create stress and instability for adolescents, potentially contributing to the development of behavioural problems and emotional distress.

The study revealed significant G×E effects in prediction of self-rated SDQ total behaviour problems, indicating that PGSs for ADHD, anxiety, neuroticism, and schizophrenia interacted with environmental factors measured at age 12. However, it is crucial to interpret this finding with caution, as the overall proportion of variance explained by these G×E was relatively small, less than 1%. It is important to acknowledge that the detection of a single G×E effect does not necessarily indicate a widespread presence of G×E. Rather, it highlights the need for further research and replication studies to establish the robustness and generalizability of the observed interaction.

Nevertheless, the finding of a significant G×E interaction underscores the importance of considering gene-environment interplay in the development of behaviour and emotional problems. Gene-environment interactions imply that the effects of genetic predispositions on behaviour are not uniform across different environmental contexts. This means that an individual's genetic makeup may influence how they respond to and interact with their environment, leading to varying developmental outcomes. However, the tiny effect size suggests that the influence of these specific genetic and environmental factors is modest compared to the overall complexity of developmental psychopathology. Individual differences in developmental psychopathology are likely shaped by a multitude of genetic variants, environmental factors, and their interactions, making it a multifaceted process that defies simple explanations.

The utilization of PGSs introduced a holistic view of the interplay between genetic predisposition and environmental factors in shaping phenotypic traits and disease susceptibilities, contrasting with traditional candidate gene studies, which often focus on the influence of individual genetic variants. This paradigm shift presents a unique set of challenges in interpreting G×E findings. One critical consideration is the average environmental context inherent within PGS effect sizes, reflecting the environmental milieu of the GWA study sample. This averaging process may obscure nuanced interactions between specific environmental factors and genetic variants, potentially leading to misinterpretation or oversimplification of G×E effects. The inherent environmental confounding captured within PGS estimates adds another layer of complexity to interpretation. Diverse environmental exposures within the discovery sample may yield context-specific findings that may not generalize across populations or environments. By acknowledging these interpretation challenges, researchers can pave the way for methodological advancements that facilitate a more nuanced understanding of the intricate interplay between genes and environment.

In addition, we observed rGE effects as examined by the mediation models, which are equally important in understanding the development of psychopathology during adolescence. Gene-environment correlation occurs when an individual's genetic predispositions influence their exposure to certain environments, which subsequently lead to behavioural outcomes. For instance, we observed a significant indirect effect for the mediation of ADHD PGS and chaos scale in predicting behaviour problems. This suggests that children with a higher

genetic predisposition for ADHD may contribute to chaotic home environments, which, in turn, may worsen the manifestations of hyperactivity and difficulties with concentration. Similarly, neuroticism PGS showed a significant indirect effect through the chaos scale. Children with a higher genetic predisposition for neuroticism may experience or elicit chaotic family environments, which could contribute to the manifestation of internalizing symptoms or emotional difficulties. Furthermore, the interaction between ADHD PGS and the "I make parent angry" item from the parental feelings scale also exhibited a significant indirect effect. This finding suggests that children with a genetic predisposition for ADHD may be more likely to experience greater levels of anger from the parents, which could adversely impact their activity levels and/or inattention.

These mediation effects suggest that genetic predispositions can influence the environment in ways that may contribute to the development of behavioural and emotional problems during adolescence. Moreover, the role of the Chaos scale as a mediator indicates that certain aspects of the home environment, such as disorganization and stress, play a crucial role in exacerbating how the genetic risk impacts behavioural outcomes. It is important to note that mediation effects do not imply causality, but rather offer insights into potential pathways through which genetic and environmental factors correlate and contribute to individual differences in developmental outcomes.

In our study, we had a sufficient sample size to detect large G×E effects that account for 1% of the variance (Duncan & Keller, 2011). While smaller G×E effects might not be easily detectable with our sample size, they are valuable for understanding the causal pathways between genes and environments (Götz et al., 2022). However, from a predictive perspective, larger G×E effects are of more immediate practical utility. The goal of prediction is to account for as much variance as possible without being concerned about the causal explanation. Prediction remains an essential first step towards explanation and has practical applications for identifying individuals at risk (Plomin et al., 2022; Plomin & von Stumm, 2022). This knowledge can be used to develop targeted interventions and support systems to improve outcomes for those at higher risk.

In our study, the G×E effects accounted for modest proportions of variance, which at the current stage of research advancement, may limit their utility for prediction purposes.

Nonetheless these findings open up new avenues for future research in developmental psychopathology. Firstly, the results emphasize the significance of early identification of both genetic and environmental candidates. By recognising individuals at risk based on their genetic predispositions and environmental exposures, early interventions have the potential to prevent or mitigate the development of psychopathology, leading to improved long-term outcomes for these individuals (Colizzi et al., 2020; Moffitt et al., 2011). Second, understanding how genetic predispositions interact with specific environmental factors can help clinicians customize treatment strategies to target the individual's unique risk profile. Interventions targeting family dynamics, parenting, and home chaos may be beneficial in reducing the risk of psychopathology in adolescents. By promoting positive and supportive family environments, clinicians can create protective factors that buffer against the influence of genetic predispositions. It is important to acknowledge that while these findings provide valuable insights into the complex nature of developmental psychopathology, they are long way from being robust enough to guide precise individual-level predictions or targeted interventions. As the field of G×E research progresses, it will be crucial to accumulate more substantial effect sizes, increase sample sizes and conduct replication studies.

# Chapter 6— General Discussion

The four empirical chapters of this thesis have explored several questions related to genetic and environmental influences on child and adolescent psychopathology, focusing on neurodevelopmental disorders and behaviour problems. While the findings of each study are discussed in detail in the Discussion section of every empirical chapter, this final chapter of my thesis aims to provide a general discussion by highlighting core findings and reflecting upon the broader implications of this research for understanding developmental psychopathology.

In Chapter 2, I presented the results of a comprehensive meta-analysis that explored the genetic and environmental underpinnings of neurodevelopmental disorders (NDDs) and their co-occurrence with disruptive, impulse control and conduct disorders (DICCs) in childhood and adolescence. Through a meta-analysis of 296 independent studies with a cumulative sample size of 4 million participants, the study assessed the extent to which genetic and environmental factors influence individual variation in NDDs and their relationship with other developmental disorders. The findings of this meta-analysis hold substantial implications for understanding the complex nature of NDDs and their genetic and environmental foundations. Identifying a genetic overlap between different NDD categories and their co-occurrence with DICCs suggests shared underlying mechanisms that transcend diagnostic boundaries. The finding of an uneven distribution of genetics research, which has been predominantly focused on disorders such as autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD), highlights gaps in understanding of the aetiology of the remaining NDD categories. This could serve as a call to action for future research to address these gaps and explore the genetic and environmental underpinnings of less-studied NDDs, such as intellectual disabilities and motor disorders, and their co-occurrences.

While exposing the uneven distribution of research efforts in behaviour genetics, this meta-analysis also notes substantial geographical variations in aetiology and a lack of racial and cultural diversity among samples. These limitations stress the need for more inclusive research and emphasise the importance of balanced attention across various diagnostic categories and participant populations for improved applicability and generalizability of

findings. Overall, the meta-analysis contributed to our understanding of the genetic underpinnings of NDDs and their co-occurrence with other developmental conditions. synthesising a vast array of studies underscored the complexity of NDD aetiology, highlighting the substantial contributions of genetic and environmental factors. The identification of shared genetic factors across different NDD categories and their co-occurrence with diverse developmental conditions challenges traditional diagnostic boundaries, advocating for a more holistic and integrated approach to understanding these disorders. These findings emphasise the need for comprehensive assessment strategies and highlight the importance of considering co-occurrence in formulating effective interventions and preventive measures to address the multifaceted nature of NDDs.

Chapter 3 investigated the utility of DNA-based prediction of behaviour problems across development. The study aimed to enhance the predictive power of genome-wide polygenic scores (PGSs) by employing the cross-trait, longitudinal, and trans-situational approaches. We constructed latent composites of behaviour problems and explored the potential of the multi-PGS prediction in various developmental contexts, using PGSs derived from genome-wide association (GWA) studies of psychiatric disorders and personality traits. We investigated whether aggregated PGSs can improve predictive power and provide insights into the genetic basis of behaviour problems. The study discussed mechanisms underlying improved prediction and the potential for gene-environment interplay research to be facilitated by aggregation techniques. This paper contributed to the field of behaviour genetics by demonstrating how DNA-based prediction can enhance our understanding of behaviour problems across different developmental stages and how the use of multiple PGSs to predict behaviour problems is a promising approach that builds upon the growing body of knowledge regarding the genetic basis of complex traits. In this study, we also found that the cross-trait, longitudinal, and trans-situational approaches have the potential to enhance predictive power. This approach acknowledges the dynamic nature of behaviour problems across development and the importance of considering multiple sources of information, such as different measurements and raters. The study showcases the potential for a more holistic understanding of behaviour problems by integrating data from various stages of development and different contexts. The recognition that environmental factors can also influence genetic predisposition emphasises the complexity of behaviour problems and the need for method refinement to account for how these environments interact with genetic propensities to shape emotional and behavioural outcomes. In addition to DNA-based prediction, this chapter also

investigated the genetic aetiology of behaviour problems using the twin methodology. Polygenic scores-based research into behaviour problems may enhance our understanding beyond twin studies by identifying the proportion of variance accounted for by specific genetic variants associated with complex traits, as opposed to the broad heritability estimates provided by twin studies, which also consider the impact of rare variants and gene-gene interactions.

Aiming for a comprehensive discussion of the importance and potential impact of genetic investigations into developmental psychopathology, we must confront the broader ethical and social issues surrounding this line of research. Ethical and social considerations extend beyond methodological rigour to issues linked to diversity, the societal impact of research and transparent public dissemination of findings. Exploring the genetic and environmental aetiology of developmental psychopathology, one must be aware of the potential for stigmatization and the importance of engaging in collaborative practices and adopting diverse perspectives. The reliance on PGSs and the observed disparities in their predictive power among different populations, particularly with a Eurocentric bias, introduces another critical ethical and scientific consideration that involves the inclusion and protection of vulnerable populations (A. R. Martin, Kanai, et al., 2019; Popejoy & Fullerton, 2016; "Whose Genomics?," 2019). Polygenic scores are currently more accurate in predicting complex traits, including psychopathology, for individuals of European descent (Vilhjálmsson et al., 2015a). This discrepancy is not due to inherent biological differences but rather stems from the underrepresentation of non-European populations in GWA studies (A. R. Martin, Kanai, et al., 2019). Developmental psychopathology often manifests differently across diverse populations due to a complex interplay of genetic, environmental, and cultural factors (D. W. Belsky et al., 2019). The fact that 80% of participants in DNA-based research are of European descent, while they constitute only 16% of the global population, highlights a substantial skew in the demographics of research samples ("Genetics for All," 2019). If the data used to develop PGSs predominantly comes from one ethnic or cultural group, it may not accurately capture the risk factors in other populations. Ethical guidelines must underscore the importance of cultural sensitivity, respecting diverse backgrounds and ensuring that research methods do not sustain biases or reinforce stereotypes.

Not only is the Eurocentric bias prevalent in GWA investigations but also in behaviour genetics studies that employ twin and family models (Gidziela, Ahmadzadeh, et al., 2023;

"Whose Genomics?," 2019). This is concerning because the prevalence and manifestation of developmental disorders vary across different regions, cultures, and ethnicities (Institute for Health Metrics and Evaluation, 2019). To address the Eurocentric bias in behaviour genetics research, there is a need for concerted efforts to enhance diversity in research samples, ensuring that research methodologies are culturally inclusive and do not perpetuate systemic biases. This includes increased collaboration with researchers and participants from non-Western regions and the development of methodologies that consider and account for ancestral diversity. Recent initiatives, such as the East London Genes & Health (ELGH) (Finer et al., 2020), the Born in Bradford Multi-Ethnic Family Cohort Study (Wright et al., 2013), and the African Partnerships through the H3Africa Consortium (Ramsay & Sankoh, 2016), play a pivotal role in minimizing Eurocentric bias in genetic research by contributin to a more representative understanding of the genetic determinants of health.
Nevertheless, the challenge of enrolling minority populations in medical research persists despite mandates like the NIH Revitalization Act, which emphasises their inclusion (Baquet et al., 2008; Freedman et al., 1995; Paskett et al., 2008; Svensson et al., 2012). Barriers such as lack of time, inconvenient locations, socio-cultural factors and limited awareness hinder participation, leading to the overrepresentation of Europeans in medical research (Farmer et al., 2007; Svensson et al., 2012; Wendler et al., 2006). Only by embracing a more inclusive and global perspective in genetic research can we hope to unravel the complexities of developmental disorders across diverse populations and develop more universally applicable insights for diagnosis, treatment, and prevention ("Genetics for All," 2019).

In Chapter 4, the focus shifted to the intricate role of nonshared environmental (NSE) factors in shaping behaviour problems from childhood to adulthood. A nonshared environment, which includes unique experiences that differ between siblings, often remains overshadowed by genetic and shared environmental factors in behaviour genetics research.
The common oversight of the NSE relates to the measurement, specifically a reliance on questionnaire ratings for assessing behaviour problems. These standard measurement practice in research but one that inherently carries constraints because the evaluation draws on input from parents, teachers, and the twins themselves, limiting the depth of behavioral insights. Research indicates that alternative assessment methods, such as observational measures, may yield more robust results (Pike, McGuire, et al., 1996; Turkheimer & Waldron, 2000). However, the choice between assessment methods entails trade-offs. Observational measures offer an objective lens, capturing nuances that questionnaires might overlook, potentially

providing a more accurate reflection of environmental influences. Yet, a broader challenge surfaces in the limited availability of objective measures in the literature, highlighting the need for future research to explore and incorporate more diverse and objective assessment tools. Conversely, self-report questionnaires tap into perceptions and subjective experiences of the environment (Plomin et al., 1994). Nonshared environment research faces a general limitation wherein assessments of the family environment traditionally prioritize variations between families rather than considering unique circumstances within each family (Asbury et al., 2017; Daniels & Plomin, 1985). To address this gap, there is a recognized need for additional measures that specifically capture the within-family environment for each child. It is crucial to recognize that the causes of environmental differences between families may not necessarily align with the causes of differences within families (Plomin & Daniels, 1987).

Chapter 4 addressed the analytic imbalance related to behaviour genetic research primarily exploring nature and nurture and omitting the NSE component (Harris, 1998). The study employed a multivariate longitudinal twin modelling approach, which dissects the contributions of NSE, genetics, and shared environment to behaviour problems from early childhood to adulthood. The investigation of NSE, distinct from genetics and shared environment, highlighted the 'missing NSE' gap— the shortfall in identifying specific environmental factors that would account for the NSE variance of behaviour problem symptoms (Turkheimer, 2011). From a research perspective, acknowledging the role of NSE factors prompts a re-evaluation of study designs and data collection methodologies. Researchers are urged to develop more sophisticated and comprehensive tools to capture the diversity of environmental experiences contributing to behaviour problems. The 'missing heritability' gap in understanding the genetic basis of behavioural traits has been addressed through GWA studies utilizing DNA chips (Plomin, 2019). A parallel breakthrough in NSE research could be achieved with the RNA chip, that offers a snapshot of environmental effects, as well as focusing on epigenetic changes, measured through DNA methylation (Bell & Spector, 2011; Feil & Fraga, 2012; von Stumm & d'Apice, 2022; C. C. Y. Wong et al., 2014). However, both transcriptomics and epigenomics are tissue-specific, and accessing the relevant tissue, the brain, poses a challenge. Another avenue for understanding NSE lies in technological advancements in remote real-time monitoring through wearables, smartphones, and social media data (Adjerid & Kelley, 2018). These efforts would lead to a more accurate depiction of how the NSE impacts the emergence and persistence of phenotypes. However, the difficulty in establishing causality warrants cautious interpretation of correlations between

environmental measures and behaviour problems, as the primary goal is to identify predictive NSE factors rather than providing causal explanations (Plomin & von Stumm, 2022; Yarkoni & Westfall, 2017).

The cumulative insights from Chapters 2 to 4 lay the foundation for the central inquiry of Chapter 5— evaluating the interplay between genetic and environmental factors in the development of adolescent psychopathology. This chapter aims to bridge the insights gained from previous chapters to comprehensively analyse the complex interplay between genes and environments in shaping the trajectory of developmental psychopathology, considering both how genetic and environmental factors correlate and interact. By drawing on the nuanced understanding of genetic propensity and environmental influences, this chapter provided a more integrated perspective on the aetiology and progression of adolescent psychopathology. The findings demonstrated that both genetic and environmental factors contribute to the development of psychopathology, although the interactions between them are relatively small, which could be attributed to several factors. Firstly, the limited predictive power of the psychiatric PGSs does not capture the full complexity of genetic influences on developmental psychopathology (Plomin et al., 2022). Additionally, the statistical power of our study, while sufficient for detecting large G×E effects of >1%, is not insufficient to identify subtle effects (L. E. Duncan & Keller, 2011; Plomin et al., 2022). The inherent complexity of rGE in psychiatric outcomes adds another layer of challenge. Acknowledging the role of rGE is crucial, as it unveils that individuals, influenced by their genetic predispositions, might actively seek or shape environments that align with their inherent propensities. Overlooking rGE can result in misinterpretations and misidentification of authentic G×E effects (Plomin & Viding, 2022).

The study also emphasises the importance of adolescents' perceptions of their own environments, which were stronger predictors of adolescent psychopathology, compared to parent-rated measures. This suggests that adolescent interpretations of their environments influence their emotional and behavioural functioning during adolescence. Therefore, comprehensively assessing developmental psychopathology needs to extend beyond traditional measurement scales, embracing a more nuanced approach through symptom-level analyses and evaluations of daily functioning (Markon, 2010; Russell & Gajos, 2020). Daily functioning measures assess the practical impact of symptoms on an individual's ability to navigate various life domains, emphasising adaptive functioning and independence (Russell

& Gajos, 2020). Additionally, incorporating sleep patterns and biological markers, such as cortisol levels, offers a deeper insight into the intricate interplay of psychological and physiological factors (Malanchini et al., 2021; Meltzer, 2017; Sadeh, 2015). This multimodal assessment, grounded in real-world contexts and ecological validity, seeks to capture the complexity of developmental psychopathology, enabling more precise evaluations and facilitating G×E research.

Despite the small effect sizes of observed gene-environment interactions (G×E), the findings hold the predictive potential. This predictive capacity matters, even if the underlying causal mechanisms are not fully understood. The aim of prediction is to maximize the proportion of variance accounted for, without necessitating a detailed causal understanding. In practical terms, while small effect sizes limit the immediate clinical applications, this chapter provides a thorough investigation of gene-environment interplay in adolescent psychopathology, paving the way for future research aiming to select environmental candidates that combine with polygenic risk and predict psychiatric outcomes.

Collectively, the findings presented in this thesis highlight the necessity of considering both genetic and environmental factors in understanding the multifaceted nature of developmental psychopathology. The integration of genetic information and aggregation techniques, as demonstrated in Chapters 3 and 4, offers a promising approach to enhancing prediction and gaining insights into the underlying mechanisms. Recognition of the 'missing NSE' gap in Chapter 4 emphasises the complexity of the environmental influences and calls for innovative methods to capture these elusive factors accurately.

The impact of developmental psychopathology research extends beyond the scientific community. Chapters 2 and 3, exploring the genetic underpinnings of NDDs and polygenic prediction of childhood behaviour problems, raise ethical questions about how these findings are communicated to the broader public (Gidziela, Ahmadzadeh, et al., 2022; Gidziela, Rimfeld, et al., 2022). Researchers must be mindful of the potential societal implications and ensure that dissemination is accurate and balanced. Striking a balance between scientific rigour and accessible communication is an ethical responsibility, preventing the misinterpretation of findings (“Embracing Communication,” 2021). The historical misuse of genetic information to justify discrimination and violence against marginalised groups adds an extra layer of responsibility to researchers in human genetics, reinforcing the need for

clear and accessible communication (Martschenko et al., 2021; Pascoe, 2009). One of the efforts to enhance public understanding of genetic research is introducing the FAQs on Genomic Studies (FoGs) database (Martschenko et al., 2021). This database, collecting FAQ documents accompanying GWA publications on behavioural and social traits, explains and interprets the results in an accessible manner. This initiative contributes to responsible reporting and mitigates the risk of misinterpretation by encouraging researchers to include FAQs in their studies and providing a template for their creation.

The matter of dissemination becomes even more critical when it comes to PGS research, necessitating a commitment to transparency regarding their predictive power and scope. Given the potential for deterministic interpretation, it is crucial to convey that PGSs represent only one component of multifaceted traits influenced by a complex interplay between genetic and environmental factors (Sud et al., 2023; Wray et al., 2021). The responsible sharing of PGS research findings demands issues of stigmatisation and discrimination to be integral to the public discourse surrounding PGS research (Lewis & Green, 2021). Researchers, and stakeholders can contribute to a more informed and ethically responsible public understanding of genetic effects on developmental psychopathology and polygenic prediction by integrating these principles into communication strategies.

In the intricate landscape of developmental psychopathology, focusing on how psychological and behavioural development unfolds across the lifespan, translating research findings into practical applications presents dynamic challenges (Rutter & Sroufe, 2000). Navigating the complex interplay of genetic and environmental factors requires a nuanced understanding to bridge the gap between scientific findings and real-world interventions for the wellbeing of individuals across diverse developmental trajectories. Reflecting on the limitations of developmental psychopathology research necessitates an open acknowledgement of what impedes the research-to-practice translation, considering the multifactorial nature of developmental processes, issues of predictive power, generalisability and interdisciplinary communication.

The multifactorial nature of developmental psychopathology highlights the complex interplay of genetic and environmental factors in the emergence and persistence of symptoms (Rutter & Silberg, 2002). This interplay contributes to the research-to-practice gap in understanding and addressing developmental psychopathology due to the limited impact of the G×E,

explaining only small proportions of variance (Plomin et al., 2022). Although these findings contribute valuable insights into risk prediction, being the first step towards the explanation of mechanisms underlying variability in developmental phenotypes (Plomin & von Stumm, 2022), their practical utility for precise individual-level predictions or targeted interventions remains distant. It is evident that as the field of gene-environment interplay research progresses, efforts must focus on accumulating more substantial effect sizes to attain clinical applicability (Plomin et al., 2022). A much more feasible immediate utility of gene-environment research of developmental psychopathology includes refining the measures and predictive models to better understand the multifactorial nature of developmental disorders at the level of scientific investigations.

The research-to-practice gap in developmental psychopathology is even more pronounced in research involving the PGSs. While these scores have proven valuable in predicting physiological outcomes (Inouye et al., 2018; Oram et al., 2016; Padilla-Martínez et al., 2020) and shedding light on behavioural traits (Gidziela, Rimfeld, et al., 2022), their translation into practical applications for identifying and addressing developmental psychopathology is limited. One key challenge of translating the PGS findings into practical interventions is the modest predictive power of PGSs for behaviour and emotional problems, accounting for less than 6% of differences in this domain (Gidziela, Rimfeld, et al., 2022). The current level of predictive power is insufficient for correctly identifying children at risk of developmental disorders, however, despite their current effect sizes, PGSs can still prove valuable in clinical research. For instance, a twofold greater risk of a depression diagnosis was observed for individuals in the highest decile of the internalising PGS, compared to those in the lowest decile (Gidziela, Rimfeld, et al., 2022). It is essential to note, however, that these findings may not be universally applicable to other sample populations. Despite this limitation, PGSs remain a valuable tool in behaviour genetics research, particularly when combined with other environmental factors.

Polygenic scores exhibit varying levels of utility in predicting real-life outcomes, with some being highly precise. For cardiovascular diseases, for example, studies have shown that a high PGS can be as effective at predicting the risk of heart problems as other lifestyle risk factors that are usually considered by medical practitioners, for example, smoking and body mass index (Aragam & Natarajan, 2020; Inouye et al., 2018). Polygenic scores have also been found to predict the risk of diabetes (Bonifacio et al., 2018), with greater than 80%

accuracy for type 1 diabetes (Perry et al., 2018). Using PGSs, it might be possible to diagnose young adults with diabetes who might need insulin treatment (Padilla-Martínez et al., 2020) and to differentiate between different types of diabetes (e.g., type 1 versus type 2) (Oram et al., 2016; Patel et al., 2016). In addition to the promising accuracy of PGSs in predicting health outcomes, recall-by-genotype studies stand out as a complementary avenue (Nurm et al., 2022). Recall-by-genotype studies involve recalling individuals based on disease-related genotypes to gather detailed clinical and phenotypic information. Recall-by-genotype studies have proven useful in the context of familial hypercholesterolemia, an autosomal-dominant genetic disorder associated with elevated cholesterol levels (Nurm et al., 2022). One longitudinal recall-by-genotype study conducted within the Estonian Biobank, involving 34 recalled participants and 291 controls revealed substantial differences in familial hypercholesterolemia diagnoses and lipid-lowering treatment prescriptions between study groups (Nurm et al., 2022). Although recall-by-genotype studies typically focus of single-gene disorders, a recent study of Alzheimer's disease implemented the polygenic approach and recruited clinically asymptomatic participants who scored at the high and low extremes of the Alzheimer's disease PGS (Lancaster et al., 2023). This integration enhanced the sensitivity and specificity of genetic risk assessment, potentially leading to more comprehensive insights into the genetic architecture of complex traits like Alzheimer's disease (Lancaster et al., 2023). Implementing PGSs in recall-by-genotype studies can improve the efficiency and power of the studies, facilitating the detection and assessments of individuals with increased genetic risk for particular disorders (Lancaster et al., 2023). With a high level of accuracy, greater precision in diagnosis could result in lifestyle changes or targeted use of medication to effectively treat, or even slow down the progression of the condition before the symptoms have manifested. Moreover, as research progresses, polygenic scores may contribute to the development of innovative treatments tailored to an individual's genetic profile, maximizing efficacy and minimizing side effects.

The future of PGSs holds great promise in revolutionizing personalized medicine and enhancing our understanding of genetic factors influencing various traits and health conditions (Plomin & von Stumm, 2022). In fields such as mental health, PGSs could contribute to a deeper understanding of the genetic basis of conditions like depression, anxiety, and schizophrenia. This knowledge may pave the way for more effective therapeutic approaches and destigmatize mental health issues by emphasizing their biological underpinnings (Jorm et al., 1997; Wahl, 1987). However, other studies suggest that revealing

the genetic basis of certain mental health conditions, like schizophrenia, can have complex implications for stigma and shame and that these reactions depend on framing of genetic information and public understanding of genetics (Bennett et al., 2008). With countries like Finland and Estonia already incorporating DNA testing into their national health services and trials underway in the United Kingdom, the prospect of routine DNA testing at birth is on the horizon (Gidziela, Rimfeld, et al., 2022). However, as the Chinese government ambitiously aims to sequence the DNA of a substantial percentage of newborns, discussions about maximizing clinical benefits and minimizing risks become paramount (Gidziela, Rimfeld, et al., 2022; Metzl, 2019b). Some argue that these scores, while powerful, may never singularly serve as reliable predictors of polygenic diseases (Wray et al., 2021). While the medical applications of DNA testing primarily focus on predicting and preventing disorders, the broader use of polygenic information introduces ethical considerations, emphasizing the urgency of establishing responsible guidelines and frameworks to navigate the evolving landscape of genomic medicine.

Another issue making research-to-practice translation challenging refers to the limited generalizability of the findings. Research findings based on specific populations or contexts can hinder the development of universally applicable interventions. When a study is confined to particular groups or scenarios, its relevance to a broader demographic spectrum diminishes. Factors such as participants' background, socioeconomic status (SES), and cultural attributes are crucial in shaping developmental outcomes. A socioeconomic bias may emerge when the study predominantly involves a specific economic class, leading to recommendations that might not resonate with those from different financial backgrounds. When voluntary participation is a feature of population-based studies, individuals with higher SES are often overrepresented, leading to a skewed sample that may not accurately reflect the broader population (Jousilahti et al., 2005; Vo et al., 2023). Factors frequently used to measure SES include sociodemographic characteristics, such as education, occupation, and income (Hatch et al., 2011; Mackenbach et al., 2008). Research consistently shows that individuals with lower SES are less likely to participate in health surveys (Harald et al., 2007; Lorant et al., 2007; Søgaard et al., 2004; Tolonen et al., 2006). To overcome this bias, researchers increasingly turn to high-quality national registers with individual-level data (Vo et al., 2023). By comparing the sociodemographic characteristics of participants and non-participants, researchers can gain insights into the nature and extent of selection bias. This understanding is critical for making more accurate assumptions and drawing reliable

conclusions in population-based studies, ensuring that research findings are applicable and relevant across diverse socioeconomic strata. Addressing the issue of high SES bias in research is crucial for promoting equity and improving the overall quality of research. Implications for intervention and policy are contingent on the inclusivity of the research findings. Narrow sample characteristics could limit the practicality of proposed interventions, impeding the development of practical applications that cater to the diverse needs of populations. Because genetic effects are inseparable from environmental and social contexts (Abdellaoui et al., 2019; Gidziela, Ahmadzadeh, et al., 2023; Rimfeld, Krapohl, et al., 2018; Silventoinen et al., 2020), ignoring the lack of socioeconomic diversity in sample characteristics risks oversimplifying conclusions and missing the nuanced dynamics that shape developmental psychopathology. Balancing precision phenotyping, generalizability, and sample size in developmental psychopathology research is a nuanced challenge. While detailed phenotypic data allows for a fine-grained understanding of individual differences, achieving broader applicability requires consideration of generalizability to diverse populations. Register data, with its potential for large sample sizes, offers an opportunity to enhance statistical power but may entail sacrificing some precision.

This research-to-practice crisis stems from the inherent complexity of understanding and addressing developmental psychopathology, necessitating a multidisciplinary approach involving various fields such as psychology, genetics, and neuroscience (Cicchetti & Toth, 2006; Eisenberg & Pellmar, 2000; Nelson et al., 2002; Sroufe & Rutter, 1984). The collaborative efforts within consortia, such as CAPICE (Childhood and Adolescence Psychopathology: unravelling the complex aetiology by a Large Interdisciplinary Collaboration in Europe), reflect a significant shift in genetic research in developmental psychopathology (Rajula et al., 2022). CAPICE, in conjunction with the EAGLE (EArly Genetics and Life course Epidemiology) consortium, has leveraged methodological advancements in the field of psychiatric genetics to address fundamental questions in child psychiatry (Middeldorp et al., 2019; Rajula et al., 2022). These questions span from understanding the genetic variants and biological pathways contributing to the continuity of symptoms from childhood to adulthood, unravelling the associations of developmental psychopathology with early life and familial risk factors, probing into the role of epigenetic factors, to predicting which children are at higher risk for poorer outcomes (Rajula et al., 2022). By identifying novel targets for existing pharmacological agents, these collaborative endeavours contribute to the advancement of precision medicine in child psychiatry (Breen et

al., 2016; Gaspar et al., 2019; Gaspar & Breen, 2017; So et al., 2017). The prospect of having better prediction tools offers the opportunity to tailor interventions specifically to children at high or low risk for the persistence of symptoms, thereby optimising treatment outcomes. A model for collaborative, multidisciplinary research in developmental psychopathology contributes to translating research findings into tangible benefits for clinical practice and broader society and minimizing the research-to-practice crisis.

This thesis contributes significantly to the field of developmental psychopathology by shedding light on the intricate interplay between genetics and environment in shaping developmental outcomes. The insights gained from this thesis expand our theoretical understanding and hold practical implications for intervention and prevention strategies targeting developmental disorders and behavioural problems in children and adolescents. The ethical and social considerations highlighted in this thesis draw attention to the responsibility researchers bear in communicating findings transparently, avoiding stigmatisation, and addressing the Eurocentric bias in genetic research. The challenges of translating research into practice, especially in the context of PGSs, highlight the need to refine measures, consider environmental factors, and navigate ethical concerns related to privacy and discrimination. The research-to-practice crisis is further characterised by limited generalizability, emphasising the importance of diverse and inclusive research samples to ensure the relevance and applicability of interventions across different populations.

Despite these challenges, collaborative efforts represent a promising avenue for multidisciplinary research in developmental psychopathology. These collaborations hold the potential to bridge the gap between research and practice, offering insights that could inform the development of targeted interventions and prevention strategies. As we navigate the complexities of understanding and addressing developmental psychopathology, it is clear that a multidimensional approach—one that integrates genetic, environmental, and social perspectives—is essential for advancing both scientific knowledge and the wellbeing of individuals across diverse developmental trajectories. The ethical and social considerations embedded in developmental psychopathology research are integral to its responsible conduct and application.

# References


Abdellaoui, A., Hugh-Jones, D., Yengo, L., Kemper, K. E., Nivard, M. G., Veul, L., Holtz, Y., Zietsch, B. P., Frayling, T. M., Wray, N. R., Yang, J., Verweij, K. J. H., & Visscher, P. M. (2019). Genetic correlates of social stratification in Great Britain. Nature Human Behaviour, 3(12). https://doi.org/10.1038/s41562-019-0757-5

Adjerid, I., & Kelley, K. (2018). Big data in psychology: A framework for research advancement. *American Psychologist*, *73*(7). https://doi.org/10.1037/amp0000190

Ainley, J., & Bourke, S. (1992). Student views of primary schooling. *Research Papers in Education*, *7*(2). https://doi.org/10.1080/0267152920070202

Akingbuwa, W. A., Hammerschlag, A. R., Jami, E. S., Allegrini, A. G., Karhunen, V., Sallis, H., Ask, H., Askeland, R. B., Baselmans, B., Diemer, E., Hagenbeek, F. A., Havdahl, A., Hottenga, J. J., Mbarek, H., Rivadeneira, F., Tesli, M., Van Beijsterveldt, C., Breen, G., Lewis, C. M., … Middeldorp, C. M. (2020). Genetic Associations between Childhood Psychopathology and Adult Depression and Associated Traits in 42998 Individuals: A Meta-analysis. *JAMA Psychiatry*, *77*(7). https://doi.org/10.1001/jamapsychiatry.2020.0527

Alarcón, M., DeFries, J. C., & Fulker, D. W. (1995). Etiology of individual differences in reading performance: A test of sex limitation. *Behavior Genetics*, *25*(1). https://doi.org/10.1007/BF02197238

Alarcón, M., DeFries, J. C., Light, J. G., & Pennington, B. F. (1997). A Twin Study of Mathematics Disability. *Journal of Learning Disabilities*, *30*(6). https://doi.org/10.1177/002221949703000605

Albiñana, C., Zhu, Z., Schork, A. J., Ingason, A., Aschard, H., Brikell, I., Bulik, C. M., Petersen, L. V., Agerbo, E., Grove, J., Nordentoft, M., Hougaard, D. M., Werge, T., Børglum, A. D., Mortensen, P. B., McGrath, J. J., Neale, B. M., Privé, F., & Vilhjálmsson, B. J. (2023). Multi-PGS enhances polygenic prediction by combining 937 polygenic scores. *Nature Communications*, *14*(1). https://doi.org/10.1038/s41467-023-40330-w

Alexander, R. A., Scozzaro, M. J., & Borodkin, L. J. (1989). Statistical and empirical examination of the chi-square test for homogeneity of correlations in meta-analysis. *Psychological Bulletin*, *106*(2), 329.

Allegrini, A. G., Cheesman, R., Rimfeld, K., Selzam, S., Pingault, J. B., Eley, T. C., & Plomin, R. (2020). The p factor: genetic analyses support a general dimension of psychopathology in

childhood and adolescence. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *61*(1). https://doi.org/10.1111/jcpp.13113

Allegrini, A. G., Karhunen, V., Coleman, J. R. I., Selzam, S., Rimfeld, K., von Stumm, S., Pingault, J. B., & Plomin, R. (2020). Multivariable G-E interplay in the prediction of educational achievement. *PLoS Genetics*, *16*(11). https://doi.org/10.1371/journal.pgen.1009153

Allegrini, A. G., Selzam, S., Rimfeld, K., von Stumm, S., Pingault, J. B., & Plomin, R. (2019). Genomic prediction of cognitive traits in childhood and adolescence. *Molecular Psychiatry*, *24*(6). https://doi.org/10.1038/s41380-019-0394-4

Anckarsäter, H., Lundström, S., Kollberg, L., Kerekes, N., Palm, C., Carlström, E., Långström, N., Magnusson, P. K. E., Halldner, L., Bölte, S., Gillberg, C., Gumpert, C., Råstam, M., & Lichtenstein, P. (2011). The child and adolescent twin study in Sweden (CATSS). *Twin Research and Human Genetics*, *14*(6). https://doi.org/10.1375/twin.14.6.495

Andersson, A., Tuvblad, C., Chen, Q., Du Rietz, E., Cortese, S., Kuja-Halkola, R., & Larsson, H. (2020). Research Review: The strength of the genetic overlap between ADHD and other psychiatric symptoms – a systematic review and meta-analysis. In *Journal of Child Psychology and Psychiatry and Allied Disciplines* (Vol. 61, Issue 11). https://doi.org/10.1111/jcpp.13233

Anney, R. J. L., Ripke, S., Anttila, V., Grove, J., Holmans, P., Huang, H., Klei, L., Lee, P. H., Medland, S. E., Neale, B., Robinson, E., Weiss, L. A., Zwaigenbaum, L., Yu, T. W., Wittemeyer, K., Willsey, A. J., Wijsman, E. M., Werge, T., Wassink, T. H., … Consortium, T. A. S. D. W. G. of T. P. G. (2017). Meta-analysis of GWAS of over 16,000 individuals with autism spectrum disorder highlights a novel locus at 10q24.32 and a significant overlap with schizophrenia. *Molecular Autism*, *8*(1), 21. https://doi.org/10.1186/s13229-017-0137-9

APA, A. P. A. (2022). Diagnostic and statistical manual of mental disorders: FIFTH EDITION - TEXT REVISION - DSM-5-TR. In *American Psychiatric Publishi ng*.

Aragam, K. G., & Natarajan, P. (2020). Polygenic Scores to Assess Atherosclerotic Cardiovascular Disease Risk: Clinical Perspectives and Basic Implications. *Circulation Research*, *126*(9). https://doi.org/10.1161/CIRCRESAHA.120.315928

Armitage, J. M., Wang, R. A. H., Davis, O. S. P., & Haworth, C. M. A. (2022). A Polygenic Approach to Understanding Resilience to Peer Victimisation. *Behavior Genetics*, *52*(1). https://doi.org/10.1007/s10519-021-10085-5

Arnau-Soler, A., Macdonald-Dunlop, E., Adams, M. J., Clarke, T. K., MacIntyre, D. J., Milburn, K., Navrady, L., Hayward, C., McIntosh, A. M., & Thomson, P. A. (2019). Genome-wide by

environment interaction studies of depressive symptoms and psychosocial stress in UK Biobank and Generation Scotland. *Translational Psychiatry*, *9*(1). https://doi.org/10.1038/s41398-018-0360-y

Arnold, P. D., Askland, K. D., Barlassina, C., Bellodi, L., Bienvenu, O. J., Black, D., Bloch, M., Brentani, H., Burton, C. L., Camarena, B., Cappi, C., Cath, D., Cavallini, M., Conti, D., Cook, E., Coric, V., Cullen, B. A., Cusi, D., Davis, L. K., … Zai, G. (2018). Revealing the complex genetic architecture of obsessive-compulsive disorder using meta-analysis. *Molecular Psychiatry*, *23*(5). https://doi.org/10.1038/mp.2017.154

Asbury, K., Dunn, J. F., Pike, A., & Plomin, R. (2003). Nonshared Environmental Influences on Individual Differences in Early Behavioral Development: A Monozygotic Twin Differences Study. *Child Development*, *74*(3). https://doi.org/10.1111/1467-8624.00577

Asbury, K., Moran, N., & Plomin, R. (2017). Do MZ twins have discordant experiences of friendship? A qualitative hypothesis-generating MZ twin differences study. *PLoS ONE*, *12*(7). https://doi.org/10.1371/journal.pone.0180521

Association, A. P. (1994). Diagnostic criteria from DSM-IV. *Washington DC: American Psychiatry Association*.

Association, A. P. (2015). *Neurodevelopmental disorders: DSM-5® selections*. American Psychiatric Pub.

Astrom, R. L., Wadsworth, S. J., Olson, R. K., Willcutt, E. G., & DeFries, J. C. (2011). DeFries-fulker analysis of longitudinal reading performance data from twin pairs ascertained for reading difficulties and from their nontwin siblings. *Behavior Genetics*, *41*(5). https://doi.org/10.1007/s10519-011-9445-6

Autism Speaks. (2022). *AGRE—Autism Genetic Resource Exchange*.

Avenevoli, S., Swendsen, J., He, J. P., Burstein, M., & Merikangas, K. R. (2015). Major Depression in the National Comorbidity Survey–Adolescent Supplement: Prevalence, Correlates, and Treatment. *Journal of the American Academy of Child and Adolescent Psychiatry*, *54*(1). https://doi.org/10.1016/j.jaac.2014.10.010

Bailey, A., Le Couteur, A., Gottesman, I., Bolton, P., Simonoff, E., Yuzda, E., & Rutter, M. (2013). Autism as a strongly genetic disorder: Evidence from a british twin study. In *The Science of Mental Health: Volume 2: Autism*.

Baio, J., Wiggins, L., Christensen, D. L., Maenner, M. J., Daniels, J., Warren, Z., Kurzius-Spencer, M., Zahorodny, W., Rosenberg, C. R., White, T., Durkin, M. S., Imm, P., Nikolaou, L., Yeargin-Allsopp, M., Lee, L. C., Harrington, R., Lopez, M., Fitzgerald, R. T., Hewitt, A., … Dowling, N. F. (2018). Prevalence of autism spectrum disorder among children aged 8

Years - Autism and developmental disabilities monitoring network, 11 Sites, United States, 2014. *MMWR Surveillance Summaries*, *67*(6). https://doi.org/10.15585/mmwr.ss6706a1

Bakermans-Kranenburg, M. J., & Van IJzendoorn, M. H. (2007). Research Review: Genetic vulnerability or differential susceptibility in child development: The case of attachment. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *48*(12). https://doi.org/10.1111/j.1469-7610.2007.01801.x

Balduzzi, S., Rücker, G., & Schwarzer, G. (2019). How to perform a meta-analysis with R: A practical tutorial. *Evidence-Based Mental Health*, *22*(4). https://doi.org/10.1136/ebmental-2019-300117

Baquet, C. R., Mishra, S. I., Commiskey, P., Ellison, G. L., & DeShields, M. (2008). Breast cancer epidemiology in blacks and whites: Disparities in incidence, mortality, survival rates and histology. *Journal of the National Medical Association*, *100*(5). https://doi.org/10.1016/s0027-9684(15)31294-3

Bares, C. B., Chartier, K. G., Karriker-Jaffe, K. J., Aliev, F., Mustanski, B., & Dick, D. (2020). Exploring how Family and Neighborhood Stressors Influence Genetic Risk for Adolescent Conduct Problems and Alcohol Use. *Journal of Youth and Adolescence*, *49*(7). https://doi.org/10.1007/s10964-019-01098-9

Baron, R. M., & Kenny, D. A. (1986). The moderator-mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology*, *51*(6). https://doi.org/10.1037//0022-3514.51.6.1173

Bartels, M., Boomsma, D. I., Hudziak, J. J., Rietveld, M. J. H., Van Beijsterveldt, T. C. E. M., & Van Den Oord, E. J. C. G. (2004). Disentangling Genetic, Environmental, and Rater Effects on Internalizing and Externalizing Problem Behavior in 10-year-old Twins. *Twin Research*, *7*(2). https://doi.org/10.1375/136905204323016140

Baselmans, B. M. L., Yengo, L., van Rheenen, W., & Wray, N. R. (2021). Risk in Relatives, Heritability, SNP-Based Heritability, and Genetic Correlations in Psychiatric Disorders: A Review. In *Biological Psychiatry* (Vol. 89, Issue 1). https://doi.org/10.1016/j.biopsych.2020.05.034

Bates, S., Hastie, T., & Tibshirani, R. (2023). Cross-validation: what does it estimate and how well does it do it? *Journal of the American Statistical Association*, 1–12.

Bates, T. C., Castles, A., Coltheart, M., Gillespie, N., Wright, M., & Martin, N. G. (2004). Behaviour genetic analyses of reading and spelling: A component processes approach. *Australian Journal of Psychology*, *56*(2). https://doi.org/10.1080/00049530410001734847

Bayard, F., Nymberg Thunell, C., Abé, C., Almeida, R., Banaschewski, T., Barker, G., Bokde, A. L. W., Bromberg, U., Büchel, C., Quinlan, E. B., Desrivières, S., Flor, H., Frouin, V., Garavan, H., Gowland, P., Heinz, A., Ittermann, B., Martinot, J. L., Martinot, M. L. P., … Petrovic, P. (2020). Distinct brain structure and behavior related to ADHD and conduct disorder traits. *Molecular Psychiatry*, *25*(11). https://doi.org/10.1038/s41380-018-0202-6

Behar, L. B. (1977). The Preschool Behavior Questionnaire. *Journal of Abnormal Child Psychology*, *5*(3). https://doi.org/10.1007/BF00913697

Bell, J. T., & Spector, T. D. (2011). A twin approach to unraveling epigenetics. In *Trends in Genetics* (Vol. 27, Issue 3). https://doi.org/10.1016/j.tig.2010.12.005

Belsky, D. W., Caspi, A., Arseneault, L., Corcoran, D. L., Domingue, B. W., Harris, K. M., Houts, R. M., Mill, J. S., Moffitt, T. E., Prinz, J., Sugden, K., Wertz, J., Williams, B., & Odgers, C. L. (2019). Genetics and the geography of health, behaviour and attainment. In *Nature Human Behaviour* (Vol. 3, Issue 6). https://doi.org/10.1038/s41562-019-0562-1

Belsky, D. W., & Harden, K. P. (2019). Phenotypic Annotation: Using Polygenic Scores to Translate Discoveries From Genome-Wide Association Studies From the Top Down. *Current Directions in Psychological Science*, *28*(1). https://doi.org/10.1177/0963721418807729

Belsky, J., Bakermans-Kranenburg, M. J., & Van Ijzendoorn, M. H. (2007). For better and for worse: Differential susceptibility to environmental influences. *Current Directions in Psychological Science*, *16*(6). https://doi.org/10.1111/j.1467-8721.2007.00525.x

Bennett, L., Thirlaway, K., & Murray, A. J. (2008). The stigmatising implications of presenting schizophrenia as a genetic disease. *Journal of Genetic Counseling*, *17*(6). https://doi.org/10.1007/s10897-008-9178-8

Bereiter, C. (1963). Some persisting dilemmas in the measurement of change. *Problems in Measuring Change*, *2*.

Betjemann, R. S., Johnson, E. P., Barnard, H., Boada, R., Filley, C. M., Filipek, P. A., Willcutt, E. G., Defries, J. C., & Pennington, B. F. (2010). Genetic covariation between brain volumes and IQ, reading performance, and processing speed. *Behavior Genetics*, *40*(2). https://doi.org/10.1007/s10519-009-9328-2

Bigby, C. (2012). Social inclusion and people with intellectual disability and challenging behaviour: A systematic review. In *Journal of Intellectual and Developmental Disability* (Vol. 37, Issue 4). https://doi.org/10.3109/13668250.2012.721878

Bishop, D. V. M. (2001). Genetic influences on language impairment and literacy problems in children: Same or different? *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *42*(2). https://doi.org/10.1017/S002196300100662X

Bishop, D. V. M. (2002). Motor immaturity and specific speech and language impairment: Evidence for a common genetic basis. *American Journal of Medical Genetics, Part B: Neuropsychiatric Genetics*, *114*(1). https://doi.org/10.1002/ajmg.1630

Bishop, D. V. M. (2005). DeFries-Fulker analysis of twin data with skewed distributions: Cautions and recommendations from a study of children's use of verb inflections. *Behavior Genetics*, *35*(4). https://doi.org/10.1007/s10519-004-1834-7

Bishop, D. V. M. (2010). Which neurodevelopmental disorders get researched and why? *PLoS ONE*, *5*(11). https://doi.org/10.1371/journal.pone.0015112

Bishop, D. V. M., Adams, C. V., & Norbury, C. F. (2004). Using nonword repetition to distinguish genetic and environmental influences on early literacy development: A study of 6-year-old twins. *American Journal of Medical Genetics - Neuropsychiatric Genetics*, *129 B*(1). https://doi.org/10.1002/ajmg.b.30065

Bishop, D. V. M., Adams, C. V., & Norbury, C. F. (2006). Distinct genetic influences on grammar and phonological short-term memory deficits: Evidence from 6-year-old twins. *Genes, Brain and Behavior*, *5*(2). https://doi.org/10.1111/j.1601-183X.2005.00148.x

Bishop, D. V. M., & Hayiou-Thomas, M. E. (2008). Heritability of specific language impairment depends on diagnostic criteria. *Genes, Brain and Behavior*, *7*(3). https://doi.org/10.1111/j.1601-183X.2007.00360.x

Bishop, D. V. M., Laws, G., Adams, C., & Norbury, C. F. (2006). High heritability of speech and language impairments in 6-year-old twins demonstrated using parent and teacher report. *Behavior Genetics*, *36*(2). https://doi.org/10.1007/s10519-005-9020-0

Bishop, D. V. M., North, T., & Donlan, C. (1996). Nonword repetition as a behavioural marker for inherited language impairment: Evidence from a twin study. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *37*(4). https://doi.org/10.1111/j.1469-7610.1996.tb01420.x

Bogdan, R., Baranger, D. A. A., & Agrawal, A. (2018). Polygenic Risk Scores in Clinical Psychology: Bridging Genomic Risk to Individual Differences. *Annual Review of Clinical Psychology*, *14*. https://doi.org/10.1146/annurev-clinpsy-050817-084847

Bonifacio, E., Beyerlein, A., Hippich, M., Winkler, C., Vehik, K., Weedon, M. N., Laimighofer, M., Hattersley, A. T., Krumsiek, J., Frohnert, B. I., Steck, A. K., Hagopian, W. A., Krischer, J. P., Lernmark, Å., Rewers, M. J., She, J. X., Toppari, J., Akolkar, B., Oram, R. A., …

Ziegler, A. G. (2018). Genetic scores to stratify risk of developing multiple islet autoantibodies and type 1 diabetes: A prospective study in children. *PLoS Medicine*, *15*(4). https://doi.org/10.1371/journal.pmed.1002548

Boomsma, D. I., van Beijsterveldt, T. C. E. M., Odintsova, V. V., Neale, M. C., & Dolan, C. V. (2021). Genetically Informed Regression Analysis: Application to Aggression Prediction by Inattention and Hyperactivity in Children and Adults. *Behavior Genetics*, *51*(3). https://doi.org/10.1007/s10519-020-10025-9

Border, R., Johnson, E. C., Evans, L. M., Smolen, A., Berley, N., Sullivan, P. F., & Keller, M. C. (2019). No support for historical candidate gene or candidate gene-by-interaction hypotheses for major depression across multiple large samples. *American Journal of Psychiatry*, *176*(5). https://doi.org/10.1176/appi.ajp.2018.18070881

Borenstein, M., Higgins, J. P. T., Hedges, L. V., & Rothstein, H. R. (2017). Basics of meta-analysis: I2 is not an absolute measure of heterogeneity. *Research Synthesis Methods*, *8*(1). https://doi.org/10.1002/jrsm.1230

Boyce, W. T., Frank, E., Jensen, P. S., Kessler, R. C., Nelson, C. A., & Steinberg, L. (1998). Social context in developmental psychopathology: Recommendations for future research from the MacArthur Network on Psychopathology and Development. *Development and Psychopathology*, *10*(2). https://doi.org/10.1017/S0954579498001552

Breen, G., Li, Q., Roth, B. L., O'Donnell, P., Didriksen, M., Dolmetsch, R., O'Reilly, P. F., Gaspar, H. A., Manji, H., Huebel, C., Kelsoe, J. R., Malhotra, D., Bertolino, A., Posthuma, D., Sklar, P., Kapur, S., Sullivan, P. F., Collier, D. A., & Edenberg, H. J. (2016). Translating genome-wide association findings into new therapeutics for psychiatry. In *Nature Neuroscience* (Vol. 19, Issue 11). https://doi.org/10.1038/nn.4411

Brikell, I., Kuja-Halkola, R., Larsson, J. O., Lahey, B. B., Kuntsi, J., Lichtenstein, P., Rydelius, P. A., & Larsson, H. (2016). Relative Immaturity in Childhood and Attention-Deficit/Hyperactivity Disorder Symptoms From Childhood to Early Adulthood: Exploring Genetic and Environmental Overlap Across Development. *Journal of the American Academy of Child and Adolescent Psychiatry*, *55*(10). https://doi.org/10.1016/j.jaac.2016.06.014

Brimo, K., Dinkler, L., Gillberg, C., Lichtenstein, P., Lundström, S., & Åsberg Johnels, J. (2021). The co-occurrence of neurodevelopmental problems in dyslexia. *Dyslexia*, *27*(3). https://doi.org/10.1002/dys.1681

Bronsard, G., Botbol, M., & Tordjman, S. (2010). Aggression in low functioning children and adolescents with autistic disorder. *PLoS ONE*, *5*(12). https://doi.org/10.1371/journal.pone.0014358

Brooker, R. J., Moore, M. N., Van Hulle, C. A., Beekman, C. R., Begnoche, J. P., Lemery-Chalfant, K., & Goldsmith, H. H. (2020). Attentional Control Explains Covariation Between Symptoms of Attention-Deficit/Hyperactivity Disorder and Anxiety During Adolescence. *Journal of Research on Adolescence*, *30*(1). https://doi.org/10.1111/jora.12506

Browner, W. S., Newman, T. B., Cummings, S. R., & Grady, D. G. (2022). *Designing clinical research*. Lippincott Williams & Wilkins.

Bulik-Sullivan, B., Loh, P. R., Finucane, H. K., Ripke, S., Yang, J., Patterson, N., Daly, M. J., Price, A. L., Neale, B. M., Corvin, A., Walters, J. T. R., Farh, K. H., Holmans, P. A., Lee, P., Collier, D. A., Huang, H., Pers, T. H., Agartz, I., Agerbo, E., … O'Donovan, M. C. (2015). LD score regression distinguishes confounding from polygenicity in genome-wide association studies. *Nature Genetics*, *47*(3). https://doi.org/10.1038/ng.3211

Burt, S. A. (2009). Rethinking Environmental Contributions to Child and Adolescent Psychopathology: A Meta-Analysis of Shared Environmental Influences. *Psychological Bulletin*, *135*(4). https://doi.org/10.1037/a0015702

Burt, S. A., Krueger, R. F., McGue, M., & Iacono, W. (2003). Parent-child conflict and the comorbidity among childhood externalizing disorders. *Archives of General Psychiatry*, *60*(5). https://doi.org/10.1001/archpsyc.60.5.505

Burt, S. A., Krueger, R. F., McGue, M., & Iacono, W. G. (2001). Sources of covariation among attention-deficit/hyperactivity disorder, oppositional defiant disorder, and conduct disorder: The importance of shared environment. *Journal of Abnormal Psychology*, *110*(4). https://doi.org/10.1037/0021-843X.110.4.516

Burt, S. A., Larsson, H., Lichtenstein, P., & Klump, K. L. (2012). Additional evidence against shared environmental contributions to attention-deficit/hyperactivity problems. *Behavior Genetics*, *42*, 711–721.

Burt, S. A., McGue, M., Krueger, R. F., & Iacono, W. G. (2005). Sources of covariation among the child-externalizing disorders: Informant effects and the shared environment. *Psychological Medicine*, *35*(8). https://doi.org/10.1017/S0033291705004770

Caspi, A., Houts, R. M., Belsky, D. W., Goldman-Mellor, S. J., Harrington, H., Israel, S., Meier, M. H., Ramrakha, S., Shalev, I., Poulton, R., & Moffitt, T. E. (2014). The p factor: One general psychopathology factor in the structure of psychiatric disorders? *Clinical Psychological Science*, *2*(2). https://doi.org/10.1177/2167702613497473

Caspi, A., McCray, J., Moffitt, T. E., Mill, J., Martin, J., Craig, I. W., Taylor, A., & Poulton, R. (2002). Role of genotype in the cycle of violence in maltreated children. *Science*, *297*(5582). https://doi.org/10.1126/science.1072290

Caspi, A., Moffitt, T. E., Morgan, J., Rutter, M., Taylor, A., Arseneault, L., Tully, L., Jacobs, C., Kim-Cohen, J., & Polp-Tomas, M. (2004). Maternal Expressed Emotion Predicts Children's Antisocial Behavior Problems: Using Monozygotic-Twin Differences to Identify Environmental Effects on Behavioral Development. *Developmental Psychology*, *40*(2). https://doi.org/10.1037/0012-1649.40.2.149

Caspi, A., Sugden, K., Moffitt, T. E., Taylor, A., Craig, I. W., Harrington, H. L., McClay, J., Mill, J., Martin, J., Braithwaite, A., & Poulton, R. (2003). Influence of life stress on depression: Moderation by a polymorphism in the 5-HTT gene. *Science*, *301*(5631). https://doi.org/10.1126/science.1083968

Castles, A., Datta, H., Gayan, J., & Olson, R. K. (1999). Varieties of Developmental Reading Disorder: Genetic and Environmental Influences. *Journal of Experimental Child Psychology*, *72*(2). https://doi.org/10.1006/jecp.1998.2482

Chabris, C. F., Lee, J. J., Cesarini, D., Benjamin, D. J., & Laibson, D. I. (2015). The Fourth Law of Behavior Genetics. *Current Directions in Psychological Science*, *24*(4). https://doi.org/10.1177/0963721415580430

Chang, Z., Lichtenstein, P., Asherson, P. J., & Larsson, H. (2013). Developmental twin study of attention problems: High heritabilities throughout development. *JAMA Psychiatry*, *70*(3). https://doi.org/10.1001/jamapsychiatry.2013.287

Chang, Z., Lichtenstein, P., & Larsson, H. (2012). The effects of childhood ADHD symptoms on early-onset substance use: A Swedish twin study. *Journal of Abnormal Child Psychology*, *40*(3). https://doi.org/10.1007/s10802-011-9575-6

Cheesman, R., Purves, K. L., Pingault, J. B., Breen, G., Rijsdij k, F., Plomin, R., & Eley, T. C. (2018). Extracting stability increases the SNP heritability of emotional problems in young people. *Translational Psychiatry*, *8*(1). https://doi.org/10.1038/s41398-018-0269-5

Cheesman, R., Selzam, S., Ronald, A., Dale, P. S., McAdams, T. A., Eley, T. C., & Plomin, R. (2017). Childhood behaviour problems show the greatest gap between DNA-based and twin heritability. *Translational Psychiatry*, *7*(12). https://doi.org/10.1038/s41398-017-0046-x

Chen, Q., Kuja-Halkola, R., Sjölander, A., Serlachius, E., Cortese, S., Faraone, S. V., Almqvist, C., & Larsson, H. (2017). Shared familial risk factors between attention-deficit/hyperactivity disorder and overweight/obesity – a population-based familial coaggregation study in

Sweden. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *58*(6). https://doi.org/10.1111/jcpp.12686

Chen, T. J., Ji, C. Y., Wang, S. S., Lichtenstein, P., Larsson, H., & Chang, Z. (2016). Genetic and environmental influences on the relationship between ADHD symptoms and internalizing problems: A Chinese twin study. *American Journal of Medical Genetics, Part B: Neuropsychiatric Genetics*, *171*(7). https://doi.org/10.1002/ajmg.b.32411

Cheung, C. H. M., Fazier-Wood, A. C., Asherson, P., Rijsdijk, F., & Kuntsi, J. (2014). Shared cognitive impairments and aetiology in ADHD symptoms and reading difficulties. *PLoS ONE*, *9*(6). https://doi.org/10.1371/journal.pone.0098590

Child care and child development: results from the NICHD study of early child care and youth development. (2005). *Choice Reviews Online*, *43*(04). https://doi.org/10.5860/choice.43-2279

Christensen, D. L., Baio, J., Van Naarden Braun, K., Bilder, D., Charles, J., Constantino, J. N., Daniels, J., Durkin, M. S., Fitzgerald, R. T., Kurzius-Spencer, M., Lee, L. C., Pettygrove, S., Robinson, C., Schulz, E., Wells, C., Wingate, M. S., Zahorodny, W., & Yeargin-Allsopp, M. (2016). Prevalence and characteristics of autism spectrum disorder among children aged 8 years - Autism and developmental disabilities monitoring network, 11 sites, United States, 2012. *MMWR Surveillance Summaries*, *65*(3). https://doi.org/10.15585/mmwr.ss6503a1

Christopher, M. E., Hulslander, J., Byrne, B., Samuelsson, S., Keenan, J. M., Pennington, B., DeFries, J. C., Wadsworth, S. J., Willcutt, E., & Olson, R. K. (2013). The genetic and environmental etiologies of individual differences in early reading growth in Australia, the United States, and Scandinavia. *Journal of Experimental Child Psychology*, *115*(3). https://doi.org/10.1016/j.jecp.2013.03.008

Cicchetti, D., & Cohen, D. J. (1995). Perspectives on developmental psychopathology. *Theory and Methods*, *1*.

Cicchetti, D., Rogosch, F. A., & Thibodeau, E. L. (2012). The effects of child maltreatment on early signs of antisocial behavior: Genetic moderation by tryptophan hydroxylase, serotonin transporter, and monoamine oxidase A genes. *Development and Psychopathology*, *24*(3). https://doi.org/10.1017/S0954579412000442

Cicchetti, D., & Toth, S. L. (2006). Building bridges and crossing them: Translational research in developmental psychopathology. In *Development and Psychopathology* (Vol. 18, Issue 3). https://doi.org/10.1017/S0954579406060317

Cicchetti, D., Toth, S. L., & Hennessy, K. (1989). Research on the Consequences of Child Maltreatment and Its Application to Educational Settings. *Topics in Early Childhood Special Education*, *9*(2). https://doi.org/10.1177/027112148900900204

Clemmensen, L., Vernal, D. L., & Steinhausen, H. C. (2012). A systematic review of the long-term outcome of early onset schizophrenia. *BMC Psychiatry*, *12*. https://doi.org/10.1186/1471-244X-12-150

Cohen, J., Cohen, P., West, S. G., & Aiken, L. S. (2013). *Applied multiple regression/correlation analysis for the behavioral sciences*. Routledge.

Cole, J., Ball, H. A., Martin, N. C., Scourfield, J., & Mcguffin, P. (2009). Genetic Overlap Between Measures of Hyperactivity/Inattention and Mood in Children and Adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry*, *48*(11). https://doi.org/10.1097/CHI.0b013e3181b7666e

Coleman, J. R. I., Gaspar, H. A., Bryois, J., Byrne, E. M., Forstner, A. J., Holmans, P. A., de Leeuw, C. A., Mattheisen, M., McQuillin, A., Whitehead Pavlides, J. M., Pers, T. H., Ripke, S., Stahl, E. A., Steinberg, S., Trubetskoy, V., Trzaskowski, M., Wang, Y., Abbott, L., Abdellaoui, A., … Breen, G. (2020). The Genetics of the Mood Disorder Spectrum: Genome-wide Association Analyses of More Than 185,000 Cases and 439,000 Controls. *Biological Psychiatry*, *88*(2). https://doi.org/10.1016/j.biopsych.2019.10.015

Colizzi, M., Lasalvia, A., & Ruggeri, M. (2020). Prevention and early intervention in youth mental health: Is it time for a multidisciplinary and trans-diagnostic model for care? In *International Journal of Mental Health Systems* (Vol. 14, Issue 1). https://doi.org/10.1186/s13033-020-00356-9

Collins, F. (2010). *The language of life: DNA and the revolution in personalised medicine*. Profile Books.

Colman, I., Murray, J., Abbott, R. A., Maughan, B., Kuh, D., Croudace, T. J., & Jones, P. B. (2009). Outcomes of conduct problems in adolescence: 40 Year follow-up of national cohort. *BMJ (Online)*, *338*(7688). https://doi.org/10.1136/bmj.a2981

Colodro-Conde, L., Couvy-Duchesne, B., Zhu, G., Coventry, W. L., Byrne, E. M., Gordon, S., Wright, M. J., Montgomery, G. W., Madden, P. A. F., Ripke, S., Eaves, L. J., Heath, A. C., Wray, N. R., Medland, S. E., & Martin, N. G. (2018). A direct test of the diathesis–stress model for depression. *Molecular Psychiatry*, *23*(7). https://doi.org/10.1038/mp.2017.130

Colvert, E., Tick, B., McEwen, F., Stewart, C., Curran, S. R., Woodhouse, E., Gillan, N., Hallett, V., Lietz, S., Garnett, T., Ronald, A., Plomin, R., Rijsdijk, F., Happé, F., & Bolton, P. (2015). Heritability of autism spectrum disorder in a UK population-based twin sample. *JAMA Psychiatry*, *72*(5). https://doi.org/10.1001/jamapsychiatry.2014.3028

Constantino, J. N., Hudziak, J. J., & Todd, R. D. (2003). Deficits in reciprocal social behavior in male twins: Evidence for a genetically independent domain of psychopathology. *Journal of*

*the American Academy of Child and Adolescent Psychiatry*, *42*(4). https://doi.org/10.1097/01.CHI.0000046811.95464.21

Constantino, J. N., & Todd, R. D. (2003). Autistic traits in the general population: A twin study. *Archives of General Psychiatry*, *60*(5). https://doi.org/10.1001/archpsyc.60.5.524

Coolidge, F. L., Thede, L. L., & Young, S. E. (2000). Heritability and the comorbidity of attention deficit hyperactivity disorder with behavioral disorders and executive function deficits: A preliminary investigation. *Developmental Neuropsychology*, *17*(3). https://doi.org/10.1207/S15326942DN1703_1

Cox, J. L., Holden, J. M., & Sagovsky, R. (1987). Detection of Postnatal Depression: Development of the 10-item Edinburgh Postnatal Depression scale. *British Journal of Psychiatry*, *150*(JUNE). https://doi.org/10.1192/bjp.150.6.782

Crosbie, J., Arnold, P., Paterson, A., Swanson, J., Dupuis, A., Li, X., Shan, J., Goodale, T., Tam, C., Strug, L. J., & Schachar, R. J. (2013). Response inhibition and ADHD traits: Correlates and heritability in a community sample. *Journal of Abnormal Child Psychology*, *41*(3). https://doi.org/10.1007/s10802-012-9693-9

Curran, S., Rijsdijk, F., Martin, N., Marusic, K., Asherson, P., Taylor, E., & Sham, P. (2003). CHIP: Defining a dimension of the vulnerability to attention deficit hyperactivity disorder (ADHD) using sibling and individual data of children in a community-based sample. *American Journal of Medical Genetics - Neuropsychiatric Genetics*, *119 B*(1). https://doi.org/10.1002/ajmg.b.20002

Dale, P. S., Rice, M. L., Rimfeld, K., & Hayiou-Thomas, M. E. (2018). Grammar clinical marker yields substantial heritability for language impairments in 16-year-old twins. *Journal of Speech, Language, and Hearing Research*, *61*(1). https://doi.org/10.1044/2017_JSLHR-L-16-0364

Daniels, D., & Plomin, R. (1985). Differential Experience of Siblings in the Same Family. *Developmental Psychology*, *21*(5). https://doi.org/10.1037/0012-1649.21.5.747

Daucourt, M. C., Haughbrook, R., van Bergen, E., & Hart, S. A. (2020). The association of parent-reported executive functioning, reading, and math is explained by nature, not nurture. *Developmental Psychology*. https://doi.org/10.1037/dev0001126

Davis, C. J., Gayán, J., Knopik, V. S., Smith, S. D., Cardon, L. R., Pennington, B. F., Olson, R. K., & Defries, J. C. (2001). Etiology of reading difficulties and rapid naming: The Colorado twin study of reading disability. *Behavior Genetics*, *31*(6). https://doi.org/10.1023/A:1013305730430

Davis, L. K., Yu, D., Keenan, C. L., Gamazon, E. R., Konkashbaev, A. I., Derks, E. M., Neale, B. M., Yang, J., Lee, S. H., Evans, P., Barr, C. L., Bellodi, L., Benarroch, F., Berrio, G. B., Bienvenu, O. J., Bloch, M. H., Blom, R. M., Bruun, R. D., Budman, C. L., … Scharf, J. M. (2013). Partitioning the Heritability of Tourette Syndrome and Obsessive Compulsive Disorder Reveals Differences in Genetic Architecture. *PLoS Genetics*, *9*(10). https://doi.org/10.1371/journal.pgen.1003864

Davis, O. S. P., Band, G., Pirinen, M., Haworth, C. M. A., Meaburn, E. L., Kovas, Y., Harlaar, N., Docherty, S. J., Hanscombe, K. B., Trzaskowski, M., Curtis, C. J. C., Strange, A., Freeman, C., Bellenguez, C., Su, Z., Pearson, R., Vukcevic, D., Langford, C., Deloukas, P., … Spencer, C. C. A. (2014). The correlation between reading and mathematics ability at age twelve has a substantial genetic component. *Nature Communications*, *5*. https://doi.org/10.1038/ncomms5204

Davis, O. S. P., Kovas, Y., Harlaar, N., Busfield, P., McMillan, A., Frances, J., Petrill, S. A., Dale, P. S., & Plomin, R. (2008). Generalist genes and the Internet generation: Etiology of learning abilities by web testing at age 10. *Genes, Brain and Behavior*, *7*(4). https://doi.org/10.1111/j.1601-183X.2007.00370.x

de Zeeuw, E. L., van Beijsterveldt, C. E. M., Ehli, E. A., de Geus, E. J. C., & Boomsma, D. I. (2017). Attention Deficit Hyperactivity Disorder Symptoms and Low Educational Achievement: Evidence Supporting A Causal Hypothesis. *Behavior Genetics*, *47*(3). https://doi.org/10.1007/s10519-017-9836-4

de Zeeuw, E. L., van Beijsterveldt, C. E. M., Lubke, G. H., Glasner, T. J., & Boomsma, D. I. (2015). Childhood ODD and ADHD Behavior: The Effect of Classroom Sharing, Gender, Teacher Gender and Their Interactions. *Behavior Genetics*, *45*(4). https://doi.org/10.1007/s10519-015-9712-z

Deater-Deckard, K. (2000). Parenting and child behavioral adjustment in early childhood: A quantitative genetic approach to studying family processes. *Child Development*, *71*(2). https://doi.org/10.1111/1467-8624.00158

Deater-Deckard, K. (2001). Annotation: Recent research examining the role of peer relationships in the development of psychopathology. In *Journal of Child Psychology and Psychiatry and Allied Disciplines* (Vol. 42, Issue 5). https://doi.org/10.1017/S0021963001007272

Deater-Deckard, K., Dodge, K. A., Bates, J. E., & Pettit, G. S. (1998). Multiple risk factors in the development of externalizing behavior problems: Group and individual differences. *Development and Psychopathology*, *10*(3). https://doi.org/10.1017/S0954579498001709

DeFries, J. C., & Alarcón, M. (1996). Genetics of specific reading disability. *Mental Retardation and Developmental Disabilities Research Reviews*, *2*(1). https://doi.org/10.1002/(SICI)1098-2779(1996)2:1<39::AID-MRDD7>3.0.CO;2-S

Defries, J. C., Fulker, D. W., & Labuda, M. C. (1987). Evidence for a genetic aetiology in reading disability of twins. *Nature*, *329*(6139). https://doi.org/10.1038/329537a0

DeFries, J. C., Knopik, V. S., & Wadsworth, S. J. (1999). Colorado twin study of reading disability. *Reading and Attention Disorders: Neurobiological Correlates*, 17–41.

Del Re, A. C., Hoyt, W. T., & Del Re, M. A. C. (2022). *Package 'MAd.'*

Demontis, D., Walters, G. B., Athanasiadis, G., Walters, R., Therrien, K., Nielsen, T. T., Farajzadeh, L., Voloudakis, G., Bendl, J., Zeng, B., Zhang, W., Grove, J., Als, T. D., Duan, J., Satterstrom, F. K., Bybjerg-Grauholm, J., Bækved-Hansen, M., Gudmundsson, O. O., Magnusson, S. H., … Børglum, A. D. (2023). Genome-wide analyses of ADHD identify 27 risk loci, refine the genetic architecture and implicate several cognitive domains. *Nature Genetics*, *55*(2). https://doi.org/10.1038/s41588-022-01285-8

Demontis, D., Walters, R. K., Martin, J., Mattheisen, M., Als, T. D., Agerbo, E., Baldursson, G., Belliveau, R., Bybjerg-Grauholm, J., Bækvad-Hansen, M., Cerrato, F., Chambert, K., Churchhouse, C., Dumont, A., Eriksson, N., Gandal, M., Goldstein, J. I., Grasby, K. L., Grove, J., … Neale, B. M. (2019). Discovery of the first genome-wide significant risk loci for attention deficit/hyperactivity disorder. *Nature Genetics*, *51*(1). https://doi.org/10.1038/s41588-018-0269-7

Deng, W., Zou, X., Deng, H., Li, J., Tang, C., Wang, X., & Guo, X. (2015). The relationship among genetic heritability, environmental effects, and autism spectrum disorders: 37 pairs of ascertained twin study. *Journal of Child Neurology*, *30*(13), 1794–1799.

Derks, E. M., Dolan, C. V., Hudziak, J. J., Neale, M. C., & Boomsma, D. I. (2007). Assessment and etiology of attention deficit hyperactivity disorder and oppositional defiant disorder in boys and girls. *Behavior Genetics*, *37*(4). https://doi.org/10.1007/s10519-007-9153-4

Derks, E. M., Hudziak, J. J., Dolan, C. V., Van Beijsterveldt, T. C. E. M., Verhulst, F. C., & Boomsma, D. I. (2008). Genetic and environmental influences on the relation between attention problems and attention deficit hyperactivity disorder. *Behavior Genetics*, *38*(1). https://doi.org/10.1007/s10519-007-9178-8

Derks, E. M., Hudziak, J. J., Van Beijsterveldt, C. E., Dolan, C. V., & Boomsma, D. I. (2006). Genetic analyses of maternal and teacher ratings on attention problems in 7-year-old Dutch twins. *Behavior Genetics*, *36*(6). https://doi.org/10.1007/s10519-006-9084-5

Dethorne, L. S., Hart, S. A., Petril, S. A., Deater-Deckard, K., Thompson, L. A., Schatschneider, C., & Davison, M. D. (2006). Children's history of speech-language difficulties: Genetic influences and associations with reading- related measures. *Journal of Speech, Language, and Hearing Research*, *49*(6). https://doi.org/10.1044/1092-4388(2006/092)

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 Ddsorder, and oppositional defiant disorder symptoms. *Journal of Abnormal Child Psychology*, *33*(2). https://doi.org/10.1007/s10802-005-1829-8

Dietrich, K. N., Eskenazi, B., Schantz, S., Yolton, K., Rauh, V. A., Johnson, C. B., Alkon, A., Canfield, R. L., Pessah, I. N., & Berman, R. F. (2005). Principles and practices of neurodevelopmental assessment in children: Lessons learned from the Centers for Children's Environmental Health and Disease Prevention Research. In *Environmental Health Perspectives* (Vol. 113, Issue 10). https://doi.org/10.1289/ehp.7672

Dionne, G., Touchette, E., Forget-Dubois, N., Petit, D., Tremblay, R. E., Montplaisir, J. Y., & Boivin, M. (2011). Associations between sleep-wake consolidation and language development in early childhood: A longitudinal twin study. *Sleep*, *34*(8). https://doi.org/10.5665/SLEEP.1148

Do, E. K., Haberstick, B. C., Williams, R. B., Lessem, J. M., Smolen, A., Siegler, I. C., & Fuemmeler, B. F. (2019). The role of genetic and environmental influences on the association between childhood ADHD symptoms and BMI. *International Journal of Obesity*, *43*(1). https://doi.org/10.1038/s41366-018-0236-5

Dolan, C. V., de Zeeuw, E. L., Zayats, T., van Beijsterveldt, C. E. M., & Boomsma, D. I. (2020). The (Broad-Sense) Genetic Correlations Among Four Measures of Inattention and Hyperactivity in 12 Year Olds. *Behavior Genetics*, *50*(4). https://doi.org/10.1007/s10519-020-10002-2

Domingue, B. W., Kanopka, K., Mallard, T. T., Trejo, S., & Tucker-Drob, E. M. (2022). Modeling Interaction and Dispersion Effects in the Analysis of Gene-by-Environment Interaction. *Behavior Genetics*, *52*(1). https://doi.org/10.1007/s10519-021-10090-8

D'Onofrio, B. M., Slutske, W. S., Turkheimer, E., Emery, R. E., Harden, K. P., Heath, A. C., Madden, P. A. F., & Martin, N. G. (2007). Intergenerational transmission of childhood conduct problems: A children of twins study. *Archives of General Psychiatry*, *64*(7). https://doi.org/10.1001/archpsyc.64.7.820

Drabick, D. A. G., & Kendall, P. C. (2010). Developmental Psychopathology and the Diagnosis of Mental Health Problems Among Youth. *Clinical Psychology: Science and Practice*, *17*(4). https://doi.org/10.1111/j.1468-2850.2010.01219.x

Du Rietz, E., Pettersson, E., Brikell, I., Ghirardi, L., Chen, Q., Hartman, C., Lichtenstein, P., Larsson, H., & Kuja-Halkola, R. (2021a). Overlap between attention-deficit hyperactivity disorder and neurodevelopmental, externalising and internalising disorders: Separating unique from general psychopathology effects. *British Journal of Psychiatry*, *218*(1). https://doi.org/10.1192/bjp.2020.152

Du Rietz, E., Pettersson, E., Brikell, I., Ghirardi, L., Chen, Q., Hartman, C., Lichtenstein, P., Larsson, H., & Kuja-Halkola, R. (2021b). Overlap between attention-deficit hyperactivity disorder and neurodevelopmental, externalising and internalising disorders: separating unique from general psychopathology effects. *The British Journal of Psychiatry*, *218*(1), 35–42.

Dudbridge, F. (2013). Power and Predictive Accuracy of Polygenic Risk Scores. *PLoS Genetics*, *9*(3). https://doi.org/10.1371/journal.pgen.1003348

Duncan, L. E., & Keller, M. C. (2011). A critical review of the first 10 years of candidate gene-by-environment interaction research in psychiatry. In *American Journal of Psychiatry* (Vol. 168, Issue 10). https://doi.org/10.1176/appi.ajp.2011.11020191

Duncan, L. E., Ratanatharathorn, A., Aiello, A. E., Almli, L. M., Amstadter, A. B., Ashley-Koch, A. E., Baker, D. G., Beckham, J. C., Bierut, L. J., Bisson, J., Bradley, B., Chen, C. Y., Dalvie, S., Farrer, L. A., Galea, S., Garrett, M. E., Gelernter, J. E., Guffanti, G., Hauser, M. A., … Koenen, K. C. (2018). Largest GWAS of PTSD (N=20 070) yields genetic overlap with schizophrenia and sex differences in heritability. *Molecular Psychiatry*, *23*(3). https://doi.org/10.1038/mp.2017.77

Duncan, L., Shen, H., Gelaye, B., Meijsen, J., Ressler, K., Feldman, M., Peterson, R., & Domingue, B. (2019). Analysis of polygenic risk score usage and performance in diverse human populations. *Nature Communications*, *10*(1). https://doi.org/10.1038/s41467-019-11112-0

Dunn, J., & Plomin, R. (1990). *Separate lives: why siblings are so different.* Basic Books.

Dworzynski, K., Happé, F., Bolton, P., & Ronald, A. (2009). Relationship between symptom domains in autism spectrum disorders: A population based twin study. *Journal of Autism and Developmental Disorders*, *39*(8). https://doi.org/10.1007/s10803-009-0736-1

Dworzynski, K., Remington, A., Rijsdijk, F., Howell, P., & Plomin, R. (2007). Genetic etiology in cases of recovered and persistent stuttering in an unselected, longitudinal sample of young

twins. *American Journal of Speech-Language Pathology*, *16*(2). https://doi.org/10.1044/1058-0360(2007/021)

Dworzynski, K., Ronald, A., Hayiou-Thomas, M. E., McEwan, F., Happé, F., Bolton, P., & Plomin, R. (2008). Developmental path between language and autistic-like impairments: A twin study. *Infant and Child Development*, *17*(2). https://doi.org/10.1002/icd.536

Eaves, L. J., Silberg, J. L., Meyer, J. M., Maes, H. H., Simonoff, E., Pickles, A., Rutter, M., Reynolds, C. A., Heath, A. C., Truett, K. R., Neale, M. C., Erikson, M. T., Loeber, R., & Hewitt, J. K. (1997). Genetics and developmental psychopathology: 2. The main effects of genes and environment on behavioral problems in the Virginia Twin Study of Adolescent Behavioral Development. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *38*(8). https://doi.org/10.1111/j.1469-7610.1997.tb01614.x

Eaves, L., Rutter, M., Silberg, J. L., Shillady, L., Maes, H., & Pickles, A. (2000). Genetic and environmental causes of covariation in interview assessments of disruptive behavior in child and adolescent twins. *Behavior Genetics*, *30*(4). https://doi.org/10.1023/A:1026553518272

Ebejer, J. L., Coventry, W. L., Byrne, B., Willcutt, E. G., Olson, R. K., Corley, R., & Samuelsson, S. (2010). Genetic and environmental influences on inattention, hyperactivity-impulsivity, and reading: Kindergarten to grade 2. *Scientific Studies of Reading*, *14*(4). https://doi.org/10.1080/10888430903150642

Ebejer, J. L., Medland, S. E., van der Werf, J., J Wright, M., Henders, A. K., Gillespie, N. A., Hickie, I. B., Martin, N. G., & Duffy, D. L. (2015). Contrast Effects and Sex Influence Maternal and Self-Report Dimensional Measures of Attention-Deficit Hyperactivity Disorder. *Behavior Genetics*, *45*(1). https://doi.org/10.1007/s10519-014-9670-x

Edelbrock, C., Rende, R., Plomin, R., & Thompson, L. A. (1995). A Twin Study of Competence and Problem Behavior in Childhood and Early Adolescence. *Journal of Child Psychology and Psychiatry*, *36*(5). https://doi.org/10.1111/j.1469-7610.1995.tb01328.x

Ehringer, M. A., Rhee, S. H., Young, S., Corley, R., & Hewitt, J. K. (2006). Genetic and environmental contributions to common psychopathologies of childhood and adolescence: A study of twins and their siblings. *Journal of Abnormal Child Psychology*, *34*(1). https://doi.org/10.1007/s10802-005-9000-0

Eilertsen, E. M., Gjerde, L. C., Kendler, K. S., Røysamb, E., Aggen, S. H., Gustavson, K., Reichborn-Kjennerud, T., & Ystrom, E. (2019). Development of ADHD symptoms in preschool children: Genetic and environmental contributions. *Development and Psychopathology*, *31*(4). https://doi.org/10.1017/S0954579418000731

Eisenberg, L., & Pellmar, T. C. (2000). *Bridging disciplines in the brain, behavioral, and clinical sciences*.

Eley, T. C., Bolton, D., O'Connor, T. G., Perrin, S., Smith, P., & Plomin, R. (2003). A twin study of anxiety-related behaviours in pre-school children. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *44*(7). https://doi.org/10.1111/1469-7610.00179

Eley, T. C., McAdams, T. A., Rijsdijk, F. V., Lichtenstein, P., Narusyte, J., Reiss, D., Spotts, E. L., Ganiban, J. M., & Neiderhiser, J. M. (2015). The Intergenerational Transmission of Anxiety: A Children-of-Twins Study. *The American Journal of Psychiatry*, *172*(7). https://doi.org/10.1176/appi.ajp.2015.14070818

Ellis, E. M., & Thal, D. J. (2008). Early Language Delay and Risk for Language Impairment. *Perspectives on Language Learning and Education*, *15*(3). https://doi.org/10.1044/lle15.3.93

Embracing communication. (2021). In *Nature Genetics* (Vol. 53, Issue 9). https://doi.org/10.1038/s41588-021-00942-8

Erbeli, F., Hart, S. A., & Taylor, J. (2018). Longitudinal Associations Among Reading-Related Skills and Reading Comprehension: A Twin Study. *Child Development*, *89*(6). https://doi.org/10.1111/cdev.12853

Erbeli, F., Hart, S. A., & Taylor, J. (2019). Genetic and Environmental Influences on Achievement Outcomes Based on Family History of Learning Disabilities Status. *Journal of Learning Disabilities*, *52*(2). https://doi.org/10.1177/0022219418775116

Falconer, D. S. (1996). *Introduction to quantitative genetics*. Pearson Education India.

Faraone, S. V., Biederman, J., & Mick, E. (2006). The age-dependent decline of attention deficit hyperactivity disorder: A meta-analysis of follow-up studies. In *Psychological Medicine* (Vol. 36, Issue 2). https://doi.org/10.1017/S003329170500471X

Faraone, S. V., & Larsson, H. (2019). Genetics of attention deficit hyperactivity disorder. In *Molecular Psychiatry* (Vol. 24, Issue 4). https://doi.org/10.1038/s41380-018-0070-0

Farmer, D. F., Jackson, S. A., Camacho, F., & Hall, M. A. (2007). Attitudes of African American and low socioeconomic status white women toward medical research. *Journal of Health Care for the Poor and Underserved*, *18*(1). https://doi.org/10.1353/hpu.2007.0008

Fedko, I. O., Wesseldijk, L. W., Nivard, M. G., Hottenga, J. J., van Beijsterveldt, C. E. M., Middeldorp, C. M., Bartels, M., & Boomsma, D. I. (2017). Heritability of Behavioral Problems in 7-Year Olds Based on Shared and Unique Aspects of Parental Views. *Behavior Genetics*, *47*(2). https://doi.org/10.1007/s10519-016-9823-1

Feil, R., & Fraga, M. F. (2012). Epigenetics and the environment: Emerging patterns and implications. In *Nature Reviews Genetics* (Vol. 13, Issue 2). https://doi.org/10.1038/nrg3142

Finer, S., Martin, H. C., Khan, A., Hunt, K. A., Maclaughlin, B., Ahmed, Z., Ashcroft, R., Durham, C., Macarthur, D. G., McCarthy, M. I., Robson, J., Trivedi, B., Griffiths, C., Wright, J., Trembath, R. C., & Van Heel, D. A. (2020). Cohort Profile: East London Genes & Health (ELGH), a community-based population genomics and health study in British Bangladeshi and British Pakistani people. *International Journal of Epidemiology*, *49*(1). https://doi.org/10.1093/ije/dyz174

Fletcher, T. D. (2010). psychometric: Applied Psychometric Theory. *R Package Version*.

Fliers, E., Vermeulen, S., Rijsdijk Mar, F., Altink, I., Buschgens, C., Rommelse, N., Faraone, S., Sergeant, J., Buitelaar, J., & Franke, B. (2009). ADHD and poor motor performance from a family genetic perspective. *Journal of the American Academy of Child and Adolescent Psychiatry*, *48*(1). https://doi.org/10.1097/CHI.0b013e31818b1ca2

Forty, L., Kelly, M., Jones, L., Jones, I., Barnes, E., Caesar, S., Fraser, C., Gordon-Smith, K., Griffiths, E., Craddock, N., & Smith, D. J. (2010). Reducing the Hypomania Checklist (HCL-32) to a 16-item version. *Journal of Affective Disorders*, *124*(3). https://doi.org/10.1016/j.jad.2010.01.004

Frazier, T. W., Thompson, L., Youngstrom, E. A., Law, P., Hardan, A. Y., Eng, C., & Morris, N. (2014). A twin study of heritable and shared environmental contributions to autism. *Journal of Autism and Developmental Disorders*, *44*(8). https://doi.org/10.1007/s10803-014-2081-2

Freedman, L. S., Simon, R., Foulkes, M. A., Friedman, L., Geller, N. L., Gordon, D. J., & Mowery, R. (1995). Inclusion of women and minorities in clinical trials and the NIH Revitalization Act of 1993 - The perspective of NIH clinical trialists. *Controlled Clinical Trials*, *16*(5). https://doi.org/10.1016/0197-2456(95)00048-8

Frick, P. J. (1998). *Conduct Disorders and Severe Antisocial Behavior*. Springer US. https://doi.org/10.1007/978-1-4615-5343-4

Frick, P. J. (2004). Inventory of callous–unemotional traits. *PLoS One*.

Frick, P. J., & Loney, B. R. (1999). Outcomes of Children and Adolescents with Oppositional Defiant Disorder and Conduct Disorder. In *Handbook of Disruptive Behavior Disorders*. https://doi.org/10.1007/978-1-4615-4881-2_24

Friend, A., Defries, J. C., Olson, R. K., Pennington, B., Harlaar, N., Byrne, B., Samuelsson, S., Willcutt, E. G., Wadsworth, S. J., Corley, R., & Keenan, J. M. (2009). Heritability of high reading ability and its interaction with parental education. *Behavior Genetics*, *39*(4). https://doi.org/10.1007/s10519-009-9263-2

Friend, A., DeFries, J. C., Wadsworth, S. J., & Olson, R. K. (2007). Genetic and environmental influences on word recognition and spelling deficits as a function of age. *Behavior Genetics*, *37*(3). https://doi.org/10.1007/s10519-007-9145-4

Fushiki, T. (2011). Estimation of prediction error by using K-fold cross-validation. *Statistics and Computing*, *21*(2). https://doi.org/10.1007/s11222-009-9153-8

Gandal, M. J., Haney, J. R., Parikshak, N. N., Leppa, V., Ramaswami, G., Hartl, C., Schork, A. J., Appadurai, V., Buil, A., Werge, T. M., Liu, C., White, K. P., Horvath, S., & Geschwind, D. H. (2018). Shared molecular neuropathology across major psychiatric disorders parallels polygenic overlap. *Science*, *359*(6376). https://doi.org/10.1126/science.aad6469

Garon-Carrier, G., Boivin, M., Kovas, Y., Feng, B., Brendgen, M., Vitaro, F., Séguin, J. R., Tremblay, R. E., & Dionne, G. (2017). Persistent Genetic and Family-Wide Environmental Contributions to Early Number Knowledge and Later Achievement in Mathematics. *Psychological Science*, *28*(12). https://doi.org/10.1177/0956797617721480

Gaspar, H. A., & Breen, G. (2017). Drug enrichment and discovery from schizophrenia genome-wide association results: An analysis and visualisation approach. *Scientific Reports*, *7*(1). https://doi.org/10.1038/s41598-017-12325-3

Gaspar, H. A., Gerring, Z., Hübel, C., Middeldorp, C. M., Derks, E. M., & Breen, G. (2019). Using genetic drug-target networks to develop new drug hypotheses for major depressive disorder. *Translational Psychiatry*, *9*(1). https://doi.org/10.1038/s41398-019-0451-4

Gayán, J., & Olson, R. K. (2001). Genetic and environmental influences on orthographic and phonological skills in children with reading disabilities. *Developmental Neuropsychology*, *20*(2). https://doi.org/10.1207/S15326942DN2002_3

Gayán, J., & Olson, R. K. (2003). Genetic and environmental influences on individual differences in printed word recognition. *Journal of Experimental Child Psychology*, *84*(2). https://doi.org/10.1016/S0022-0965(02)00181-9

Genetics for all. (2019). In *Nature Genetics* (Vol. 51, Issue 4). https://doi.org/10.1038/s41588-019-0394-y

Gialluisi, A., Andlauer, T. F. M., Mirza-Schreiber, N., Moll, K., Becker, J., Hoffmann, P., Ludwig, K. U., Czamara, D., Pourcain, B. S., Honbolygó, F., Tóth, D., Csépe, V., Huguet, G., Chaix, Y., Iannuzzi, S., Demonet, J. F., Morris, A. P., Hulslander, J., Willcutt, E. G., … Schulte-Körne, G. (2021). Genome-wide association study reveals new insights into the heritability and genetic correlates of developmental dyslexia. *Molecular Psychiatry*, *26*(7). https://doi.org/10.1038/s41380-020-00898-x

Gidziela, A., Ahmadzadeh, Y. I., Michelini, G., Allegrini, A. G., Agnew-Blais, J., Lau, L. Y., Duret, M., Procopio, F., Daly, E., Ronald, A., Rimfeld, K., & Malanchini, M. (2023). A meta-analysis of genetic effects associated with neurodevelopmental disorders and co-occurring conditions. *Nature Human Behaviour*, *7*(4). https://doi.org/10.1038/s41562-023-01530-y

Gidziela, A., Ahmadzadeh, Y., Michelini, G., Allegrini, A., Agnew-Blais, J., Lau, L. Y., Duret, M., Procopio, F., Daly, E., Ronald, A., Rimfeld, K., & Malanchini, M. (2022). Genetic influences on neurodevelopmental disorders and their overlap with co-occurring conditions in childhood and adolescence A meta-analysis. In *Research Square*. https://doi.org/10.21203/rs.3.rs-1442476/v1

Gidziela, A., Malanchini, M., Rimfeld, K., McMillan, A., Ronald, A., Viding, E., Pike, A., Asbury, K., Eley, T. C., von Stumm, S., & Plomin, R. (2023). Explaining the influence of non-shared environment (NSE) on symptoms of behaviour problems from preschool to adulthood: mind the missing NSE gap. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *64*(5). https://doi.org/10.1111/jcpp.13729

Gidziela, A., Rimfeld, K., Malanchini, M., Allegrini, A. G., McMillan, A., Selzam, S., Ronald, A., Viding, E., von Stumm, S., Eley, T. C., & Plomin, R. (2021). Using DNA to predict behaviour problems from preschool to adulthood. In *medRxiv*. https://doi.org/10.1101/2021.02.15.21251308

Gidziela, A., Rimfeld, K., Malanchini, M., Allegrini, A. G., McMillan, A., Selzam, S., Ronald, A., Viding, E., von Stumm, S., Eley, T. C., & Plomin, R. (2022). Using DNA to predict behaviour problems from preschool to adulthood. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *63*(7). https://doi.org/10.1111/jcpp.13519

Gillberg, C. (2010). The ESSENCE in child psychiatry: Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations. *Research in Developmental Disabilities*, *31*(6). https://doi.org/10.1016/j.ridd.2010.06.002

Gillis, J. J., DeFries, J. C., & Fulker, D. W. (1992). Confirmatory factor analysis of reading and mathematics performance: A twin study. *Acta Geneticae Medicae et Gemellologiae*, *41*(4). https://doi.org/10.1017/S0001566000002142

Goodman. (1997). The Strengths and Difficulties Questionnaire_ A Research Note - Goodman - 1997 - Journal of Child Psychology and Psychiatry - Wiley Online Library. *J. Child Psychol. Psychiat*, *38*(5).

Goodman, R. (2001). Psychometric properties of the strengths and difficulties questionnaire. *Journal of the American Academy of Child and Adolescent Psychiatry*, *40*(11). https://doi.org/10.1097/00004583-200111000-00015

Götz, F. M., Gosling, S. D., & Rentfrow, P. J. (2022). Small Effects: The Indispensable Foundation for a Cumulative Psychological Science. *Perspectives on Psychological Science*, *17*(1). https://doi.org/10.1177/1745691620984483

Gould, K. L., Coventry, W. L., Olson, R. K., & Byrne, B. (2018). Gene-Environment Interactions in ADHD: The Roles of SES and Chaos. *Journal of Abnormal Child Psychology*, *46*(2). https://doi.org/10.1007/s10802-017-0268-7

Grasby, K. L., & Coventry, W. L. (2016). Longitudinal Stability and Growth in Literacy and Numeracy in Australian School Students. *Behavior Genetics*, *46*(5). https://doi.org/10.1007/s10519-016-9796-0

Gregory, A. M., Eley, T. C., O'Connor, T. G., & Plomin, R. (2004). Etiologies of associations between childhood sleep and behavioral problems in a large twin sample. *Journal of the American Academy of Child and Adolescent Psychiatry*, *43*(6). https://doi.org/10.1097/01.chi/0000122798.47863.a5

Greven, C. U., Asherson, P., Rijsdijk, F. V., & Plomin, R. (2011). A longitudinal twin study on the association between inattentive and hyperactive-impulsive ADHD symptoms. *Journal of Abnormal Child Psychology*, *39*(5). https://doi.org/10.1007/s10802-011-9513-7

Greven, C. U., Harlaar, N., Dale, P. S., & Plomin, R. (2011). Genetic Overlap between ADHD Symptoms and Reading is largely Driven by Inattentiveness rather than Hyperactivity-Impulsivity. *Journal of the Canadian Academy of Child and Adolescent Psychiatry*, *20*(1).

Greven, C. U., Kovas, Y., Willcutt, E. G., Petrill, S. A., & Plomin, R. (2014). Evidence for shared genetic risk between ADHD symptoms and reduced mathematics ability: A twin study. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *55*(1). https://doi.org/10.1111/jcpp.12090

Greven, C. U., Rijsdijk, F. V., Asherson, P., & Plomin, R. (2012). A longitudinal twin study on the association between ADHD symptoms and reading. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *53*(3). https://doi.org/10.1111/j.1469-7610.2011.02445.x

Greven, C. U., Rijsdijk, F. V., & Plomin, R. (2011). A twin study of ADHD symptoms in early adolescence: Hyperactivity- impulsivity and inattentiveness show substantial genetic overlap but also genetic specificity. *Journal of Abnormal Child Psychology*, *39*(2). https://doi.org/10.1007/s10802-010-9451-9

Groen-Blokhuis, M. M., Middeldorp, C. M., Kan, K. J., Abdellaoui, A., Van Beijsterveldt, C. E. M., Ehli, E. A., Davies, G. E., Scheet, P. A., Xiao, X., Hudziak, J. J., Hottenga, J. J., Neale, B. M., & Boomsma, D. I. (2014). Attention-deficit/hyperactivity disorder polygenic risk scores predict attention problems in a population-based sample of children. *Journal of the American Academy of Child and Adolescent Psychiatry*, *53*(10). https://doi.org/10.1016/j.jaac.2014.06.014

Grotzinger, A. D., Mallard, T. T., Akingbuwa, W. A., Ip, H. F., Adams, M. J., Lewis, C. M., McIntosh, A. M., Grove, J., Dalsgaard, S., Lesch, K. P., Strom, N., Meier, S. M., Mattheisen, M., Børglum, A. D., Mors, O., Breen, G., Mors, O., Meier, S. M., Lee, P. H., … Nivard, M. G. (2022). Genetic architecture of 11 major psychiatric disorders at biobehavioral, functional genomic and molecular genetic levels of analysis. *Nature Genetics*, *54*(5). https://doi.org/10.1038/s41588-022-01057-4

Grotzinger, A. D., Rhemtulla, M., de Vlaming, R., Ritchie, S. J., Mallard, T. T., Hill, W. D., Ip, H. F., Marioni, R. E., McIntosh, A. M., Deary, I. J., Koellinger, P. D., Harden, K. P., Nivard, M. G., & Tucker-Drob, E. M. (2019). Genomic structural equation modelling provides insights into the multivariate genetic architecture of complex traits. *Nature Human Behaviour*, *3*(5). https://doi.org/10.1038/s41562-019-0566-x

Grove, J., Ripke, S., Als, T. D., Mattheisen, M., Walters, R. K., Won, H., Pallesen, J., Agerbo, E., Andreassen, O. A., Anney, R., Awashti, S., Belliveau, R., Bettella, F., Buxbaum, J. D., Bybjerg-Grauholm, J., Bækvad-Hansen, M., Cerrato, F., Chambert, K., Christensen, J. H., … Børglum, A. D. (2019). Identification of common genetic risk variants for autism spectrum disorder. *Nature Genetics*, *51*(3). https://doi.org/10.1038/s41588-019-0344-8

Haberstick, B. C., Lessem, J. M., Hopfer, C. J., Smolen, A., Ehringer, M. A., Timberlake, D., & Hewitt, J. K. (2005). Monoamine oxidase A (MAOA) and antisocial behaviors in the presence of childhood and adolescent maltreatment. *American Journal of Medical Genetics - Neuropsychiatric Genetics*, *135 B*(1). https://doi.org/10.1002/ajmg.b.30176

Haberstick, B. C., Timberlake, D., Hopfer, C. J., Lessem, J. M., Ehringer, M. A., & Hewitt, J. K. (2008). Genetic and environmental contributions to retrospectively reported DSM-IV childhood attention deficit hyperactivity disorder. *Psychological Medicine*, *38*(7). https://doi.org/10.1017/S0033291707001584

Hallett, V., Ronald, A., & Happé, F. (2009). Investigating the association between autistic-like and internalizing traits in a community-based twin sample. *Journal of the American Academy of Child & Adolescent Psychiatry*, *48*(6), 618–627.

Hallett, V., Ronald, A., Rijsdijk, F., & Happé, F. (2012). Disentangling the associations between autistic-like and internalizing traits: A community based twin study. *Journal of Abnormal Child Psychology*, *40*(5). https://doi.org/10.1007/s10802-011-9596-1

Hallmayer, J., Cleveland, S., Torres, A., Phillips, J., Cohen, B., Torigoe, T., Miller, J., Fedele, A., Collins, J., Smith, K., Lotspeich, L., Croen, L. A., Ozonoff, S., Lajonchere, C., Grether, J. K., & Risch, N. (2011). Genetic heritability and shared environmental factors among twin pairs with autism. *Archives of General Psychiatry*, *68*(11). https://doi.org/10.1001/archgenpsychiatry.2011.76

Happé, F. (1999). Understanding assets and deficits in autism: Why success is more interesting than failure. *The Psychologist*, *12*(11).

Harald, K., Salomaa, V., Jousilahti, P., Koskinen, S., & Vartiainen, E. (2007). Non-participation and mortality in different socioeconomic groups: The FINRISK population surveys in 1972-92. *Journal of Epidemiology and Community Health*, *61*(5). https://doi.org/10.1136/jech.2006.049908

Harlaar, N., Dale, P. S., & Plomin, R. (2007). Reading exposure: A (largely) environmental risk factor with environmentally-mediated effects on reading performance in the primary school years. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *48*(12). https://doi.org/10.1111/j.1469-7610.2007.01798.x

Harlaar, N., Kovas, Y., Dale, P. S., Petrill, S. A., & Plomin, R. (2012). Mathematics is differentially related to reading comprehension and word decoding: Evidence from a genetically sensitive design. *Journal of Educational Psychology*, *104*(3). https://doi.org/10.1037/a0027646

Harlaar, N., Spinath, F. M., Dale, P. S., & Plomin, R. (2005). Genetic influences on early word recognition abilities and disabilities: A study of 7-year-old twins. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *46*(4). https://doi.org/10.1111/j.1469-7610.2004.00358.x

Harlaar, N., Trzaskowski, M., Dale, P. S., & Plomin, R. (2014). Word Reading Fluency: Role of Genome-Wide Single-Nucleotide Polymorphisms in Developmental Stability and Correlations With Print Exposure. *Child Development*, *85*(3). https://doi.org/10.1111/cdev.12207

Harrer, M., Cuijpers, P., Furukawa, T. A., & Ebert, D. D. (2019). dmetar: Companion R Package For The Guide 'Doing Meta-Analysis in R. *R Package Version 0.0.9000*.

Harris, J. R. (1998). The nurture assumption: Why children turn out the way they do. *Adolescence*, *33*(132), 960.

Hart, D., & Marmorstein, N. R. (2009). Neighborhoods and genes and everything in between: Understanding adolescent aggression in social and biological contexts. *Development and Psychopathology*, *21*(3). https://doi.org/10.1017/S0954579409000510

Hart, S. A., Logan, J. A. R., Soden-Hensler, B., Kershaw, S., Taylor, J., & Schatschneider, C. (2013). Exploring how nature and nurture affect the development of reading: An analysis of the florida twin project on reading. *Developmental Psychology*, *49*(10). https://doi.org/10.1037/a0031348

Hart, S. A., Petrill, S. A., Thompson, L. A., & Plomin, R. (2009). The ABCs of math: A genetic analysis of mathematics and its links with reading ability and general cognitive ability. *Journal of Educational Psychology*, *101*(2), 388.

Hastie, T., Qian, J., & Tay, K. (2023). An introduction to glmnet. In *CRAN R Repositary*.

Hatch, S. L., Frissa, S., Verdecchia, M., Stewart, R., Fear, N. T., Reichenberg, A., Morgan, C., Kankulu, B., Clark, J., Gazard, B., Medcalf, R., & Hotopf, M. (2011). Identifying socio-demographic and socioeconomic determinants of health inequalities in a diverse London community: The South East London Community Health (SELCoH) study. *BMC Public Health*, *11*. https://doi.org/10.1186/1471-2458-11-861 22078667

Hawke, J. L., Stallings, M. C., Wadsworth, S. J., & DeFries, J. C. (2008). DeFries-Fulker and Pearson-Aitken model-fitting analyses of reading performance data from selected and unselected twin pairs. *Behavior Genetics*, *38*(2). https://doi.org/10.1007/s10519-008-9189-0

Hay, D. A., Bennett, K. S., Levy, F., Sergeant, J., & Swanson, J. (2007). A Twin Study of Attention-Deficit/Hyperactivity Disorder Dimensions Rated by the Strengths and Weaknesses of ADHD-Symptoms and Normal-Behavior (SWAN) Scale. *Biological Psychiatry*, *61*(5). https://doi.org/10.1016/j.biopsych.2006.04.040

Hayiou-Thomas, M. E., Dale, P. S., & Plomin, R. (2012). The etiology of variation in language skills changes with development: A longitudinal twin study of language from 2 to 12 years. *Developmental Science*, *15*(2), 233–249.

Hayiou-Thomas, M. E., Dale, P. S., & Plomin, R. (2014). Language impairment from 4 to 12 years: Prediction and etiology. *Journal of Speech, Language, and Hearing Research*, *57*(3). https://doi.org/10.1044/2013_JSLHR-L-12-0240

He, Q., & Li, J. J. (2022). A Gene-Environment Interaction Study of Polygenic Scores and Maltreatment on Childhood ADHD. *Research on Child and Adolescent Psychopathology*, *50*(3). https://doi.org/10.1007/s10802-021-00873-2

Hechtman, L., Swanson, J. M., Sibley, M. H., Stehli, A., Lakes, K. D., Owens, E. B., Mitchell, J. T., Arnold, L. E., Molina, B. S. G., Hinshaw, S. P., Jensen, P. S., Abikoff, H. B., Perez

Algorta, G., Howard, A. L., Hoza, B., Nichols, J. Q., Etcovitch, J., Houssais, S., Vitiello, B., … Stern, K. (2016). Functional Adult Outcomes 16 Years After Childhood Diagnosis of Attention-Deficit/Hyperactivity Disorder: MTA Results. *Journal of the American Academy of Child and Adolescent Psychiatry*, *55*(11). https://doi.org/10.1016/j.jaac.2016.07.774

Hensler, B. S., Schatschneider, C., Taylor, J., & Wagner, R. K. (2010). Behavioral genetic approach to the study of dyslexia. *Journal of Developmental and Behavioral Pediatrics*, *31*(7). https://doi.org/10.1097/DBP.0b013e3181ee4b70

Heutink, P., Verhuls, F. C., & Boomsma, D. I. (2006). A longitudinal twin study on IQ, executive functioning, and attention problems during childhood and early adolescence. *Acta Neurol. Belg*, *106*, 191–207.

Higgins, J. P. T., & Thompson, S. G. (2002). Quantifying heterogeneity in a meta-analysis. *Statistics in Medicine*, *21*(11). https://doi.org/10.1002/sim.1186

Higgins, J. P. T., Thompson, S. G., Deeks, J. J., & Altman, D. G. (2003). Measuring inconsistency in meta-analyses. In *British Medical Journal* (Vol. 327, Issue 7414). https://doi.org/10.1136/bmj.327.7414.557

Hill, W. D., Davies, G., Liewald, D. C., McIntosh, A. M., & Deary, I. J. (2016). Age-Dependent Pleiotropy Between General Cognitive Function and Major Psychiatric Disorders. *Biological Psychiatry*, *80*(4). https://doi.org/10.1016/j.biopsych.2015.08.033

Hirschhorn, J. N., Lohmueller, K., Byrne, E., & Hirschhorn, K. (2002). A comprehensive review of genetic association studies. In *Genetics in Medicine* (Vol. 4, Issue 2). https://doi.org/10.1097/00125817-200203000-00002

Hoekstra, R. A., Bartels, M., Van Leeuwen, M., & Boomsma, D. I. (2009). Genetic architecture of verbal abilities in children and adolescents. *Developmental Science*, *12*(6). https://doi.org/10.1111/j.1467-7687.2009.00843.x

Hoekstra, R. A., Bartels, M., Verweij, C. J. H., & Boomsma, D. I. (2007). Heritability of autistic traits in the general population. *Archives of Pediatrics and Adolescent Medicine*, *161*(4). https://doi.org/10.1001/archpedi.161.4.372

Hoekstra, R. A., Happé, F., Baron-Cohen, S., & Ronald, A. (2010). Limited genetic covariance between autistic traits and intelligence: Findings from a longitudinal twin study. *American Journal of Medical Genetics, Part B: Neuropsychiatric Genetics*, *153*(5). https://doi.org/10.1002/ajmg.b.31066

Hohnen, B., & Stevenson, J. (1999). The structure of genetic influences on general cognitive, language, phonological, and reading abilities. *Developmental Psychology*, *35*(2). https://doi.org/10.1037/0012-1649.35.2.590

Holmboe, K., Rijsdijk, F. V., Hallett, V., Happé, F., Plomin, R., & Ronald, A. (2014). Strong genetic influences on the stability of autistic traits in childhood. *Journal of the American Academy of Child and Adolescent Psychiatry*, *53*(2). https://doi.org/10.1016/j.jaac.2013.11.001

Howard, D. M., Adams, M. J., Clarke, T. K., Hafferty, J. D., Gibson, J., Shirali, M., Coleman, J. R. I., Hagenaars, S. P., Ward, J., Wigmore, E. M., Alloza, C., Shen, X., Barbu, M. C., Xu, E. Y., Whalley, H. C., Marioni, R. E., Porteous, D. J., Davies, G., Deary, I. J., … McIntosh, A. M. (2019). Genome-wide meta-analysis of depression identifies 102 independent variants and highlights the importance of the prefrontal brain regions. *Nature Neuroscience*, *22*(3). https://doi.org/10.1038/s41593-018-0326-7

Hudziak, J. J., Derks, E. M., Althoff, R. R., Rettew, D. C., & Boomsma, D. I. (2005). The genetic and environmental contributions to attention deficit hyperactivity disorder as measured by the Conners' Rating Scales - Revised. *American Journal of Psychiatry*, *162*(9). https://doi.org/10.1176/appi.ajp.162.9.1614

Hudziak, J. J., Rudiger, L. P., Neale, M. C., Heath, A. C., & Todd, R. D. (2000). A twin study of inattentive, aggressive, and anxious/depressed behaviors. *Journal of the American Academy of Child and Adolescent Psychiatry*, *39*(4). https://doi.org/10.1097/00004583-200004000-00016

Hur, Y. M. (2015). Genetic and environmental etiology of the relationship between childhood hyperactivity/inattention and conduct problems in a South Korean twin sample. *Twin Research and Human Genetics*, *18*(3). https://doi.org/10.1017/thg.2015.26

Hur, Y.-M. (2014). Increasing phenotypic and genetic variations in hyperactivity/inattention problems from age 3 to 13 years: A cross-sectional twin study. *Twin Research and Human Genetics*, *17*(6), 545–552.

Hyman, S. L., Levy, S. E., Myers, S. M., Kuo, D. Z., Apkon, C. S., Davidson, L. F., Ellerbeck, K. A., Foster, J. E. A., Noritz, G. H., O'Connor Leppert, M., Saunders, B. S., Stille, C., Yin, L., Brei, T., Davis, B. E., Lipkin, P. H., Norwood, K., Coleman, C., Mann, M., … Paul, L. (2020). Identification, evaluation, and management of children with autism spectrum disorder. *Pediatrics*, *145*(1). https://doi.org/10.1542/PEDS.2019-3447

Inouye, M., Abraham, G., Nelson, C. P., Wood, A. M., Sweeting, M. J., Dudbridge, F., Lai, F. Y., Kaptoge, S., Brozynska, M., Wang, T., Ye, S., Webb, T. R., Rutter, M. K., Tzoulaki, I., Patel, R. S., Loos, R. J. F., Keavney, B., Hemingway, H., Thompson, J., … Samani, N. J. (2018). Genomic Risk Prediction of Coronary Artery Disease in 480,000 Adults: Implications for

Primary Prevention. *Journal of the American College of Cardiology*, *72*(16). https://doi.org/10.1016/j.jacc.2018.07.079

Insel, T., Cuthbert, B., Garvey, M., Heinssen, R., Pine, D. S., Quinn, K., Sanislow, C., & Wang, P. (2010). Research Domain Criteria (RDoC): Toward a new classification framework for research on mental disorders. In *American Journal of Psychiatry* (Vol. 167, Issue 7). https://doi.org/10.1176/appi.ajp.2010.09091379

Institute for Health Metrics and Evaluation. (2017). Global Burden of Disease Study 2016 (GBD 2016) Results. *Global Burden of Disease Collaborative Network*, *2016*(Gbd 2016).

Institute for Health Metrics and Evaluation. (2019). Global Burden of Disease Study 2019 (GBD 2019). In *Global Burden of Disease Study* (Vol. 2019, Issue Gbd).

iPSYCH. (n.d.). *About iPSYCH*. 2022.

Jaffee, S. R., Caspi, A., Moffitt, T. E., Dodge, K. A., Rutter, M., Taylor, A., & Tully, L. A. (2005). Nature× nurture: Genetic vulnerabilities interact with physical maltreatment to promote conduct problems. *Development and Psychopathology*, *17*(1), 67–84.

Jaffee, S. R., Hanscombe, K. B., Haworth, C. M. A., Davis, O. S. P., & Plomin, R. (2012). Chaotic Homes and Children's Disruptive Behavior: A Longitudinal Cross-Lagged Twin Study. *Psychological Science*, *23*(6). https://doi.org/10.1177/0956797611431693

Jami, E. S., Hammerschlag, A. R., Ip, H. F., Allegrini, A. G., Benyamin, B., Border, R., Diemer, E. W., Jiang, C., Karhunen, V., Lu, Y., Lu, Q., Mallard, T. T., Mishra, P. P., Nolte, I. M., Palviainen, T., Peterson, R. E., Sallis, H. M., Shabalin, A. A., Tate, A. E., … Middeldorp, C. M. (2022). Genome-wide Association Meta-analysis of Childhood and Adolescent Internalizing Symptoms. *Journal of the American Academy of Child and Adolescent Psychiatry*, *61*(7). https://doi.org/10.1016/j.jaac.2021.11.035

Jansen, P. R., Watanabe, K., Stringer, S., Skene, N., Bryois, J., Hammerschlag, A. R., de Leeuw, C. A., Benjamins, J. S., Muñoz-Manchado, A. B., Nagel, M., Savage, J. E., Tiemeier, H., White, T., Agee, M., Alipanahi, B., Auton, A., Bell, R. K., Bryc, K., Elson, S. L., … Posthuma, D. (2019). Genome-wide analysis of insomnia in 1,331,010 individuals identifies new risk loci and functional pathways. *Nature Genetics*, *51*(3). https://doi.org/10.1038/s41588-018-0333-3

Johnson, W., McGue, M., & Iacono, W. G. (2005). Disruptive behavior and school grades: Genetic and environmental relations in 11-year-olds. *Journal of Educational Psychology*, *97*(3). https://doi.org/10.1037/0022-0663.97.3.391

Jones, A. P., Larsson, H., Ronald, A., Rijsdijk, F., Busfield, P., Mcmillan, A., Plomin, R., & Viding, E. (2009). Phenotypic and aetiological associations between psychopathic tendencies,

autistic traits, and emotion attribution. *Criminal Justice and Behavior*, *36*(11). https://doi.org/10.1177/0093854809342949

Jorm, A. F., Korten, A. E., Jacomb, P. A., Christensen, H., Rodgers, B., & Pollitt, P. (1997). Public beliefs about causes and risk factors for depression and schizophrenia. *Social Psychiatry and Psychiatric Epidemiology*, *32*(3). https://doi.org/10.1007/bf00794613

Jousilahti, P., Salomaa, V., Kuulasmaa, K., Niemelä, M., & Vartiainen, E. (2005). Total and cause specific mortality among participants and non-participants of population based health surveys: A comprehensive follow up of 54 372 Finnish men and women. *Journal of Epidemiology and Community Health*, *59*(4). https://doi.org/10.1136/jech.2004.024349

Kan, K. J., Dolan, C. V., Nivard, M. G., Middeldorp, C. M., Van Beijsterveldt, C. E. M., Willemsen, G., & Boomsma, D. I. (2013). Genetic and environmental stability in attention problems across the lifespan: Evidence from the netherlands twin register. In *Journal of the American Academy of Child and Adolescent Psychiatry* (Vol. 52, Issue 1). https://doi.org/10.1016/j.jaac.2012.10.009

Kan, K. J., Van Beijsterveldt, C. E. M., Bartels, M., & Boomsma, D. I. (2014). Assessing genetic influences on behavior: Informant and context dependency as illustrated by the analysis of attention problems. *Behavior Genetics*, *44*(4). https://doi.org/10.1007/s10519-014-9657-7

Kandaswamy, R., Allegrini, A., Nancarrow, A. F., Cave, S. N., Plomin, R., & Von Stumm, S. (2022). Predicting Alcohol Use from Genome-Wide Polygenic Scores, Environmental Factors, and Their Interactions in Young Adulthood. *Psychosomatic Medicine*, *84*(2). https://doi.org/10.1097/PSY.0000000000001005

Karlsson Linnér, R., Biroli, P., Kong, E., Meddens, S. F. W., Wedow, R., Fontana, M. A., Lebreton, M., Tino, S. P., Abdellaoui, A., Hammerschlag, A. R., Nivard, M. G., Okbay, A., Rietveld, C. A., Timshel, P. N., Trzaskowski, M., Vlaming, R. de, Zünd, C. L., Bao, Y., Buzdugan, L., … Wagner, G. G. (2019). Genome-wide association analyses of risk tolerance and risky behaviors in over 1 million individuals identify hundreds of loci and shared genetic influences. *Nature Genetics*, *51*(2). https://doi.org/10.1038/s41588-018-0309-3

Karlsson Linnér, R., Mallard, T. T., Barr, P. B., Sanchez-Roige, S., Madole, J. W., Driver, M. N., Poore, H. E., de Vlaming, R., Grotzinger, A. D., Tielbeek, J. J., Johnson, E. C., Liu, M., Rosenthal, S. B., Ideker, T., Zhou, H., Kember, R. L., Pasman, J. A., Verweij, K. J. H., Liu, D. J., … Dick, D. M. (2021). Multivariate analysis of 1.5 million people identifies genetic associations with traits related to self-regulation and addiction. *Nature Neuroscience*, *24*(10). https://doi.org/10.1038/s41593-021-00908-3

Keenan, J. M., Betjemann, R. S., Wadsworth, S. J., Defries, J. C., & Olson, R. K. (2006). Genetic and environmental influences on reading and listening comprehension. *Journal of Research in Reading*, *29*(1). https://doi.org/10.1111/j.1467-9817.2006.00293.x

Keith Conners, C., Sitarenios, G., Parker, J. D. A., & Epstein, J. N. (1998). The revised Conners' Parent Rating Scale (CPRS-R): Factor structure, reliability, and criterion validity. *Journal of Abnormal Child Psychology*, *26*(4). https://doi.org/10.1023/A:1022602400621

Kendler, K. S., Ohlsson, H., Edwards, A. C., Lichtenstein, P., Sundquist, K., & Sundquist, J. (2016). A novel sibling-based design to quantify genetic and shared environmental effects: Application to drug abuse, alcohol use disorder and criminal behavior. *Psychological Medicine*, *46*(8). https://doi.org/10.1017/S003329171500224X

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the national comorbidity survey replication. In *Archives of General Psychiatry* (Vol. 62, Issue 6). https://doi.org/10.1001/archpsyc.62.6.593

Khan, K., Hall, C. L., Bethan Davies, E., Hollis, C., & Glazebrook, C. (2019). The effectiveness of web-based interventions delivered to children and young people with neurodevelopmental disorders: Systematic review and meta-analysis. In *Journal of Medical Internet Research* (Vol. 21, Issue 11). https://doi.org/10.2196/13478

Kim, S., Greene, D. J., Bihun, E. C., Koller, J. M., Hampton, J. M., Acevedo, H., Reiersen, A. M., Schlaggar, B. L., & Black, K. J. (2019). Provisional Tic Disorder is not so transient. *Scientific Reports*, *9*(1). https://doi.org/10.1038/s41598-019-40133-4

Kim-Cohen, J., Caspi, A., Taylor, A., Williams, B., Newcombe, R., Craig, I. W., & Moffitt, T. E. (2006). MAOA, maltreatment, and gene-environment interaction predicting children's mental health: New evidence and a meta-analysis. *Molecular Psychiatry*, *11*(10). https://doi.org/10.1038/sj.mp.4001851

Kmet, L. M., Lee, R. C., & Cook, Linda, S. (2020). Standard quality assessment criteria for evaluating primary research papers from a variety of fields. In *Archives of Pathology & Laboratory Medicine* (Vol. 144, Issue 9).

Knopik, V. S., Alarcón, M., & DeFries, J. C. (1997). Comorbidity of mathematics and reading deficits: Evidence for a genetic etiology. *Behavior Genetics*, *27*(5). https://doi.org/10.1023/A:1025622400239

Knopik, V. S., Heath, A. C., Bucholz, K. K., Madden, P. A. F., & Waldron, M. (2009). Genetic and environmental influences on externalizing behavior and alcohol problems in adolescence:

A female twin study. *Pharmacology Biochemistry and Behavior*, *93*(3). https://doi.org/10.1016/j.pbb.2009.03.011

Knopik, V. S., Neiderhiser, J. M., DeFries, J. C., & Plomin, R. (2017). *Behavioral genetics*. Worth Publishers, Macmillan Learning New York.

Knopik, V. S., Smith, S. D., Cardon, L., Pennington, B., Gayan, J., Olson, R. K., & DeFries, J. C. (2002). Differential genetic etiology of reading component processes as a function of IQ. *Behavior Genetics*, *32*(3). https://doi.org/10.1023/A:1016069012111

Kovas, Y., Haworth, C. M. A., Harlaar, N., Petrill, S. A., Dale, P. S., & Plomin, R. (2007). Overlap and specificity of genetic and environmental influences on mathematics and reading disability in 10-year-old twins. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *48*(9). https://doi.org/10.1111/j.1469-7610.2007.01748..x

Kovas, Y., Voronin, I., Kaydalov, A., Malykh, S. B., Dale, P. S., & Plomin, R. (2013). Literacy and Numeracy Are More Heritable Than Intelligence in Primary School. *Psychological Science*, *24*(10). https://doi.org/10.1177/0956797613486982

Krapohl, E., Patel, H., Newhouse, S., Curtis, C. J., Von Stumm, S., Dale, P. S., Zabaneh, D., Breen, G., O'Reilly, P. F., & Plomin, R. (2018). Multi-polygenic score approach to trait prediction. *Molecular Psychiatry*, *23*(5). https://doi.org/10.1038/mp.2017.163

Ksinan, A. J., Smith, R. L., Barr, P. B., & Vazsonyi, A. T. (2022). The Associations of Polygenic Scores for Risky Behaviors and Parenting Behaviors with Adolescent Externalizing Problems. *Behavior Genetics*, *52*(1). https://doi.org/10.1007/s10519-021-10079-3

Kuhn, M. (2008). Building predictive models in R using the caret package. *Journal of Statistical Software*, *28*(5). https://doi.org/10.18637/jss.v028.i05

Kuja-Halkola, R., Lichtenstein, P., D'Onofrio, B. M., & Larsson, H. (2015). Codevelopment of ADHD and externalizing behavior from childhood to adulthood. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *56*(6). https://doi.org/10.1111/jcpp.12340

Kuntsi, J., Gayán, J., & Stevenson, J. (2000). Parents' and teachers' ratings of problem behaviours in children: Genetic and contrast effects. *Twin Research*, *3*(4). https://doi.org/10.1375/136905200320565229

Kuntsi, J., Pinto, R., Price, T. S., van der Meere, J. J., Frazier-Wood, A. C., & Asherson, P. (2014). The separation of ADHD inattention and hyperactivity-impulsivity symptoms: pathways from genetic effects to cognitive impairments and symptoms. *Journal of Abnormal Child Psychology*, *42*, 127–136.

Kuntsi, J., Rijsdijk, F., Ronald, A., Asherson, P., & Plomin, R. (2005). Genetic influences on the stability of attention-deficit/hyperactivity disorder symptoms from early to middle childhood. *Biological Psychiatry*, *57*(6). https://doi.org/10.1016/j.biopsych.2004.12.032

Kuntsi, J., & Stevenson, J. (2001). Psychological mechanisms in hyperactivity: II The role of genetic factors. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *42*(2). https://doi.org/10.1017/S0021963001006710

Kuo, P. H., Lin, C. C. H., Yang, H. J., Soong, W. T., & Chen, W. J. (2004). A Twin Study of Competence and Behavioral/Emotional Problems among Adolescents in Taiwan. *Behavior Genetics*, *34*(1). https://doi.org/10.1023/B:BEGE.0000009477.70657.9d

Lahey, B. B., & Loeber, R. (1994). Framework for a Developmental Model of Oppositional Defiant Disorder and Conduct Disorder. In *Disruptive Behavior Disorders in Childhood*. https://doi.org/10.1007/978-1-4899-1501-6_6

Lancaster, T., Creese, B., Escott-Price, V., Driver, I., Menzies, G., Khan, Z., Corbett, A., Ballard, C., Williams, J., & Murphy, K. (2023). Proof-of-concept recall-by-genotype study of extremely low and high Alzheimer's polygenic risk reveals autobiographical deficits and cingulate cortex correlates. *Alzheimer's Research & Therapy*, *15*(1), 213.

Larsson, H., Anckarsater, H., Råstam, M., Chang, Z., & Lichtenstein, P. (2012). Childhood attention-deficit hyperactivity disorder as an extreme of a continuous trait: A quantitative genetic study of 8,500 twin pairs. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *53*(1). https://doi.org/10.1111/j.1469-7610.2011.02467.x

Larsson, H., Dilshad, R., Lichtenstein, P., & Barker, E. D. (2011). Developmental trajectories of DSM-IV symptoms of attention-deficit/ hyperactivity disorder: Genetic effects, family risk and associated psychopathology. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *52*(9). https://doi.org/10.1111/j.1469-7610.2011.02379.x

Larsson, H., Lichtenstein, P., & Larsson, J. O. (2006). Genetic contributions to the development of ADHD subtypes from childhood to adolescence. *Journal of the American Academy of Child and Adolescent Psychiatry*, *45*(8). https://doi.org/10.1097/01.chi.0000222787.57100.d8

Larsson, J. O., Larsson, H., & Lichtenstein, P. (2004). Genetic and environmental contributions to stability and change of ADHD symptoms between 8 and 13 years of age: A longitudinal twin study. *Journal of the American Academy of Child and Adolescent Psychiatry*, *43*(10). https://doi.org/10.1097/01.chi.0000135622.05219.bf

Lau, J. Y. F., & Eley, T. C. (2006). Changes in genetic and environmental influences on depressive symptoms across adolescence and young adulthood. *British Journal of Psychiatry*, *189*(NOV.). https://doi.org/10.1192/bjp.bp.105.018721

Lazaroo, N. K., Bates, T. C., Hansell, N. K., Wright, M. J., Martin, N. G., & Luciano, M. (2019). Genetic structure of IQ, phonemic decoding skill, and academic achievement. *Frontiers in Genetics*, *10*(MAR). https://doi.org/10.3389/fgene.2019.00195

Lee, J. J., Wedow, R., Okbay, A., Kong, E., Maghzian, O., Zacher, M., Nguyen-Viet, T. A., Bowers, P., Sidorenko, J., Karlsson Linnér, R., Fontana, M. A., Kundu, T., Lee, C., Li, H., Li, R., Royer, R., Timshel, P. N., Walters, R. K., Willoughby, E. A., … Turley, P. (2018). Gene discovery and polygenic prediction from a genome-wide association study of educational attainment in 1.1 million individuals. *Nature Genetics*, *50*(8). https://doi.org/10.1038/s41588-018-0147-3

Lee, S. H., Ripke, S., Neale, B. M., Faraone, S. V., Purcell, S. M., Perlis, R. H., Mowry, B. J., Thapar, A., Goddard, M. E., Witte, J. S., Absher, D., Agartz, I., Akil, H., Amin, F., Andreassen, O. A., Anjorin, A., Anney, R., Anttila, V., Arking, D. E., … Wray, N. R. (2013). Genetic relationship between five psychiatric disorders estimated from genome-wide SNPs. *Nature Genetics*, *45*(9). https://doi.org/10.1038/ng.2711

Lemery-Chalfant, K., Doelger, L., & Goldsmith, H. H. (2008). Genetic relations between effortful and attentional control and symptoms of psychopathology in middle childhood. *Infant and Child Development*, *17*(4 SPEC. ISS.). https://doi.org/10.1002/icd.581

Levy, F., Hay, D. A., McStephen, M., Wood, C., & Waldman, I. (1997). Attention-deficit hyperactivity disorder: A category or a continuum? Genetic analysis of a large-scale twin study. *Journal of the American Academy of Child and Adolescent Psychiatry*, *36*(6). https://doi.org/10.1097/00004583-199706000-00009

Lewis, G. J., Haworth, C. M. A., & Plomin, R. (2014). Identical genetic influences underpin behavior problems in adolescence and basic traits of personality. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *55*(8). https://doi.org/10.1111/jcpp.12156

Lewis, G. J., & Plomin, R. (2015). Heritable influences on behavioural problems from early childhood to mid-adolescence: Evidence for genetic stability and innovation. *Psychological Medicine*, *45*(10). https://doi.org/10.1017/S0033291715000173

Lichtenstein, P., Carlström, E., Råstam, M., Gillberg, C., & Anckarsäter, H. (2010). The genetics of autism spectrum disorders and related neuropsychiatric disorders in childhood. *American Journal of Psychiatry*, *167*(11). https://doi.org/10.1176/appi.ajp.2010.10020223

Lifford, K. J., Harold, G. T., & Thapar, A. (2009). Parent-child hostility and child ADHD symptoms: A genetically sensitive and longitudinal analysis. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *50*(12). https://doi.org/10.1111/j.1469-7610.2009.02107.x

Light, J. G., Pennington, B. F., Gilger, J. W., & DeFries, J. C. (1995). Reading Disability and Hyperactivity Disorder: Evidence for a Common Genetic Etiology. *Developmental Neuropsychology*, *11*(3). https://doi.org/10.1080/87565649509540623

Lim, M., & Hastie, T. (2015). Learning Interactions via Hierarchical Group-Lasso Regularization. *Journal of Computational and Graphical Statistics*, *24*(3). https://doi.org/10.1080/10618600.2014.938812

Little, C. W., Hart, S. A., Schatschneider, C., & Taylor, J. (2016). Examining Associations Among ADHD, Homework Behavior, and Reading Comprehension: A Twin Study. *Journal of Learning Disabilities*, *49*(4). https://doi.org/10.1177/0022219414555715

Lockhart, C., Bright, J., Ahmadzadeh, Y., Breen, G., Bristow, S., Boyd, A., Downs, J., Hotopf, M., Palaiologou, E., Rimfeld, K., Maxwell, J., Malanchini, M., McAdams, T. A., McMillan, A., Plomin, R., & Eley, T. C. (2023). Twins Early Development Study (TEDS): A genetically sensitive investigation of mental health outcomes in the mid-twenties. *JCPP Advances*, *3*(2), e12154. https://doi.org/10.1002/JCV2.12154

Loehlin, J. C., & Nichols, R. C. (1976). *Heredity, environment, and personality: A study of 850 sets of twins*. University of Texas Press.

Logan, J. A. R., Hart, S. A., Cutting, L., Deater-Deckard, K., Schatschneider, C., & Petrill, S. (2013). Reading development in young children: Genetic and environmental influences. *Child Development*, *84*(6). https://doi.org/10.1111/cdev.12104

LoParo, D., & Waldman, I. (2014). Twins' Rearing Environment Similarity and Childhood Externalizing Disorders: A Test of the Equal Environments Assumption. *Behavior Genetics*, *44*(6). https://doi.org/10.1007/s10519-014-9685-3

López-León, S., Janssens, A. C. J. W., González-Zuloeta Ladd, A. M., Del-Favero, J., Claes, S. J., Oostra, B. A., & Van Duijn, C. M. (2008). Meta-analyses of genetic studies on major depressive disorder. *Molecular Psychiatry*, *13*(8). https://doi.org/10.1038/sj.mp.4002088

Lorant, V., Demarest, S., Miermans, P. J., & Van oyen, H. (2007). Survey error in measuring socio-economic risk factors of health status: A comparison of a survey and a census. *International Journal of Epidemiology*, *36*(6). https://doi.org/10.1093/ije/dym191

Luciano, M., Hagenaars, S. P., Davies, G., Hill, W. D., Clarke, T. K., Shirali, M., Harris, S. E., Marioni, R. E., Liewald, D. C., Fawns-Ritchie, C., Adams, M. J., Howard, D. M., Lewis, C. M., Gale, C. R., McIntosh, A. M., & Deary, I. J. (2018). Association analysis in over 329,000 individuals identifies 116 independent variants influencing neuroticism. *Nature Genetics*, *50*(1). https://doi.org/10.1038/s41588-017-0013-8

Lundström, S., Chang, Z., Kerekes, N., Gumpert, C. H., Rästam, M., Gillberg, C., Lichtenstein, P., & Anckarsäter, H. (2011). Autistic-like traits and their association with mental health problems in two nationwide twin cohorts of children and adults. *Psychological Medicine*, *41*(11). https://doi.org/10.1017/S0033291711000377

Lundström, S., Chang, Z., Råstam, M., Gillberg, C., Larsson, H., Anckarsäter, H., & Lichtenstein, P. (2012). Autism spectrum disorders and autisticlike traits: Similar etiology in the extreme end and the normal variation. *Archives of General Psychiatry*, *69*(1). https://doi.org/10.1001/archgenpsychiatry.2011.144

Lundström, S., Haworth, C. M. A., Carlström, E., Gillberg, C., Mill, J., Råstam, M., Hultman, C. M., Ronald, A., Anckarsäter, H., Plomin, R., Lichtenstein, P., & Reichenberg, A. (2010). Trajectories leading to autism spectrum disorders are affected by paternal age: Findings from two nationally representative twin studies. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *51*(7). https://doi.org/10.1111/j.1469-7610.2010.02223.x

Mackenbach, J. P., Stirbu, I., Roskam, A.-J. R., Schaap, M. M., Menvielle, G., Leinsalu, M., & Kunst, A. E. (2008). Socioeconomic Inequalities in Health in 22 European Countries. *New England Journal of Medicine*, *358*(23). https://doi.org/10.1056/nejmsa0707519

Malanchini, M., Engelhardt, L. E., Grotzinger, A. D., Harden, K. P., & Tucker-Drob, E. M. (2019). "Same But Different": Associations Between Multiple Aspects of Self-Regulation, Cognition, and Academic Abilities. *Journal of Personality and Social Psychology*, *117*(6). https://doi.org/10.1037/pspp0000224

Malanchini, M., Engelhardt, L. E., Raffington, L. A., Sabhlok, A., Grotzinger, A. D., Briley, D. A., Madole, J. W., Freis, S. M., Patterson, M. W., Harden, K. P., & Tucker-Drob, E. M. (2021). Weak and uneven associations of home, neighborhood, and school environments with stress hormone output across multiple timescales. *Molecular Psychiatry*, *26*(9). https://doi.org/10.1038/s41380-020-0747-z

Malanchini, M., Rimfeld, K., Wang, Z., Petrill, S. A., Tucker-Drob, E. M., Plomin, R., & Kovas, Y. (2020). Genetic factors underlie the association between anxiety, attitudes and performance in mathematics. *Translational Psychiatry*, *10*(1). https://doi.org/10.1038/s41398-020-0711-3

Malanchini, M., Smith-Woolley, E., Ayorech, Z., Rimfeld, K., Krapohl, E., Vuoksimaa, E., Korhonen, T., Bartels, M., Van Beijsterveldt, T. C. E. M., Rose, R. J., Lundström, S., Anckarsäter, H., Kaprio, J., Lichtenstein, P., Boomsma, D. I., & Plomin, R. (2019). Aggressive behaviour in childhood and adolescence: The role of smoking during pregnancy,

evidence from four twin cohorts in the EU-ACTION consortium. *Psychological Medicine*, *49*(4). https://doi.org/10.1017/S0033291718001344

Malanchini, M., Wang, Z., Voronin, I., Schenker, V. J., Plomin, R., Petrill, S. A., & Kovas, Y. (2017). Reading self-perceived ability, enjoyment and achievement: A genetically informative study of their reciprocal links over time. *Developmental Psychology*, *53*(4). https://doi.org/10.1037/dev0000209

Manolio, T. A., Collins, F. S., Cox, N. J., Goldstein, D. B., Hindorff, L. A., Hunter, D. J., McCarthy, M. I., Ramos, E. M., Cardon, L. R., Chakravarti, A., Cho, J. H., Guttmacher, A. E., Kong, A., Kruglyak, L., Mardis, E., Rotimi, C. N., Slatkin, M., Valle, D., Whittemore, A. S., … Visscher, P. M. (2009). Finding the missing heritability of complex diseases. In *Nature* (Vol. 461, Issue 7265). https://doi.org/10.1038/nature08494

Markon, K. E. (2010). Modeling psychopathology structure: A symptom-level analysis of Axis i and II disorders. *Psychological Medicine*, *40*(2). https://doi.org/10.1017/S0033291709990183

Marlow, A. J., Fisher, S. E., Richardson, A. J., Francks, C., Talcott, J. B., Monaco, A. P., Stein, J. F., & Cardon, L. R. (2001). Investigation of quantitative measures related to reading disability in a large sample of sib-pairs from the UK. *Behavior Genetics*, *31*(2). https://doi.org/10.1023/A:1010209629021

Martin, A. R., Daly, M. J., Robinson, E. B., Hyman, S. E., & Neale, B. M. (2019). Predicting Polygenic Risk of Psychiatric Disorders. In *Biological Psychiatry* (Vol. 86, Issue 2). https://doi.org/10.1016/j.biopsych.2018.12.015

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*(4). https://doi.org/10.1038/s41588-019-0379-x

Martin, J., Hamshere, M. L., Stergiakouli, E., O'Donovan, M. C., & Thapar, A. (2014). Genetic risk for attention-deficit/hyperactivity disorder contributes to neurodevelopmental traits in the general population. *Biological Psychiatry*, *76*(8). https://doi.org/10.1016/j.biopsych.2014.02.013

Martin, J., Khramtsova, E. A., Goleva, S. B., Blokland, G. A. M., Traglia, M., Walters, R. K., Hübel, C., Coleman, J. R. I., Breen, G., Børglum, A. D., Demontis, D., Grove, J., Werge, T., Bralten, J., Bulik, C. M., Lee, P. H., Mathews, C. A., Peterson, R. E., Winham, S. J., … Stahl, E. (2021). Examining Sex-Differentiated Genetic Effects Across Neuropsychiatric and Behavioral Traits. *Biological Psychiatry*, *89*(12). https://doi.org/10.1016/j.biopsych.2020.12.024

Martin, J., Walters, R. K., Demontis, D., Mattheisen, M., Lee, S. H., Robinson, E., Brikell, I., Ghirardi, L., Larsson, H., Lichtenstein, P., Eriksson, N., Agee, M., Alipanahi, B., Auton, A., Bell, R. K., Bryc, K., Elson, S. L., Fontanillas, P., Furlotte, N. A., … Børglum, A. D. (2018). A Genetic Investigation of Sex Bias in the Prevalence of Attention-Deficit/Hyperactivity Disorder. *Biological Psychiatry*, *83*(12). https://doi.org/10.1016/j.biopsych.2017.11.026

Martin, N. C., Levy, F., Pieka, J., & Hay, D. A. (2006). A genetic study of Attention Deficit Hyperactivity Disorder, Conduct Disorder, Oppositional Defiant Disorder and Reading Disability: Aetiological overlaps and implications. *International Journal of Disability, Development and Education*, *53*(1). https://doi.org/10.1080/10349120500509992

Martin, N. C., Piek, J. P., & Hay, D. (2006). DCD and ADHD: A genetic study of their shared aetiology. *Human Movement Science*, *25*(1). https://doi.org/10.1016/j.humov.2005.10.006

Martin, N. G., & Eaves, L. J. (1977). The genetical analysis of covariance structure. *Heredity*, *38*(1). https://doi.org/10.1038/hdy.1977.9

Martin, N., Scourfield, J., & McGuffin, P. (2002). Observer effects and heritability of childhood attention-deficit hyperactivity disorder symptoms. *The British Journal of Psychiatry : The Journal of Mental Science*, *180*. https://doi.org/10.1192/bjp.180.3.260

Martschenko, D. O., Domingue, B. W., Matthews, L. J., & Trejo, S. (2021). FoGS provides a public FAQ repository for social and behavioral genomic discoveries. In *Nature Genetics* (Vol. 53, Issue 9). https://doi.org/10.1038/s41588-021-00929-5

Masten, A. S., & Curtis, W. J. (2000). Integrating competence and psychopathology: Pathways toward a comprehensive science of adaptation in development. *Development and Psychopathology*, *12*(3). https://doi.org/10.1017/S095457940000314X

Mataix-Cols, D., Isomura, K., Pérez-Vigil, A., Chang, Z., Rück, C., Johan Larsson, K., Leckman, J. F., Serlachius, E., Larsson, H., & Lichtenstein, P. (2015). Familial risks of tourette syndrome and chronic tic disorders a population-based cohort study. *JAMA Psychiatry*, *72*(8). https://doi.org/10.1001/jamapsychiatry.2015.0627

Matheny, A. P., Wachs, T. D., Ludwig, J. L., & Phillips, K. (1995). Bringing order out of chaos: Psychometric characteristics of the confusion, hubbub, and order scale. *Journal of Applied Developmental Psychology*, *16*(3). https://doi.org/10.1016/0193-3973(95)90028-4

May, T., Sciberras, E., Brignell, A., & Williams, K. (2017). Autism spectrum disorder: Updated prevalence and comparison of two birth cohorts in a nationally representative Australian sample. *BMJ Open*, *7*(5). https://doi.org/10.1136/bmjopen-2016-015549

Mazefsky, C. A., Goin-Kochel, R. P., Riley, B. P., & Maes, H. H. (2008). Genetic and environmental influences on symptom domains in twins and siblings with autism. *Research in Autism Spectrum Disorders*, *2*(2). https://doi.org/10.1016/j.rasd.2007.08.002

McAdams, T. A., Hannigan, L. J., Eilertsen, E. M., Gjerde, L. C., Ystrom, E., & Rijsdijk, F. V. (2018). Revisiting the Children-of-Twins Design: Improving Existing Models for the Exploration of Intergenerational Associations. *Behavior Genetics*, *48*(5). https://doi.org/10.1007/s10519-018-9912-4

McCauley, J. B., Elias, R., & Lord, C. (2020). Trajectories of co-occurring psychopathology symptoms in autism from late childhood to adulthood. *Development and Psychopathology*, *32*(4). https://doi.org/10.1017/S0954579420000826

McDowell, M. J., & Lesslie, J. M. (2018). Long-term outcomes for children with neurodevelopmental disorders: Are they core business for paediatricians? *Journal of Paediatrics and Child Health*, *54*(5). https://doi.org/10.1111/jpc.13871

McGovern, C. W., & Sigman, M. (2005). Continuity and change from early childhood to adolescence in autism. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *46*(4). https://doi.org/10.1111/j.1469-7610.2004.00361.x

McGregor, K. K. (2020). How we fail children with developmental language disorder. *Language, Speech, and Hearing Services in Schools*, *51*(4). https://doi.org/10.1044/2020_LSHSS-20-00003

McGue, M., & Bouchard, T. J. (1984). Adjustment of twin data for the effects of age and sex. *Behavior Genetics*, *14*(4). https://doi.org/10.1007/BF01080045

McLoughlin, G., Ronald, A., Kuntsi, J., Asherson, P., & Plomin, R. (2007). Genetic support for the dual nature of attention deficit hyperactivity disorder: Substantial genetic overlap between the inattentive and hyperactive-impulsive components. *Journal of Abnormal Child Psychology*, *35*(6). https://doi.org/10.1007/s10802-007-9149-9

Mehlmann-Wicks, J. (2020). Autism spectrum disorder. *The British Medical Association Is the Trade Union and Professional Body for Doctors in the UK*.

Meier, S. M., Trontti, K., Purves, K. L., Als, T. D., Grove, J., Laine, M., Pedersen, M. G., Bybjerg-Grauholm, J., Bækved-Hansen, M., Sokolowska, E., Mortensen, P. B., Hougaard, D. M., Werge, T., Nordentoft, M., Breen, G., Børglum, A. D., Eley, T. C., Hovatta, I., Mattheisen, M., & Mors, O. (2019). Genetic Variants Associated with Anxiety and Stress-Related Disorders: A Genome-Wide Association Study and Mouse-Model Study. *JAMA Psychiatry*, *76*(9). https://doi.org/10.1001/jamapsychiatry.2019.1119

Meltzer, L. J. (2017). Sleep and Developmental Psychopathology: Introduction to the Special Issue. In *Journal of Clinical Child and Adolescent Psychology* (Vol. 46, Issue 2). https://doi.org/10.1080/15374416.2016.1220316

Merwood, A., Asherson, P., & Larsson, H. (2013). Genetic associations between the ADHD symptom dimensions and Cloninger's temperament dimensions in adult twins. *European Neuropsychopharmacology*, *23*(6). https://doi.org/10.1016/j.euroneuro.2012.10.003

Merwood, A., Chen, W., Rijsdijk, F., Skirrow, C., Larsson, H., Thapar, A., Kuntsi, J., & Asherson, P. (2014). Genetic associations between the symptoms of attention-deficit/ hyperactivity disorder and emotional lability in child and adolescent twins. *Journal of the American Academy of Child and Adolescent Psychiatry*, *53*(2). https://doi.org/10.1016/j.jaac.2013.11.006

Messer, S. C., Angold, A., Costello, E. J., & Loeber, R. (1995). Development of a short questionnaire for use in epidemiological studies of depression in children and adolescents: Factor composition and structure across development. *International Journal of Methods in Psychiatric Research*, *5*(4).

Metzl, J. (2019a). *Hacking Darwin: Genetic engineering and the future of humanity*. Sourcebooks, Inc.

Metzl, J. (2019b). *Hacking Darwin: Genetic engineering and the future of humanity*. Sourcebooks, Inc.

Micalizzi, L., Brick, L. A., Marraccini, M. E., Benca-Bachman, C. E., Palmer, R. H. C., & Knopik, V. S. (2021). Single nucleotide polymorphism heritability and differential patterns of genetic overlap between inattention and four neurocognitive factors in youth. *Development and Psychopathology*, *33*(1), 76–86.

Michelini, G., Eley, T. C., Gregory, A. M., & McAdams, T. A. (2015). Aetiological overlap between anxiety and attention deficit hyperactivity symptom dimensions in adolescence. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *56*(4). https://doi.org/10.1111/jcpp.12318

Middeldorp, C. M., Felix, J. F., Mahajan, A., & McCarthy, M. I. (2019). The early growth genetics (Egg) and early genetics and lifecourse epidemiology (eagle) consortia: Design, results and future prospects. *European Journal of Epidemiology*, *34*(3). https://doi.org/10.1007/s10654-019-00502-9

Middeldorp, C. M., Hammerschlag, A. R., Ouwens, K. G., Groen-Blokhuis, M. M., St. Pourcain, B., Greven, C. U., Pappa, I., Tiesler, C. M. T., Ang, W., Nolte, I. M., Vilor-Tejedor, N., Bacelis, J., Ebejer, J. L., Zhao, H., Davies, G. E., Ehli, E. A., Evans, D. M., Fedko, I. O.,

Guxens, M., … Boomsma, D. I. (2016). A Genome-Wide Association Meta-Analysis of Attention-Deficit/Hyperactivity Disorder Symptoms in Population-Based Pediatric Cohorts. *Journal of the American Academy of Child and Adolescent Psychiatry*, *55*(10). https://doi.org/10.1016/j.jaac.2016.05.025

Mikolajewski, A. J., Allan, N. P., Hart, S. A., Lonigan, C. J., & Taylor, J. (2013). Negative affect shares genetic and environmental influences with symptoms of childhood internalizing and externalizing disorders. *Journal of Abnormal Child Psychology*, *41*(3). https://doi.org/10.1007/s10802-012-9681-0

Mimeau, C., Dionne, G., Feng, B., Brendgen, M., Vitaro, F., Tremblay, R. E., & Boivin, M. (2018). The Genetic and Environmental Etiology of the Association between Vocabulary and Syntax in First Grade. *Language Learning and Development*, *14*(2). https://doi.org/10.1080/15475441.2018.1427589

Moffitt, T. E. (1993). The neuropsychology of conduct disorder. *Development and Psychopathology*, *5*(1–2). https://doi.org/10.1017/S0954579400004302

Moffitt, T. E. (2005). The new look of behavioral genetics in developmental psychopathology: Gene-environment interplay in antisocial behaviors. In *Psychological Bulletin* (Vol. 131, Issue 4). https://doi.org/10.1037/0033-2909.131.4.533

Moffitt, T. E., Arseneault, L., Belsky, D., Dickson, N., Hancox, R. J., Harrington, H. L., Houts, R., Poulton, R., Roberts, B. W., Ross, S., Sears, M. R., Thomson, W. M., & Caspi, A. (2011). A gradient of childhood self-control predicts health, wealth, and public safety. *Proceedings of the National Academy of Sciences of the United States of America*, *108*(7). https://doi.org/10.1073/pnas.1010076108

Moffitt, T. E., Caspi, A., Rutter, M., & Silva, P. A. (2009). Sex Differences in Antisocial Behaviour Conduct Disorder, Delinquency, and Violence in the Dunedin Longitudinal Study. *DECP Debate*, *1*(131). https://doi.org/10.53841/bpsdeb.2009.1.131.34

Mogensen, N., Larsson, H., Lundholm, C., & Almqvist, C. (2011). Association between childhood asthma and ADHD symptoms in adolescence - A prospective population-based twin study. *Allergy: European Journal of Allergy and Clinical Immunology*, *66*(9). https://doi.org/10.1111/j.1398-9995.2011.02648.x

Molenaar, D., Middeldorp, C., van Beijsterveldt, T., & Boomsma, D. I. (2015). Analysis of Behavioral and Emotional Problems in Children Highlights the Role of Genotype × Environment Interaction. *Child Development*, *86*(6). https://doi.org/10.1111/cdev.12451

Moruzzi, S., Rijsdijk, F., & Battaglia, M. (2014). A twin study of the relationships among inattention, hyperactivity/ impulsivity and sluggish cognitive tempo problems. *Journal of Abnormal Child Psychology*, *42*(1). https://doi.org/10.1007/s10802-013-9725-0

Mullins, N., Forstner, A. J., O'Connell, K. S., Coombes, B., Coleman, J. R. I., Qiao, Z., Als, T. D., Bigdeli, T. B., Børte, S., Bryois, J., Charney, A. W., Drange, O. K., Gandal, M. J., Hagenaars, S. P., Ikeda, M., Kamitaki, N., Kim, M., Krebs, K., Panagiotaropoulou, G., … Andreassen, O. A. (2021). Genome-wide association study of more than 40,000 bipolar disorder cases provides new insights into the underlying biology. *Nature Genetics*, *53*(6). https://doi.org/10.1038/s41588-021-00857-4

Mullins, N., Power, R. A., Fisher, H. L., Hanscombe, K. B., Euesden, J., Iniesta, R., Levinson, D. F., Weissman, M. M., Potash, J. B., Shi, J., Uher, R., Cohen-Woods, S., Rivera, M., Jones, L., Jones, I., Craddock, N., Owen, M. J., Korszun, A., Craig, I. W., … Lewis, C. M. (2016). Polygenic interactions with environmental adversity in the aetiology of major depressive disorder. *Psychological Medicine*, *46*(4). https://doi.org/10.1017/S0033291715002172

Nadder, T. S., Rutter, M., Silberg, J. L., Maes, H. H., & Eaves, L. J. (2002). Genetic effects on the variation and covariation of attention deficit-hyperactivity disorder (ADHD) and oppositional-defiant disorder/conduct disorder (ODD/CD) symptomatologies across informant and occasion of measurement. *Psychological Medicine*, *32*(1). https://doi.org/10.1017/s0033291701004792

Nadder, T. S., Silberg, J. L., Eaves, L. J., Maes, H. H., & Meyer, J. M. (1998). Genetic effects on ADHD symptomatology in 7- to 13-year-old twins: Results from a telephone survey. *Behavior Genetics*, *28*(2). https://doi.org/10.1023/A:1021686906396

Nagel, M., Jansen, P. R., Stringer, S., Watanabe, K., De Leeuw, C. A., Bryois, J., Savage, J. E., Hammerschlag, A. R., Skene, N. G., Muñoz-Manchado, A. B., Agee, M., Alipanahi, B., Auton, A., Bell, R. K., Bryc, K., Elson, S. L., Fontanillas, P., Furlotte, N. A., Hinds, D. A., … Posthuma, D. (2018). Meta-analysis of genome-wide association studies for neuroticism in 449,484 individuals identifies novel genetic loci and pathways. *Nature Genetics*, *50*(7). https://doi.org/10.1038/s41588-018-0151-7

Narusyte, J., Andershed, A. K., Neiderhiser, J. M., & Lichtenstein, P. (2007). Aggression as a mediator of genetic contributions to the association between negative parent-child relationships and adolescent antisocial behavior. *European Child and Adolescent Psychiatry*, *16*(2). https://doi.org/10.1007/s00787-006-0582-z

Neale, M. C., Hunter, M. D., Pritikin, J. N., Zahery, M., Brick, T. R., Kirkpatrick, R. M., Estabrook, R., Bates, T. C., Maes, H. H., & Boker, S. M. (2016). OpenMx 2.0: Extended

Structural Equation and Statistical Modeling. *Psychometrika*, *81*(2). https://doi.org/10.1007/s11336-014-9435-8

Neiderhiser, J. M., Reiss, D., & Mavis Hetherington, E. (2007). The Nonshared Environment in Adolescent Development (NEAD) project: A longitudinal family study of twins and siblings from adolescence to young adulthood. In *Twin Research and Human Genetics* (Vol. 10, Issue 1). https://doi.org/10.1375/twin.10.1.74

Nelemans, S. A., Boks, M., Lin, B., Oldehinkel, T., van Lier, P., Branje, S., & Meeus, W. (2021). Polygenic Risk for Major Depression Interacts with Parental Criticism in Predicting Adolescent Depressive Symptom Development. *Journal of Youth and Adolescence*, *50*(1). https://doi.org/10.1007/s10964-020-01353-4

Nelson, C. A., Bloom, F. E., Cameron, J. L., Amaral, D., Dahl, R. E., & Pine, D. (2002). An integrative, multidisciplinary approach to the study of brain-behavior relations in the context of typical and atypical development. *Development and Psychopathology*, *14*(3). https://doi.org/10.1017/S0954579402003061

Neuman, R. J., Heath, A., Reich, W., Bucholz, K. K., Madden, P. A. F., Sun, L., Todd, R. D., & Hudziak, J. J. (2001). Latent class analysis of ADHD and comorbid symptoms in a population sample of adolescent female twins. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *42*(7). https://doi.org/10.1111/1469-7610.00789

Newman, D. L., Moffitt, T. E., Caspi, A., & Silva, P. A. (1998). Comorbid mental disorders: Implications for treatment and sample selection. *Journal of Abnormal Psychology*, *107*(2). https://doi.org/10.1037/0021-843X.107.2.305

Newsome, J., Boisvert, D., & Wright, J. P. (2014). Genetic and environmental influences on the co-occurrence of early academic achievement and externalizing behavior. *Journal of Criminal Justice*, *42*(1). https://doi.org/10.1016/j.jcrimjus.2013.12.002

Nikolas, M. A., & Burt, S. A. (2010). Genetic and Environmental Influences on ADHD Symptom Dimensions of Inattention and Hyperactivity: A Meta-Analysis. *Journal of Abnormal Psychology*, *119*(1). https://doi.org/10.1037/a0018010

Nikolas, M. A., Klump, K. L., & Burt, S. A. (2015). Parental Involvement Moderates Etiological Influences on Attention Deficit Hyperactivity Disorder Behaviors in Child Twins. *Child Development*, *86*(1). https://doi.org/10.1111/cdev.12296

Niv, S., Tuvblad, C., Raine, A., Wang, P., & Baker, L. A. (2012). Heritability and longitudinal stability of impulsivity in adolescence. *Behavior Genetics*, *42*(3). https://doi.org/10.1007/s10519-011-9518-6

Nivard, M. G., Dolan, C. V., Kendler, K. S., Kan, K. J., Willemsen, G., Van Beijsterveldt, C. E. M., Lindauer, R. J. L., Van Beek, J. H. D. A., Geels, L. M., Bartels, M., Middeldorp, C. M., & Boomsma, D. I. (2015). Stability in symptoms of anxiety and depression as a function of genotype and environment: A longitudinal twin study from ages 3 to 63 years. *Psychological Medicine*, *45*(5). https://doi.org/10.1017/S003329171400213X

Nurm, M., Reigo, A., Nõukas, M., Leitsalu, L., Nikopensius, T., Palover, M., Annilo, T., Alver, M., Saar, A., Marandi, T., Ainla, T., Metspalu, A., Esko, T., & Tõnisson, N. (2022). Do Biobank Recall Studies Matter? Long-Term Follow-Up of Research Participants With Familial Hypercholesterolemia. *Frontiers in Genetics*, *13*. https://doi.org/10.3389/fgene.2022.936131

O'Connor, T. G., Deater-Deckard, K., Fulker, D., Rutter, M., & Plomin, R. (1998). Genotype-environment correlations in late childhood and early adolescence: antisocial behavioral problems and coercive parenting. *Developmental Psychology*, *34*(5). https://doi.org/10.1037/0012-1649.34.5.970

Office for National Statistics [ONS]. (2021). *Population estimates for the UK, England and Wales, Scotland and Northern Ireland : Mid-2020*. Statistical Bulletin.

Offord, D. R., Boyle, M. H., Racine, Y. A., Fleming, J. E., Cadman, D. T., Blum, H. M., Byrne, C., Links, P. S., Lipman, E. L., & MacMillan, H. L. (1992). Outcome, prognosis, and risk in a longitudinal follow-up study. *Journal of the American Academy of Child & Adolescent Psychiatry*, *31*(5), 916–923.

Okbay, A., Baselmans, B. M. L., De Neve, J. E., Turley, P., Nivard, M. G., Fontana, M. A., Meddens, S. F. W., Linnér, R. K., Rietveld, C. A., Derringer, J., Gratten, J., Lee, J. J., Liu, J. Z., De Vlaming, R., SAhluwalia, T., Buchwald, J., Cavadino, A., Frazier-Wood, A. C., Furlotte, N. A., … Cesarini, D. (2016). Genetic variants associated with subjective well-being, depressive symptoms, and neuroticism identified through genome-wide analyses. *Nature Genetics*, *48*(6). https://doi.org/10.1038/ng.3552

Okbay, A., Wu, Y., Wang, N., Jayashankar, H., Bennett, M., Nehzati, S. M., Sidorenko, J., Kweon, H., Goldman, G., Gjorgjieva, T., Jiang, Y., Hicks, B., Tian, C., Hinds, D. A., Ahlskog, R., Magnusson, P. K. E., Oskarsson, S., Hayward, C., Campbell, A., … Young, A. I. (2022). Polygenic prediction of educational attainment within and between families from genome-wide association analyses in 3 million individuals. *Nature Genetics*, *54*(4). https://doi.org/10.1038/s41588-022-01016-z

Oliver, B. R., Dale, P. S., & Plomin, R. (2007). Writing and reading skills as assessed by teachers in 7-year olds: A behavioral genetic approach. *Cognitive Development*, *22*(1). https://doi.org/10.1016/j.cogdev.2006.07.003

Olson, R. K., Gillis, J. J., Rack, J. P., Defries, J. C., & Fulker, D. W. (1991). Confirmatory factor analysis of word recognition and process measures in the Colorado Reading Project. *Reading and Writing*, *3*(3–4). https://doi.org/10.1007/BF00354960

O'Nions, E., Tick, B., Rijsdijk, F., Happé, F., Plomin, R., Ronald, A., & Viding, E. (2015). Examining the genetic and environmental associations between autistic social and communication deficits and psychopathic callous-unemotional traits. *PLoS ONE*, *10*(9). https://doi.org/10.1371/journal.pone.0134331

Ooki, S. (2005). Genetic and environmental influences on stuttering and tics in Japanese twin children. *Twin Research and Human Genetics*, *8*(1). https://doi.org/10.1375/1832427053435409

Oram, R. A., Patel, K., Hill, A., Shields, B., McDonald, T. J., Jones, A., Hattersley, A. T., & Weedon, M. N. (2016). A type 1 diabetes genetic risk score can aid discrimination between type 1 and type 2 diabetes in young adults. *Diabetes Care*, *39*(3). https://doi.org/10.2337/dc15-1111

Padilla-Martínez, F., Collin, F., Kwasniewski, M., & Kretowski, A. (2020). Systematic review of polygenic risk scores for type 1 and type 2 diabetes. In *International Journal of Molecular Sciences* (Vol. 21, Issue 5). https://doi.org/10.3390/ijms21051703

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., … Moher, D. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. In *The BMJ* (Vol. 372). https://doi.org/10.1136/bmj.n71

Pain, O., Glanville, K. P., Hagenaars, S. P., Selzam, S., Furtjes, A. E., Gaspar, H. A., Coleman, J. R. I., Rimfeld, K., Breen, G., Plomin, R., Folkersen, L., & Lewis, C. M. (2021). Evaluation of polygenic prediction methodology within a reference-standardized framework. *PLoS Genetics*, *17*(5 May). https://doi.org/10.1371/journal.pgen.1009021

Paloyelis, Y., Rijsdijk, F., Wood, A. C., Asherson, P., & Kuntsi, J. (2010a). The genetic association between ADHD symptoms and reading difficulties: The role of inattentiveness and IQ. *Journal of Abnormal Child Psychology*, *38*(8). https://doi.org/10.1007/s10802-010-9429-7

Paloyelis, Y., Rijsdijk, F., Wood, A. C., Asherson, P., & Kuntsi, J. (2010b). The genetic association between ADHD symptoms and reading difficulties: the role of inattentiveness and IQ. *Journal of Abnormal Child Psychology*, *38*, 1083–1095.

Pappa, I., Fedko, I. O., Mileva-Seitz, V. R., Hottenga, J. J., Bakermans-Kranenburg, M. J., Bartels, M., Van Beijsterveldt, C. E. M., Jaddoe, V. W. V., Middeldorp, C. M., Rippe, R. C. A., Rivadeneira, F., Tiemeier, H., Verhulst, F. C., Van Ijzendoorn, M. H., & Boomsma, D. I. (2015). Single Nucleotide Polymorphism Heritability of Behavior Problems in Childhood: Genome-Wide Complex Trait Analysis. *Journal of the American Academy of Child and Adolescent Psychiatry*, *54*(9). https://doi.org/10.1016/j.jaac.2015.06.004

Pardiñas, A. F., Holmans, P., Pocklington, A. J., Escott-Price, V., Ripke, S., Carrera, N., Legge, S. E., Bishop, S., Cameron, D., Hamshere, M. L., Han, J., Hubbard, L., Lynham, A., Mantripragada, K., Rees, E., MacCabe, J. H., McCarroll, S. A., Baune, B. T., Breen, G., … Walters, J. T. R. (2018). Common schizophrenia alleles are enriched in mutation-intolerant genes and in regions under strong background selection. *Nature Genetics*, *50*(3). https://doi.org/10.1038/s41588-018-0059-2

Pascoe, P. (2009). *What comes naturally: Miscegenation law and the making of race in America*. Oxford University Press.

Paskett, E. D., Reeves, K. W., McLaughlin, J. M., Katz, M. L., McAlearney, A. S., Ruffin, M. T., Halbert, C. H., Merete, C., Davis, F., & Gehlert, S. (2008). Recruitment of minority and underserved populations in the United States: The centers for population health and health disparities experience. *Contemporary Clinical Trials*, *29*(6). https://doi.org/10.1016/j.cct.2008.07.006

Patel, K. A., Oram, R. A., Flanagan, S. E., De Franco, E., Colclough, K., Shepherd, M., Ellard, S., Weedon, M. N., & Hattersley, A. T. (2016). Type 1 diabetes genetic risk score: A novel tool to discriminate monogenic and type 1 diabetes. *Diabetes*, *65*(7). https://doi.org/10.2337/db15-1690

Pavlou, M., Ambler, G., Seaman, S., De iorio, M., & Omar, R. Z. (2016). Review and evaluation of penalised regression methods for risk prediction in low-dimensional data with few events. *Statistics in Medicine*, *35*(7). https://doi.org/10.1002/sim.6782

Peng, C. Z., Grant, J. D., Heath, A. C., Reiersen, A. M., Mulligan, R. C., & Anokhin, A. P. (2016). Familial influences on the full range of variability in attention and activity levels during adolescence: A longitudinal twin study. *Development and Psychopathology*, *28*(2). https://doi.org/10.1017/S0954579415001091

Perry, D. J., Wasserfall, C. H., Oram, R. A., Williams, M. D., Posgai, A., Muir, A. B., Haller, M. J., Schatz, D. A., Wallet, M. A., Mathews, C. E., Atkinson, M. A., & Brusko, T. M. (2018). Application of a Genetic Risk Score to Racially Diverse Type 1 Diabetes Populations Demonstrates the Need for Diversity in Risk-Modeling. *Scientific Reports*, *8*(1). https://doi.org/10.1038/s41598-018-22574-5

Peterson, R. E., Kuchenbaecker, K., Walters, R. K., Chen, C. Y., Popejoy, A. B., Periyasamy, S., Lam, M., Iyegbe, C., Strawbridge, R. J., Brick, L., Carey, C. E., Martin, A. R., Meyers, J. L., Su, J., Chen, J., Edwards, A. C., Kalungi, A., Koen, N., Majara, L., … Duncan, L. E. (2019). Genome-wide Association Studies in Ancestrally Diverse Populations: Opportunities, Methods, Pitfalls, and Recommendations. In *Cell* (Vol. 179, Issue 3). https://doi.org/10.1016/j.cell.2019.08.051

Petrill, S. A., Deater-Deckard, K., Thompson, L. A., Schatschneider, C., Dethorne, L. S., & Vandenbergh, D. J. (2007). Longitudinal genetic analysis of early reading: The Western reserve reading project. *Reading and Writing*, *20*(1–2). https://doi.org/10.1007/s11145-006-9021-2

Petrill, S. A., Hart, S. A., Harlaar, N., Logan, J., Justice, L. M., Schatschneider, C., Thompson, L., Dethorne, L. S., Deater-Deckard, K., & Cutting, L. (2010). Genetic and environmental influences on the growth of early reading skills. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *51*(6). https://doi.org/10.1111/j.1469-7610.2009.02204.x

Pettersson, E., Anckarsäter, H., Gillberg, C., & Lichtenstein, P. (2013). Different neurodevelopmental symptoms have a common genetic etiology. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *54*(12). https://doi.org/10.1111/jcpp.12113

Pettersson, E., Lichtenstein, P., Larsson, H., Song, J., Agrawal, A., Borglum, A. D., Bulik, C. M., Daly, M. J., Davis, L. K., Demontis, D., Edenberg, H. J., Grove, J., Gelernter, J., Neale, B. M., Pardiñas, A. F., Stahl, E., Walters, J. T. R., Walters, R., Sullivan, P. F., … Polderman, T. J. C. (2019). Genetic influences on eight psychiatric disorders based on family data of 4 408 646 full and half-siblings, and genetic data of 333 748 cases and controls. *Psychological Medicine*, *49*(7). https://doi.org/10.1017/S0033291718002039

Peyrot, W. J., Milaneschi, Y., Abdellaoui, A., Sullivan, P. F., Hottenga, J. J., Boomsma, D. I., & Penninx, B. W. J. H. (2014). Effect of polygenic risk scores on depression in childhood trauma. *British Journal of Psychiatry*, *205*(2). https://doi.org/10.1192/bjp.bp.113.143081

Peyrot, W. J., Van der Auwera, S., Milaneschi, Y., Dolan, C. V., Madden, P. A. F., Sullivan, P. F., Strohmaier, J., Ripke, S., Rietschel, M., Nivard, M. G., Mullins, N., Montgomery, G. W., Henders, A. K., Heat, A. C., Fisher, H. L., Dunn, E. C., Byrne, E. M., Air, T. A., Wray, N. R.,

… Nelson, E. N. (2018). Does Childhood Trauma Moderate Polygenic Risk for Depression? A Meta-analysis of 5765 Subjects From the Psychiatric Genomics Consortium. *Biological Psychiatry*, *84*(2). https://doi.org/10.1016/j.biopsych.2017.09.009

Pike, A., Hetherington, E. M., Reiss, D., & Plomin, R. (1996). Using MZ differences in the search for nonshared environmental effects. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *37*(6). https://doi.org/10.1111/j.1469-7610.1996.tb01461.x

Pike, A., McGuire, S., Hetherington, E. M., Reiss, D., & et al. (1996). Family environment and adolescent depressive symptoms and antisocial behavior: A multivariate genetic analysis. *Developmental Psychology*, *32*(4). https://doi.org/10.1037//0012-1649.32.4.590

Pingault, J. B., Rijsdijk, F., Zheng, Y., Plomin, R., & Viding, E. (2015). Developmentally dynamic genome: Evidence of genetic influences on increases and decreases in conduct problems from early childhood to adolescence. *Scientific Reports*, *5*. https://doi.org/10.1038/srep10053

Pinto, R., Rijsdijk, F., Ronald, A., Asherson, P., & Kuntsi, J. (2016). The genetic overlap of attention-deficit/hyperactivity disorder and autistic-like traits: an investigation of individual symptom scales and cognitive markers. *Journal of Abnormal Child Psychology*, *44*, 335–345.

Plomin, R. (1994). *Genetics and experience: the interplay between nature and nurture.* Sage Publications, Inc.

Plomin, R. (2004). Genetics and developmental psychology. In *Merrill-Palmer Quarterly* (Vol. 50, Issue 3). https://doi.org/10.1353/mpq.2004.0024

Plomin, R. (2011). Commentary: Why are children in the same family so different? Non-shared environment three decades later. In *International Journal of Epidemiology* (Vol. 40, Issue 3). https://doi.org/10.1093/ije/dyq144

Plomin, R. (2014). Genotype-Environment Correlation in the Era of DNA. *Behavior Genetics*, *44*(6). https://doi.org/10.1007/s10519-014-9673-7

Plomin, R. (2019). *Blueprint, with a new afterword: How DNA makes us who we are*. Mit Press.

Plomin, R., Asbury, K., & Dunn, J. (2001). Why are children in the same family so different? Nonshared environment a decade later. In *Canadian Journal of Psychiatry* (Vol. 46, Issue 3). https://doi.org/10.1177/070674370104600302

Plomin, R., & Daniels, D. (1987). Children in the same family are very different, but why? In *Behavioral and Brain Sciences* (Vol. 10, Issue 1). https://doi.org/10.1017/S0140525X00056272

Plomin, R., & Daniels, D. (2011). Why are children in the same family so different from one another? *International Journal of Epidemiology*, *40*(3). https://doi.org/10.1093/ije/dyq148

Plomin, R., DeFries, J. C., Knopik, V. S., & Neiderhiser, J. M. (2016). Top 10 Replicated Findings From Behavioral Genetics. *Perspectives on Psychological Science*, *11*(1). https://doi.org/10.1177/1745691615617439

Plomin, R., DeFries, J. C., & Loehlin, J. C. (1977). Genotype-environment interaction and correlation in the analysis of human behavior. *Psychological Bulletin*, *84*(2). https://doi.org/10.1037/0033-2909.84.2.309

Plomin, R., Gidziela, A., Malanchini, M., & Von Stumm, S. (2022). Gene-environment interaction using polygenic scores: Do polygenic scores for psychopathology moderate predictions from environmental risk to behavior problems? *Development and Psychopathology*, *34*(5). https://doi.org/10.1017/S0954579422000931

Plomin, R., Haworth, C. M. A., & Davis, O. S. P. (2009). Common disorders are quantitative traits. In *Nature Reviews Genetics* (Vol. 10, Issue 12). https://doi.org/10.1038/nrg2670

Plomin, R., & Kovas, Y. (2005). Generalist genes and learning disabilities. In *Psychological Bulletin* (Vol. 131, Issue 4). https://doi.org/10.1037/0033-2909.131.4.592

Plomin, R., Owen, M. J., & McGuffin, P. (1994). The genetic basis of complex human behaviors. *Science*, *264*(5166). https://doi.org/10.1126/science.8209254

Plomin, R., & Viding, E. (2022). Commentary: Will genomics revolutionise research on gene–environment interplay? In *Journal of Child Psychology and Psychiatry and Allied Disciplines* (Vol. 63, Issue 10). https://doi.org/10.1111/jcpp.13687

Plomin, R., & Von Stumm, S. (2018). The new genetics of intelligence. In *Nature Reviews Genetics* (Vol. 19, Issue 3). https://doi.org/10.1038/nrg.2017.104

Plomin, R., & von Stumm, S. (2022). Polygenic scores: prediction versus explanation. In *Molecular Psychiatry* (Vol. 27, Issue 1). https://doi.org/10.1038/s41380-021-01348-y

Plourde, V., Boivin, M., Brendgen, M., Vitaro, F., & Dionne, G. (2017). Phenotypic and genetic associations between reading and attention-deficit/hyperactivity disorder dimensions in adolescence. *Development and Psychopathology*, *29*(4). https://doi.org/10.1017/S0954579416001255

Plourde, V., Boivin, M., Forget-Dubois, N., Brendgen, M., Vitaro, F., Marino, C., Tremblay, R. T., & Dionne, G. (2015). Phenotypic and genetic associations between reading comprehension, decoding skills, and ADHD dimensions: Evidence from two population-based studies. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *56*(10). https://doi.org/10.1111/jcpp.12394

Polanczyk, G., De Lima, M. S., Horta, B. L., Biederman, J., & Rohde, L. A. (2007). The worldwide prevalence of ADHD: A systematic review and metaregression analysis. *American Journal of Psychiatry*, *164*(6). https://doi.org/10.1176/ajp.2007.164.6.942

Polanczyk, G. V., Salum, G. A., Sugaya, L. S., Caye, A., & Rohde, L. A. (2015). Annual research review: A meta-analysis of the worldwide prevalence of mental disorders in children and adolescents. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *56*(3). https://doi.org/10.1111/jcpp.12381

Polderman, T. J. C., Huizink, A. C., Verhulst, F. C., van Beijsterveldt, C. E. M., Boomsma, D. I., & Bartels, M. (2011). A genetic study on attention problems and academic skills: Results of a longitudinal study in twins. *Journal of the Canadian Academy of Child and Adolescent Psychiatry*, *20*(1).

Polderman, T. J. C., Posthuma, D., De Sonneville, L. M. J., Verhulst, F. C., & Boomsma, D. I. (2006). Genetic Analyses of Teacher Ratings of Problem Behavior in 5-Year-Old Twins. *Twin Research and Human Genetics*, *9*(1). https://doi.org/10.1375/twin.9.1.122

Polderman, T. J. C., Van Dongen, J., & Boomsma, D. I. (2011). The relation between ADHD symptoms and fine motor control: A genetic study. *Child Neuropsychology*, *17*(2). https://doi.org/10.1080/09297049.2010.518142

Popejoy, A. B., & Fullerton, S. M. (2016). Genomics is failing on diversity. In *Nature* (Vol. 538, Issue 7624). https://doi.org/10.1038/538161a

Posthuma, D., & Boomsma, D. I. (2000). A note on the statistical power in extended twin designs. *Behavior Genetics*, *30*(2). https://doi.org/10.1023/A:1001959306025

Preacher, K. J., & Kelley, K. (2011). Effect size measures for mediation models: Quantitative strategies for communicating indirect effects. *Psychological Methods*, *16*(2). https://doi.org/10.1037/a0022658

Price, T. S., Dale, P. S., & Plomin, R. (2004). A Longitudinal Genetic Analysis of Low Verbal and Nonverbal Cognitive Abilities in Early Childhood. *Twin Research*, *7*(2). https://doi.org/10.1375/136905204323016122

Price, T. S., Freeman, B., Craig, I., Petrill, S. A., Ebersole, L., & Plomin, R. (2000). Infant zygosity can be assigned by parental report questionnaire data. *Twin Research and Human Genetics*, *3*(3), 129–133.

Price, T. S., Simonoff, E., Asherson, P., Curran, S., Kuntsi, J., Waldman, I., & Plomin, R. (2005). Continuity and change in preschool ADHD symptoms: Longitudinal genetic analysis with contrast effects. *Behavior Genetics*, *35*(2). https://doi.org/10.1007/s10519-004-1013-x

Privé, F., Arbel, J., & Vilhjálmsson, B. J. (2020). LDpred2: Better, faster, stronger. *Bioinformatics*, *36*(22–23). https://doi.org/10.1093/bioinformatics/btaa1029

Privé, F., Aschard, H., Carmi, S., Folkersen, L., Hoggart, C., O'Reilly, P. F., & Vilhjálmsson, B. J. (2022). Portability of 245 polygenic scores when derived from the UK Biobank and applied to 9 ancestry groups from the same cohort. *American Journal of Human Genetics*, *109*(1). https://doi.org/10.1016/j.ajhg.2021.11.008

Psychiatric Genomics Consortium. (n.d.). *Psychiatric Genomics Consortium*. 2022.

Purves, K. L., Coleman, J. R. I., Meier, S. M., Rayner, C., Davis, K. A. S., Cheesman, R., Bækvad-Hansen, M., Børglum, A. D., Wan Cho, S., Jürgen Deckert, J., Gaspar, H. A., Bybjerg-Grauholm, J., Hettema, J. M., Hotopf, M., Hougaard, D., Hübel, C., Kan, C., McIntosh, A. M., Mors, O., … Eley, T. C. (2020). A major role for common genetic variation in anxiety disorders. *Molecular Psychiatry*, *25*(12). https://doi.org/10.1038/s41380-019-0559-1

Quinn, P. D., Pettersson, E., Lundström, S., Anckarsäter, H., Långström, N., Gumpert, C. H., Larsson, H., Lichtenstein, P., & D'Onofrio, B. M. (2016). Childhood attention-deficit/hyperactivity disorder symptoms and the development of adolescent alcohol problems: A prospective, population-based study of Swedish twins. *American Journal of Medical Genetics, Part B: Neuropsychiatric Genetics*, *171*(7). https://doi.org/10.1002/ajmg.b.32412

R Core Team. (2022). R Core Team 2021 R: A language and environment for statistical computing. R foundation for statistical computing. https://www.R-project.org/. *R Foundation for Statistical Computing*, *2*.

Rajula, H. S. R., Manchia, M., Agarwal, K., Akingbuwa, W. A., Allegrini, A. G., Diemer, E., Doering, S., Haan, E., Jami, E. S., Karhunen, V., Leone, M., Schellhas, L., Thompson, A., van den Berg, S. M., Bergen, S. E., Kuja-Halkola, R., Hammerschlag, A. R., Järvelin, M. R., Leval, A., … Middeldorp, C. M. (2022). Overview of CAPICE—Childhood and Adolescence Psychopathology: unravelling the complex etiology by a large Interdisciplinary Collaboration in Europe—an EU Marie Skłodowska-Curie International Training Network. *European Child and Adolescent Psychiatry*, *31*(5). https://doi.org/10.1007/s00787-020-01713-2

Ramsay, M., & Sankoh, O. (2016). African partnerships through the H3Africa Consortium bring a genomic dimension to longitudinal population studies on the continent. In *International Journal of Epidemiology* (Vol. 45, Issue 2). https://doi.org/10.1093/ije/dyv187

Rasmussen, P., & Gillberg, C. (2000). Natural outcome of ADHD with developmental coordination disorder at age 22 years: A controlled, longitudinal, community-based study.

*Journal of the American Academy of Child and Adolescent Psychiatry*, *39*(11). https://doi.org/10.1097/00004583-200011000-00017

Reef, J., Diamantopoulou, S., Van Meurs, I., Verhulst, F., & Van Der Ende, J. (2010). Predicting adult emotional and behavioral problems from externalizing problem trajectories in a 24-year longitudinal study. *European Child and Adolescent Psychiatry*, *19*(7). https://doi.org/10.1007/s00787-010-0088-6

Reef, J., Van Meurs, I., Verhulst, F. C., & Van Der Ende, J. (2010). Children's problems predict adults' DSM-IV disorders across 24 years. *Journal of the American Academy of Child and Adolescent Psychiatry*, *49*(11). https://doi.org/10.1016/j.jaac.2010.08.002

Reiss, D., & Hetherington, E. M. (2009). *The relationship code: Deciphering genetic and social influences on adolescent development* (Vol. 1). Harvard University Press.

Reiss, D., Plomin, R., Hetherington, E. M., Howe, G. W., Rovine, M. J., Tryon, A., & Hagan, M. S. (1994). The separate worlds of teenage siblings: An introduction to the study of the nonshared environment and adolescent development. In *Separate social worlds of siblings: The impact of nonshared environment on development.*

Rende, R. D., & Plomin, R. (1990). Quantitative genetics and developmental psychopathology: Contributions to understanding normal development. *Development and Psychopathology*, *2*(4). https://doi.org/10.1017/S0954579400005794

Revelle, W., & Revelle, M. W. (2015). Package 'psych.' *The Comprehensive R Archive Network*, *337*(338).

Reynolds, C. A., Hewitt, J. K., Erickson, M. T., Rutter, M., Simonoff, E., Silberg, J. L., Meyer, J., & Eaves, L. J. (1996). The genetics of children's oral reading performance. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *37*(4). https://doi.org/10.1111/j.1469-7610.1996.tb01423.x

Rhee, S. H., Waldman, I. D., Hay, D. A., & Levy, F. (1999). Sex differences in genetic and environmental influences on DSM-III-R attention-deficit/hyperactivity disorder. *Journal of Abnormal Psychology*, *108*(1). https://doi.org/10.1037/0021-843X.108.1.24

Rice, F., Harold, G. T., Boivin, J., Hay, D. F., Van Den Bree, M., & Thapar, A. (2009). Disentangling prenatal and inherited influences in humans with an experimental design. *Proceedings of the National Academy of Sciences of the United States of America*, *106*(7). https://doi.org/10.1073/pnas.0808798106

Rietveld, M. J. H., Hudziak, J. J., Bartels, M., van Beijsterveldt, C. E. M., & Boomsma, D. I. (2004). Heritability of attention problems in children: Longitudinal results from a study of

twins, age 3 to 12. In *Journal of Child Psychology and Psychiatry and Allied Disciplines* (Vol. 45, Issue 3). https://doi.org/10.1111/j.1469-7610.2004.00247.x

Rijsdijk, F. V., & Sham, P. C. (2002). Analytic approaches to twin data using structural equation models. *Briefings in Bioinformatics*, *3*(2). https://doi.org/10.1093/bib/3.2.119

Rimfeld, K., Ayorech, Z., Dale, P. S., Kovas, Y., & Plomin, R. (2016). Genetics affects choice of academic subjects as well as achievement. *Scientific Reports*, *6*. https://doi.org/10.1038/srep26373

Rimfeld, K., Kovas, Y., Dale, P. S., & Plomin, R. (2015). Pleiotropy across academic subjects at the end of compulsory education. *Scientific Reports*, *5*. https://doi.org/10.1038/srep11713

Rimfeld, K., Krapohl, E., Trzaskowski, M., Coleman, J. R. I., Selzam, S., Dale, P. S., Esko, T., Metspalu, A., & Plomin, R. (2018). Genetic influence on social outcomes during and after the Soviet era in Estonia. *Nature Human Behaviour*, *2*(4). https://doi.org/10.1038/s41562-018-0332-5

Rimfeld, K., Malanchini, M., Arathimos, R., Gidziela, A., Pain, O., McMillan, A., Ogden, R., Webster, L., Packer, A. E., Shakeshaft, N. G., Schofield, K. L., Pingault, J.-B., Allegrini, A. G., Stringaris, A., Von Stumm, S., Lewis, C. M., & Plomin, R. (2022). The consequences of a year of the COVID-19 pandemic for the mental health of young adult twins in England and Wales. *BJPsych Open*, *8*(4). https://doi.org/10.1192/bjo.2022.506

Rimfeld, K., Malanchini, M., Hannigan, L. J., Dale, P. S., Allen, R., Hart, S. A., & Plomin, R. (2019). Teacher assessments during compulsory education are as reliable, stable and heritable as standardized test scores. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *60*(12). https://doi.org/10.1111/jcpp.13070

Rimfeld, K., Malanchini, M., Krapohl, E., Hannigan, L. J., Dale, P. S., & Plomin, R. (2018). The stability of educational achievement across school years is largely explained by genetic factors. *Npj Science of Learning*, *3*(1). https://doi.org/10.1038/s41539-018-0030-0

Rimfeld, K., Malanchini, M., Spargo, T., Spickernell, G., Selzam, S., McMillan, A., Dale, P. S., Eley, T. C., & Plomin, R. (2019). Twins Early Development Study: A Genetically Sensitive Investigation into Behavioral and Cognitive Development from Infancy to Emerging Adulthood. *Twin Research and Human Genetics*, *22*(6). https://doi.org/10.1017/thg.2019.56

Ripke, S., Sanders, A. R., Kendler, K. S., Levinson, D. F., Sklar, P., Holmans, P. A., Lin, D. Y., Duan, J., Ophoff, R. A., Andreassen, O. A., Scolnick, E., Cichon, S., St. Clair, D., Corvin, A., Gurling, H., Werge, T., Rujescu, D., Blackwood, D. H. R., Pato, C. N., … Gejman, P. V. (2011). Genome-wide association study identifies five new schizophrenia loci. *Nature Genetics*, *43*(10). https://doi.org/10.1038/ng.940

Robinson, E. B., Koenen, K. C., McCormick, M. C., Munir, K., Hallett, V., Happé, F., Plomin, R., & Ronald, A. (2011). Evidence that autistic traits show the same etiology in the general population and at the quantitative extremes (5%, 2.5%, and 1%). *Archives of General Psychiatry*, *68*(11). https://doi.org/10.1001/archgenpsychiatry.2011.119

Robinson, E. B., Koenen, K. C., McCormick, M. C., Munir, K., Hallett, V., Happé, F., Plomin, R., & Ronald, A. (2012). A multivariate twin study of autistic traits in 12-year-olds: Testing the fractionable autism triad hypothesis. *Behavior Genetics*, *42*(2). https://doi.org/10.1007/s10519-011-9500-3

Robinson, N., & Bergen, S. E. (2021). Environmental Risk Factors for Schizophrenia and Bipolar Disorder and Their Relationship to Genetic Risk: Current Knowledge and Future Directions. In *Frontiers in Genetics* (Vol. 12). https://doi.org/10.3389/fgene.2021.686666

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. In *Journal of the American Academy of Child and Adolescent Psychiatry* (Vol. 60, Issue 10). https://doi.org/10.1016/j.jaac.2021.01.019

Ronald, A., Happé, F., Bolton, P., Butcher, L. M., Price, T. S., Wheelwright, S., Baron-Cohen, S., & Plomin, R. (2006). Genetic heterogeneity between the three components of the autism spectrum: A twin study. *Journal of the American Academy of Child and Adolescent Psychiatry*, *45*(6). https://doi.org/10.1097/01.chi.0000215325.13058.9d

Ronald, A., Happé, F., & Plomin, R. (2005). The genetic relationship between individual differences in social and nonsocial behaviours characteristic of autism. In *Developmental Science* (Vol. 8, Issue 5). https://doi.org/10.1111/j.1467-7687.2005.00433.x

Ronald, A., Happé, F., Price, T. S., Baron-Cohen, S., & Plomin, R. (2006). Phenotypic and genetic overlap between autistic traits at the extremes of the general population. *Journal of the American Academy of Child and Adolescent Psychiatry*, *45*(10). https://doi.org/10.1097/01.chi.0000230165.54117.41

Ronald, A., Larsson, H., Anckarsäter, H., & Lichtenstein, P. (2014). Symptoms of autism and ADHD: A swedish twin study examining their overlap. *Journal of Abnormal Psychology*, *123*(2). https://doi.org/10.1037/a0036088

Ronald, A., Simonoff, E., Kuntsi, J., Asherson, P., & Plomin, R. (2008). Evidence for overlapping genetic influences on autistic and ADHD behaviours in a community twin sample. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *49*(5). https://doi.org/10.1111/j.1469-7610.2007.01857.x

Rosenberg, J., Pennington, B. F., Willcutt, E. G., & Olson, R. K. (2012). Gene by environment interactions influencing reading disability and the inattentive symptom dimension of attention deficit/hyperactivity disorder. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *53*(3). https://doi.org/10.1111/j.1469-7610.2011.02452.x

Rosseel, Y. (2012). Lavaan: An R package for structural equation modeling. *Journal of Statistical Software*, *48*. https://doi.org/10.18637/jss.v048.i02

Roux, A. M., Shattuck, P. T., Cooper, B. P., Anderson, K. A., Wagner, M., & Narendorf, S. C. (2013). Postsecondary employment experiences among young adults with an autism spectrum disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, *52*(9). https://doi.org/10.1016/j.jaac.2013.05.019

Rovine, M. J. (2013). Estimating nonshared environment using sibling discrepancy scores. In *Separate social worlds of siblings* (pp. 33–61). Routledge.

Rovira, P., Demontis, D., Sánchez-Mora, C., Zayats, T., Klein, M., Mota, N. R., Weber, H., Garcia-Martínez, I., Pagerols, M., Vilar-Ribó, L., Arribas, L., Richarte, V., Corrales, M., Fadeuilhe, C., Bosch, R., Martin, G. E., Almos, P., Doyle, A. E., Grevet, E. H., … Ribasés, M. (2020). Shared genetic background between children and adults with attention deficit/hyperactivity disorder. *Neuropsychopharmacology*, *45*(10). https://doi.org/10.1038/s41386-020-0664-5

Rubia, K. (2011). "Cool" inferior frontostriatal dysfunction in attention-deficit/hyperactivity disorder versus "hot" ventromedial orbitofrontal-limbic dysfunction in conduct disorder: A review. In *Biological Psychiatry* (Vol. 69, Issue 12). https://doi.org/10.1016/j.biopsych.2010.09.023

Russell, M. A., & Gajos, J. M. (2020). Annual Research Review: Ecological momentary assessment studies in child psychology and psychiatry. In *Journal of Child Psychology and Psychiatry and Allied Disciplines* (Vol. 61, Issue 3). https://doi.org/10.1111/jcpp.13204

Rutter, M., & Silberg, J. (2002). Gene-environment interplay in relation to emotional and behavioral disturbance. *Annual Review of Psychology*, *53*. https://doi.org/10.1146/annurev.psych.53.100901.135223

Rutter, M., & Sroufe, L. A. (2000). Developmental psychopathology: Concepts and challenges. In *Development and Psychopathology* (Vol. 12, Issue 3). https://doi.org/10.1017/s0954579400003023

Rydell, M., Taylor, M. J., & Larsson, H. (2017). Genetic and environmental contributions to the association between ADHD and affective problems in early childhood—A Swedish

population-based twin study. *American Journal of Medical Genetics, Part B: Neuropsychiatric Genetics*, *174*(5). https://doi.org/10.1002/ajmg.b.32536

Sadeh, A. (2015). III. Sleep assessment methods. *Monographs of the Society for Research in Child Development*, *80*(1). https://doi.org/10.1111/mono.12143

Samuelsson, S., Olson, R., Wadsworth, S., Corley, R., Defries, J. C., Willcutt, E., Hulslander, J., & Byrne, B. (2007). Genetic and environmental influences on prereading skills and early reading and spelling development in the United States, Australia, and Scandinavia. *Reading and Writing*, *20*(1–2). https://doi.org/10.1007/s11145-006-9018-x

Saudino, K. J., & Plomin, R. (2007). Why are hyperactivity and academic achievement related? *Child Development*, *78*(3). https://doi.org/10.1111/j.1467-8624.2007.01044.x

Saudino, K. J., Ronald, A., & Plomin, R. (2005). The etiology of behavior problems in 7-year-old twins: Substantial genetic influence and negligible shared environmental influence for parent ratings and ratings by same and different teachers. *Journal of Abnormal Child Psychology*, *33*(1). https://doi.org/10.1007/s10802-005-0939-7

Saunders, M. C., Anckarsäter, H., Lundström, S., Hellner, C., Lichtenstein, P., & Fontaine, N. M. G. (2019). The Associations between Callous-unemotional Traits and Symptoms of Conduct Problems, Hyperactivity and Emotional Problems: A Study of Adolescent Twins Screened for Neurodevelopmental Problems. *Journal of Abnormal Child Psychology*, *47*(3). https://doi.org/10.1007/s10802-018-0439-1

Savage, J. E., Jansen, P. R., Stringer, S., Watanabe, K., Bryois, J., De Leeuw, C. A., Nagel, M., Awasthi, S., Barr, P. B., Coleman, J. R. I., Grasby, K. L., Hammerschlag, A. R., Kaminski, J. A., Karlsson, R., Krapohl, E., Lam, M., Nygaard, M., Reynolds, C. A., Trampush, J. W., … Posthuma, D. (2018). Genome-wide association meta-analysis in 269,867 individuals identifies new genetic and functional links to intelligence. *Nature Genetics*, *50*(7). https://doi.org/10.1038/s41588-018-0152-6

Scherff, A., Taylor, M., Eley, T. C., Happé, F., Charman, T., & Ronald, A. (2014). What causes internalising traits and autistic traits to co-occur in adolescence? A community-based twin study. *Journal of Abnormal Child Psychology*, *42*(4). https://doi.org/10.1007/s10802-013-9796-y

Scourfield, J., Martin, N., Eley, T. C., & McGuffin, P. (2004). The genetic relationship between social cognition and conduct problems. *Behavior Genetics*, *34*(4). https://doi.org/10.1023/B:BEGE.0000023643.49413.df

Seed, C. (2017). Hail: An Open-Source Framework for Scalable Genetic Data. *Neale Lab*.

Selzam, S., McAdams, T. A., Coleman, J. R. I., Carnell, S., O'Reilly, P. F., Plomin, R., & Llewellyn, C. H. (2018). Evidence for gene-environment correlation in child feeding: Links between common genetic variation for BMI in children and parental feeding practices. *PLoS Genetics*, *14*(11). https://doi.org/10.1371/journal.pgen.1007757

Serdarevic, F., Tiemeier, H., Jansen, P. R., Alemany, S., Xerxa, Y., Neumann, A., Robinson, E., Hillegers, M. H. J., Verhulst, F. C., & Ghassabian, A. (2020). Polygenic Risk Scores for Developmental Disorders, Neuromotor Functioning During Infancy, and Autistic Traits in Childhood. *Biological Psychiatry*, *87*(2). https://doi.org/10.1016/j.biopsych.2019.06.006

Shakeshaft, N. G., Trzaskowski, M., McMillan, A., Rimfeld, K., Krapohl, E., Haworth, C. M. A., Dale, P. S., & Plomin, R. (2013). Strong genetic influence on a UK nationwide test of educational achievement at the end of compulsory education at age 16. *PLoS ONE*, *8*(12). https://doi.org/10.1371/journal.pone.0080341

Sherman, D. K., Iacono, W. G., & McGue, M. K. (1997). Attention-deficit hyperactivity disorder dimensions: A twin study of inattention and impulsivity-hyperactivity. *Journal of the American Academy of Child and Adolescent Psychiatry*, *36*(6). https://doi.org/10.1097/00004583-199706000-00010

Siebelink, N. M., Asherson, P., Antonova, E., Bögels, S. M., Speckens, A. E., Buitelaar, J. K., & Greven, C. U. (2019). Genetic and environmental aetiologies of associations between dispositional mindfulness and ADHD traits: a population-based twin study. *European Child and Adolescent Psychiatry*, *28*(9). https://doi.org/10.1007/s00787-019-01279-8

Silberg, J., Meyer, J., Maes, H., Simonoff, E., Pickles, A., Rutter, M., Hewitt, J., Loeber, R., & Eaves, L. (1996). Genetic and environmental influences on the covariation between hyperactivity and conduct disturbance in juvenile twins. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *37*(7). https://doi.org/10.1111/j.1469-7610.1996.tb01476.x

Silventoinen, K., Jelenkovic, A., Sund, R., Latvala, A., Honda, C., Inui, F., Tomizawa, R., Watanabe, M., Sakai, N., Rebato, E., Busjahn, A., Tyler, J., Hopper, J. L., Ordoñana, J. R., Sánchez-Romera, J. F., Colodro-Conde, L., Calais-Ferreira, L., Oliveira, V. C., Ferreira, P. H., … Kaprio, J. (2020). Genetic and environmental variation in educational attainment: an individual-based analysis of 28 twin cohorts. *Scientific Reports*, *10*(1). https://doi.org/10.1038/s41598-020-69526-6

Silverman, W. K., Ginsburg, G. S., & Goedhart, A. W. (1999). Factor structure of the childhood anxiety sensitivity index. *Behaviour Research and Therapy*, *37*(9). https://doi.org/10.1016/S0005-7967(98)00189-2

Simonoff, E., Pickles, A., Hervas, A., Silberg, J. L., Rutter, M., & Eaves, L. (1998). Genetic influences on childhood hyperactivity: Contrast effects imply parental rating bias, not sibling interaction. *Psychological Medicine*, *28*(4). https://doi.org/10.1017/S0033291798006886

Singh, A. L., & Waldman, I. D. (2010). The etiology of associations between negative emotionality and childhood externalizing disorders. *Journal of Abnormal Psychology*, *119*(2). https://doi.org/10.1037/a0019342

Skuse, D. H. (2007). Rethinking the nature of genetic vulnerability to autistic spectrum disorders. *Trends in Genetics*, *23*(8). https://doi.org/10.1016/j.tig.2007.06.003

Smith, A. K., Stasi, S. M., Rhee, S. H., Corley, R. P., Young, S. E., & Hewitt, J. K. (2011). The role of attention-deficit/hyperactivity disorder in the association between verbal ability and conduct disorder. *Frontiers in Psychiatry*, *2*(MAR). https://doi.org/10.3389/fpsyt.2011.00003

So, H. C., Chau, C. K. L., Chiu, W. T., Ho, K. S., Lo, C. P., Yim, S. H. Y., & Sham, P. C. (2017). Analysis of genome-wide association data highlights candidates for drug repositioning in psychiatry. *Nature Neuroscience*, *20*(10). https://doi.org/10.1038/nn.4618

Søgaard, A. J., Selmer, R., Bjertness, E., & Thelle, D. (2004). The Oslo Health Study: The impact of self-selection in a large, population-based survey. *International Journal for Equity in Health*, *3*. https://doi.org/10.1186/1475-9276-3-3

Solberg, B. S., Zayats, T., Posserud, M. B., Halmøy, A., Engeland, A., Haavik, J., & Klungsøyr, K. (2019). Patterns of Psychiatric Comorbidity and Genetic Correlations Provide New Insights Into Differences Between Attention-Deficit/Hyperactivity Disorder and Autism Spectrum Disorder. *Biological Psychiatry*, *86*(8). https://doi.org/10.1016/j.biopsych.2019.04.021

Soler Artigas, M., Sánchez-Mora, C., Rovira, P., Richarte, V., Garcia-Martínez, I., Pagerols, M., Demontis, D., Stringer, S., Vink, J. M., Børglum, A. D., Neale, B. M., Franke, B., Faraone, S. V., Casas, M., Ramos-Quiroga, J. A., & Ribasés, M. (2020). Attention-deficit/hyperactivity disorder and lifetime cannabis use: genetic overlap and causality. *Molecular Psychiatry*, *25*(10). https://doi.org/10.1038/s41380-018-0339-3

Spinath, F. M., Price, T. S., Dale, P. S., & Plomin, R. (2004). The genetic and environmental origins of language disability and ability. *Child Development*, *75*(2). https://doi.org/10.1111/j.1467-8624.2004.00685.x

Sroufe, L. A., & Rutter, M. (1984). The Domain of Developmental Psychopathology. *Child Development*, *55*(1). https://doi.org/10.2307/1129832

St Pourcain, B., Eaves, L. J., Ring, S. M., Fisher, S. E., Medland, S., Evans, D. M., & Davey Smith, G. (2018). Developmental Changes Within the Genetic Architecture of Social

Communication Behavior: A Multivariate Study of Genetic Variance in Unrelated Individuals. *Biological Psychiatry*, *83*(7). https://doi.org/10.1016/j.biopsych.2017.09.020

St Pourcain, B., Robinson, E. B., Anttila, V., Sullivan, B. B., Maller, J., Golding, J., Skuse, D., Ring, S., Evans, D. M., & Zammit, S. (2018). ASD and schizophrenia show distinct developmental profiles in common genetic overlap with population-based social communication difficulties. *Molecular Psychiatry*, *23*(2), 263–270.

St Pourcain, B., Skuse, D. H., Mandy, W. P., Wang, K., Hakonarson, H., Timpson, N. J., Evans, D. M., Kemp, J. P., Ring, S. M., McArdle, W. L., Golding, J., & Smith, G. D. (2014). Variability in the common genetic architecture of social-communication spectrum phenotypes during childhood and adolescence. *Molecular Autism*, *5*(1). https://doi.org/10.1186/2040-2392-5-18

Stahl, E. A., Breen, G., Forstner, A. J., McQuillin, A., Ripke, S., Trubetskoy, V., Mattheisen, M., Wang, Y., Coleman, J. R. I., Gaspar, H. A., de Leeuw, C. A., Steinberg, S., Pavlides, J. M. W., Trzaskowski, M., Byrne, E. M., Pers, T. H., Holmans, P. A., Richards, A. L., Abbott, L., … Sklar, P. (2019). Genome-wide association study identifies 30 loci associated with bipolar disorder. *Nature Genetics*, *51*(5). https://doi.org/10.1038/s41588-019-0397-8

Steinberg, L. (2008). A social neuroscience perspective on adolescent risk-taking. *Developmental Review*, *28*(1). https://doi.org/10.1016/j.dr.2007.08.002

Stergiakouli, E., Davey Smith, G., Martin, J., Skuse, D. H., Viechtbauer, W., Ring, S. M., Ronald, A., Evans, D. E., Fisher, S. E., Thapar, A., & St Pourcain, B. (2017). Shared genetic influences between dimensional ASD and ADHD symptoms during child and adolescent development. *Molecular Autism*, *8*(1). https://doi.org/10.1186/s13229-017-0131-2

Stergiakouli, E., Martin, J., Hamshere, M. L., Langley, K., Evans, D. M., St Pourcain, B., Timpson, N. J., Owen, M. J., O'Donovan, M., Thapar, A., & Davey Smith, G. (2015). Shared genetic influences between attention-deficit/hyperactivity disorder (ADHD) traits in children and clinical ADHD. *Journal of the American Academy of Child and Adolescent Psychiatry*, *54*(4). https://doi.org/10.1016/j.jaac.2015.01.010

Stern, A., Agnew-Blais, J. C., Danese, A., Fisher, H. L., Matthews, T., Polanczyk, G. V., Wertz, J., & Arseneault, L. (2020). Associations between ADHD and emotional problems from childhood to young adulthood: a longitudinal genetically sensitive study. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *61*(11). https://doi.org/10.1111/jcpp.13217

Sterne, J. A. C., Egger, M., Rothstein, H. R., Sutton, A. J., & Borenstein, M. (2005). Publication bias in meta-analysis: prevention, assessment and adjustments. *Regression Methods to Detect Publication and Other Bias in Meta-analysis: John Wiley & Sons, Ltd*.

Stevenson, J. (1992). Evidence for a genetic etiology in hyperactivity in children. *Behavior Genetics*, *22*(3). https://doi.org/10.1007/BF01066665

Stevenson, J., Pennington, B. F., Gilger, J. W., DeFries, J. C., & Gillis, J. J. (1993). Hyperactivity and Spelling Disability: Testing for Shared Genetic Aetiology. *Journal of Child Psychology and Psychiatry*, *34*(7). https://doi.org/10.1111/j.1469-7610.1993.tb01779.x

Svensson, K., Ramírez, O. F., Peres, F., Barnett, M., & Claudio, L. (2012). Socioeconomic determinants associated with willingness to participate in medical research among a diverse population. *Contemporary Clinical Trials*, *33*(6). https://doi.org/10.1016/j.cct.2012.07.014

Swagerman, S. C., van Bergen, E., Dolan, C., de Geus, E. J. C., Koenis, M. M. G., Hulshoff Pol, H. E., & Boomsma, D. I. (2017). Genetic transmission of reading ability. *Brain and Language*, *172*. https://doi.org/10.1016/j.bandl.2015.07.008

Swanson, J. M., Schuck, S., Porter, M. M., Carlson, C., Hartman, C. A., Sergeant, J. A., Clevenger, W., Wasdell, M., McCleary, R., Lakes, K., & Wigal, T. (2012). Categorical and Dimensional Definitions and Evaluations of Symptoms of ADHD: History of the SNAP and the SWAN Rating Scales. *The International Journal of Educational and Psychological Assessment*, *10*(1).

Taniai, H., Nishiyama, T., Miyachi, T., Imaeda, M., & Sumi, S. (2008). Genetic influences on the broad spectrum of autism: Study of proband-ascertained twins. *American Journal of Medical Genetics, Part B: Neuropsychiatric Genetics*, *147*(6). https://doi.org/10.1002/ajmg.b.30740

Taylor, J., Allan, N., Mikolajewski, A. J., & Hart, S. A. (2013). Common genetic and nonshared environmental factors contribute to the association between socioemotional dispositions and the externalizing factor in children. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *54*(1). https://doi.org/10.1111/j.1469-7610.2012.02621.x

Taylor, J., Erbeli, F., Hart, S. A., & Johnson, W. (2020). Early classroom reading gains moderate shared environmental influences on reading comprehension in adolescence. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *61*(6). https://doi.org/10.1111/jcpp.13134

Taylor, J., & Schatschneider, C. (2010). Genetic influence on literacy constructs in kindergarten and first grade: Evidence from a diverse twin sample. *Behavior Genetics*, *40*(5). https://doi.org/10.1007/s10519-010-9368-7

Taylor, L. J., Maybery, M. T., Grayndler, L., & Whitehouse, A. J. O. (2014). Evidence for distinct cognitive profiles in autism spectrum disorders and specific language impairment. *Journal of Autism and Developmental Disorders*, *44*(1). https://doi.org/10.1007/s10803-013-1847-2

Taylor, M. J., Charman, T., Robinson, E. B., Hayiou-Thomas, M. E., Happé, F., Dale, P. S., & Ronald, A. (2014). Language and traits of autism spectrum conditions: Evidence of limited

phenotypic and etiological overlap. *American Journal of Medical Genetics, Part B: Neuropsychiatric Genetics*, *165*(7). https://doi.org/10.1002/ajmg.b.32262

Taylor, M. J., Charman, T., Robinson, E. B., Plomin, R., Happé, F., Asherson, P., & Ronald, A. (2013). Developmental associations between traits of autism spectrum disorder and attention deficit hyperactivity disorder: a genetically informative, longitudinal twin study. *Psychological Medicine*, *43*(8). https://doi.org/10.1017/S003329171200253X

Taylor, M. J., Charman, T., & Ronald, A. (2015). Where are the strongest associations between autistic traits and traits of ADHD? Evidence from a community-based twin study. *European Child & Adolescent Psychiatry*, *24*, 1129–1138.

Taylor, M. J., Gillberg, C., Lichtenstein, P., & Lundström, S. (2017). Etiological influences on the stability of autistic traits from childhood to early adulthood: Evidence from a twin study. *Molecular Autism*, *8*(1). https://doi.org/10.1186/s13229-017-0120-5

Taylor, M. J., Gustafsson, P., Larsson, H., Gillberg, C., Lundström, S., & Lichstenstein, P. (2018). Examining the Association Between Autistic Traits and Atypical Sensory Reactivity: A Twin Study. *Journal of the American Academy of Child and Adolescent Psychiatry*, *57*(2). https://doi.org/10.1016/j.jaac.2017.11.019

Taylor, M. J., Martin, J., Lu, Y., Brikell, I., Lundström, S., Larsson, H., & Lichtenstein, P. (2019a). Association of Genetic Risk Factors for Psychiatric Disorders and Traits of These Disorders in a Swedish Population Twin Sample. *JAMA Psychiatry*, *76*(3). https://doi.org/10.1001/jamapsychiatry.2018.3652

Taylor, M. J., Martin, J., Lu, Y., Brikell, I., Lundström, S., Larsson, H., & Lichtenstein, P. (2019b). Association of genetic risk factors for psychiatric disorders and traits of these disorders in a Swedish population twin sample. *JAMA Psychiatry*, *76*(3), 280–289.

Taylor, M. J., Rosenqvist, M. A., Larsson, H., Gillberg, C., D'Onofrio, B. M., Lichtenstein, P., & Lundström, S. (2020). Etiology of autism spectrum disorders and autistic traits over time. *JAMA Psychiatry*, *77*(9). https://doi.org/10.1001/jamapsychiatry.2020.0680

Thapar, A., Harrington, R., & McGuffin, P. (2001). Examining the comorbidity of ADHD-related behaviours and conduct problems using a twin study design. *British Journal of Psychiatry*, *179*(SEPT.). https://doi.org/10.1192/bjp.179.3.224

Thapar, A., Harrington, R., Ross, K., & Mcguffin, P. (2000). Does the definition of ADHD affect heritability? *Journal of the American Academy of Child and Adolescent Psychiatry*, *39*(12). https://doi.org/10.1097/00004583-200012000-00015

Thapar, A., Hervas, A., & McGuffin, P. (1995). Childhood hyperactivity scores are highly heritable and show sibling competition effects: Twin study evidence. *Behavior Genetics*, *25*(6). https://doi.org/10.1007/BF02327577

Thapar, A., Pine, D. S., Leckman, J. F., Scott, S., Snowling, M. J., & Taylor, E. (2015). Rutter's Child and Adolescent Psychiatry: Sixth Edition. In *Rutter's Child and Adolescent Psychiatry: Sixth Edition*. https://doi.org/10.1002/9781118381953

Thorell, L. B., & Wåhlstedt, C. (2006). Executive functioning deficits in relation to symptoms of ADHD and/or ODD in preschool children. *Infant and Child Development*, *15*(5). https://doi.org/10.1002/icd.475

Tick, B., Bolton, P., Happé, F., Rutter, M., & Rijsdijk, F. (2016). Heritability of autism spectrum disorders: A meta-analysis of twin studies. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *57*(5). https://doi.org/10.1111/jcpp.12499

Tielbeek, J. J., Uffelmann, E., Williams, B. S., Colodro-Conde, L., Gagnon, É., Mallard, T. T., Levitt, B. E., Jansen, P. R., Johansson, A., Sallis, H. M., Pistis, G., Saunders, G. R. B., Allegrini, A. G., Rimfeld, K., Konte, B., Klein, M., Hartmann, A. M., Salvatore, J. E., Nolte, I. M., … Posthuma, D. (2022). Uncovering the genetic architecture of broad antisocial behavior through a genome-wide association study meta-analysis. *Molecular Psychiatry*, *27*(11). https://doi.org/10.1038/s41380-022-01793-3

Tikhodeyev, O. N., & Shcherbakova, O. V. (2019). The Problem of Non-Shared Environment in Behavioral Genetics. In *Behavior Genetics* (Vol. 49, Issue 3). https://doi.org/10.1007/s10519-019-09950-1

Tolonen, H., Helakorpi, S., Talala, K., Helasoja, V., Martelin, T., & Prättälä, R. (2006). 25-Year trends and socio-demographic differences in response rates: Finnish adult health behaviour survey. *European Journal of Epidemiology*, *21*(6). https://doi.org/10.1007/s10654-006-9019-8

Tomblin, J. B., & Buckwalter, P. R. (1998). Heritability of poor language achievement among twins. *Journal of Speech, Language, and Hearing Research*, *41*(1). https://doi.org/10.1044/jslhr.4101.188

Tosto, M. G., Garon-Carrier, G., Gross, S., Petrill, S. A., Malykh, S., Malki, K., Hart, S. A., Thompson, L., Karadaghi, R. L., Yakovlev, N., Tikhomirova, T., Opfer, J. E., Mazzocco, M. M. M., Dionne, G., Brendgen, M., Vitaro, F., Tremblay, R. E., Boivin, M., & Kovas, Y. (2019). The nature of the association between number line and mathematical performance: An international twin study. *British Journal of Educational Psychology*, *89*(4). https://doi.org/10.1111/bjep.12259

Tosto, M. G., Hayiou-Thomas, M. E., Harlaar, N., Prom-Wormley, E., Dale, P. S., & Plomin, R. (2017). The genetic architecture of oral language, reading fluency, and reading comprehension: A twin study from 7 to 16 years. *Developmental Psychology*, *53*(6). https://doi.org/10.1037/dev0000297

Tosto, M. G., Malykh, S., Voronin, I., Plomin, R., & Kovas, Y. (2013). The Etiology of Individual Differences in Maths beyond IQ: Insights from 12-year Old Twins. *Procedia - Social and Behavioral Sciences*, *86*. https://doi.org/10.1016/j.sbspro.2013.08.592

Tosto, M. G., Petrill, S. A., Halberda, J., Trzaskowski, M., Tikhomirova, T. N., Bogdanova, O. Y., Ly, R., Wilmer, J. B., Naiman, D. Q., Germine, L., Plomin, R., & Kovas, Y. (2014). Why do we differ in number sense? Evidence from a genetically sensitive investigation. *Intelligence*, *43*(1). https://doi.org/10.1016/j.intell.2013.12.007

Towers, H., Sports, E., Neiderhiser, J. M., Plomin, R., Hetherington, E. M., & Reiss, D. (2000). Genetic and environmental influences on teacher ratings of the Child Behavior Checklist. *International Journal of Behavioral Development*, *24*(3). https://doi.org/10.1080/01650250050118367

Trubetskoy, V., Pardiñas, A. F., Qi, T., Panagiotaropoulou, G., Awasthi, S., Bigdeli, T. B., Bryois, J., Chen, C. Y., Dennison, C. A., Hall, L. S., Lam, M., Watanabe, K., Frei, O., Ge, T., Harwood, J. C., Koopmans, F., Magnusson, S., Richards, A. L., Sidorenko, J., … van Os, J. (2022). Mapping genomic loci implicates genes and synaptic biology in schizophrenia. *Nature*, *604*(7906). https://doi.org/10.1038/s41586-022-04434-5

Trzaskowski, M., Dale, P. S., & Plomin, R. (2013). No genetic influence for childhood behavior problems from DNA analysis. *Journal of the American Academy of Child and Adolescent Psychiatry*, *52*(10). https://doi.org/10.1016/j.jaac.2013.07.016

Trzaskowski, M., Davis, O. S. P., Defries, J. C., Yang, J., Visscher, P. M., & Plomin, R. (2013). DNA evidence for strong genome-wide pleiotropy of cognitive and learning abilities. *Behavior Genetics*, *43*(4). https://doi.org/10.1007/s10519-013-9594-x

Turkheimer, E. (2011). Still Missing. *Research in Human Development*, *8*(3–4). https://doi.org/10.1080/15427609.2011.625321

Turkheimer, E. (2012). Genome Wide Association Studies of Behavior are Social Science. In *Boston Studies in the Philosophy and History of Science* (Vol. 282). https://doi.org/10.1007/978-94-007-1951-4_3

Turkheimer, E., & Waldron, M. (2000). Nonshared environment: A theoretical, methodological, and quantitative review. *Psychological Bulletin*, *126*(1). https://doi.org/10.1037/0033-2909.126.1.78

Tuvblad, C., Zheng, M., Raine, A., & Baker, L. A. (2009). A common genetic factor explains the covariation among ADHD ODD and CD symptoms in 9-10 year old boys and girls. *Journal of Abnormal Child Psychology*, *37*(2). https://doi.org/10.1007/s10802-008-9278-9

Tye, C., Rijsdijk, F., Greven, C. U., Kuntsi, J., Asherson, P., & McLoughlin, G. (2012). Shared genetic influences on ADHD symptoms and very low-frequency EEG activity: A twin study. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *53*(6). https://doi.org/10.1111/j.1469-7610.2011.02501.x

Valentine, A. Z., Brown, B. J., Groom, M. J., Young, E., Hollis, C., & Hall, C. L. (2020). A systematic review evaluating the implementation of technologies to assess, monitor and treat neurodevelopmental disorders: A map of the current evidence. In *Clinical Psychology Review* (Vol. 80). https://doi.org/10.1016/j.cpr.2020.101870

Valentine, A. Z., Hall, S. S., Young, E., Brown, B. J., Groom, M. J., Hollis, C., & Hall, C. L. (2021). Implementation of telehealth services to assess, monitor, and treat neurodevelopmental disorders: Systematic review. In *Journal of Medical Internet Research* (Vol. 23, Issue 1). https://doi.org/10.2196/22619

Van Beijsterveldt, C. E. M., Felsenfeld, S., & Boomsma, D. I. (2010). Bivariate genetic analyses of stuttering and nonfluency in a large sample of 5-year-old twins. *Journal of Speech, Language, and Hearing Research*, *53*(3). https://doi.org/10.1044/1092-4388(2009/08-0202)

Van Beijsterveldt, C. E. M., Verhulst, F. C., Molenaar, P. C. M., & Boomsma, D. I. (2004). The Genetic Basis of Problem Behavior in 5-Year-Old Dutch Twin Pairs. *Behavior Genetics*, *34*(3). https://doi.org/10.1023/B:BEGE.0000017869.30151.fd

Vendlinski, M. K., Javaras, K. N., Van Hulle, C. A., Lemery-Chalfant, K., Maier, R., Davidson, R. J., & Goldsmith, H. H. (2014). Relative influence of genetics and shared environment on child mental health symptoms depends on comorbidity. *PLoS ONE*, *9*(7). https://doi.org/10.1371/journal.pone.0103080

Verhoef, E., Shapland, C. Y., Fisher, S. E., Dale, P. S., & St Pourcain, B. (2021). The developmental origins of genetic factors influencing language and literacy: Associations with early-childhood vocabulary. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *62*(6). https://doi.org/10.1111/jcpp.13327

Viding, E., Fontaine, N. M. G., Oliver, B. R., & Plomin, R. (2009). Negative parental discipline, conduct problems and callous-unemotional traits: Monozygotic twin differences study. *British Journal of Psychiatry*, *195*(5). https://doi.org/10.1192/bjp.bp.108.061192

Viding, E., Larsson, H., & Jones, A. P. (2008). Review. Quantitative genetic studies of antisocial behaviour. In *Philosophical Transactions of the Royal Society B: Biological Sciences* (Vol. 363, Issue 1503). https://doi.org/10.1098/rstb.2008.0037

Viding, E., & McCrory, E. (2020). Disruptive Behavior Disorders: The Challenge of Delineating Mechanisms in the Face of Heterogeneity. In *American Journal of Psychiatry* (Vol. 177, Issue 9). https://doi.org/10.1176/appi.ajp.2020.20070998

Viding, E., Spinath, F. M., Price, T. S., Bishop, D. V. M., Dale, P. S., & Plomin, R. (2004). Genetic and environmental influence on language impairment in 4-year-old same-sex and opposite-sex twins. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *45*(2). https://doi.org/10.1111/j.1469-7610.2004.00223.x

Viechtbauer, W. (2010). metafor: Meta-Analysis Package for R. *Journal of Statistical Software*, *36*(3).

Viechtbauer, W., & Cheung, M. W. L. (2010). Outlier and influence diagnostics for meta-analysis. *Research Synthesis Methods*, *1*(2). https://doi.org/10.1002/jrsm.11

Vierikko, E., Pulkkinen, L., Kaprio, J., & Rose, R. J. (2004). Genetic and environmental influences on the relationship between aggression and hyperactivity-impulsivity as rated by teachers and parents. In *Twin Research* (Vol. 7, Issue 3). https://doi.org/10.1375/136905204774200541

Vilhjálmsson, B. J., Yang, J., Finucane, H. K., Gusev, A., Lindström, S., Ripke, S., Genovese, G., Loh, P. R., Bhatia, G., Do, R., Hayeck, T., Won, H. H., Neale, B. M., Corvin, A., Walters, J. T. R., Farh, K. H., Holmans, P. A., Lee, P., Bulik-Sullivan, B., … Price, A. L. (2015a). Modeling Linkage Disequilibrium Increases Accuracy of Polygenic Risk Scores. *American Journal of Human Genetics*, *97*(4). https://doi.org/10.1016/j.ajhg.2015.09.001

Vilhjálmsson, B. J., Yang, J., Finucane, H. K., Gusev, A., Lindström, S., Ripke, S., Genovese, G., Loh, P. R., Bhatia, G., Do, R., Hayeck, T., Won, H. H., Ripke, S., Neale, B. M., Corvin, A., Walters, J. T. R., Farh, K. H., Holmans, P. A., Lee, P., … Price, A. L. (2015b). Modeling linkage disequilibrium increases accuracy of polygenic risk scores. *American Journal of Human Genetics*, *97*(4), 576–592. https://doi.org/10.1016/j.ajhg.2015.09.001

Visscher, P. M., & Goddard, M. E. (2019). From RA Fisher's 1918 paper to GWAS a century later. *Genetics*, *211*(4), 1125–1130.

Visscher, P. M., Wray, N. R., Zhang, Q., Sklar, P., McCarthy, M. I., Brown, M. A., & Yang, J. (2017). 10 Years of GWAS Discovery: Biology, Function, and Translation. In *American Journal of Human Genetics* (Vol. 101, Issue 1). https://doi.org/10.1016/j.ajhg.2017.06.005

Visscher, P. M., Yengo, L., Cox, N. J., & Wray, N. R. (2021). Discovery and implications of polygenicity of common diseases. In *Science* (Vol. 373, Issue 6562). https://doi.org/10.1126/science.abi8206

Vitaro, F., Brendgen, M., & Arseneault, L. (2009). The discordant MZ-twin method: One step closer to the holy grail of causality. *International Journal of Behavioral Development*, *33*(4). https://doi.org/10.1177/0165025409340805

Vo, C. Q., Samuelsen, P. J., Sommerseth, H. L., Wisløff, T., Wilsgaard, T., & Eggen, A. E. (2023). Comparing the sociodemographic characteristics of participants and non-participants in the population-based Tromsø Study. *BMC Public Health*, *23*(1). https://doi.org/10.1186/s12889-023-15928-w

von Stumm, S., & d'Apice, K. (2022). From Genome-Wide to Environment-Wide: Capturing the Environome. *Perspectives on Psychological Science*, *17*(1). https://doi.org/10.1177/1745691620979803

Wadsworth, S. J., DeFries, J. C., Willcutt, E. G., Pennington, B. F., & Olson, R. K. (2015). The Colorado Longitudinal Twin Study of Reading Difficulties and ADHD: Etiologies of Comorbidity and Stability. *Twin Research and Human Genetics*, *18*(6). https://doi.org/10.1017/thg.2015.66

Wadsworth, S. J., Defries, J. C., Willcutt, E. G., Pennington, B. F., & Olson, R. K. (2016). Genetic Etiologies of Comorbidity and Stability for Reading Difficulties and ADHD: A Replication Study. *Twin Research and Human Genetics*, *19*(6). https://doi.org/10.1017/thg.2016.80

Wadsworth, S. J., Olson, R. K., & Defries, J. C. (2010). Differential genetic etiology of reading difficulties as a function of IQ: An Update. *Behavior Genetics*, *40*(6). https://doi.org/10.1007/s10519-010-9349-x

Wadsworth, S. J., Olson, R. K., Pennington, B. F., & DeFries, J. C. (2000). Differential genetic etiology of reading disability as a function of IQ. *Journal of Learning Disabilities*, *33*(2). https://doi.org/10.1177/002221940003300207

Wadsworth, S. J., Olson, R. K., Willcutt, E. G., & Defries, J. C. (2012). Multiple regression analysis of reading performance data from twin pairs with reading difficulties and nontwin siblings: The augmented model. *Twin Research and Human Genetics*, *15*(1). https://doi.org/10.1375/twin.15.1.116

Wahl, O. F. (1987). Public vs. professional conceptions of schizophrenia. *Journal of Community Psychology*, *15*(2), 285–291.

Wainschtein, P., Jain, D., Zheng, Z., Aslibekyan, S., Becker, D., Bi, W., Brody, J., Carlson, J. C., Correa, A., Du, M. M., Fernandez-Rhodes, L., Ferrier, K. R., Graff, M., Guo, X., He, J.,

Heard-Costa, N. L., Highland, H. M., Hirschhorn, J. N., Howard-Claudio, C. M., … Visscher, P. M. (2022). Assessing the contribution of rare variants to complex trait heritability from whole-genome sequence data. *Nature Genetics*, *54*(3). https://doi.org/10.1038/s41588-021-00997-7

Walters, R. K., Polimanti, R., Johnson, E. C., McClintick, J. N., Adams, M. J., Adkins, A. E., Aliev, F., Bacanu, S. A., Batzler, A., Bertelsen, S., Biernacka, J. M., Bigdeli, T. B., Chen, L. S., Clarke, T. K., Chou, Y. L., Degenhardt, F., Docherty, A. R., Edwards, A. C., Fontanillas, P., … Agrawal, A. (2018). Transancestral GWAS of alcohol dependence reveals common genetic underpinnings with psychiatric disorders. *Nature Neuroscience*, *21*(12). https://doi.org/10.1038/s41593-018-0275-1

Warrier, V., & Baron-Cohen, S. (2018). Genetic contribution to "theory of mind" in adolescence. *Scientific Reports*, *8*(1). https://doi.org/10.1038/s41598-018-21737-8

Waszczuk, M. A., Zavos, H. M. S., & Eley, T. C. (2021). Why do depression, conduct, and hyperactivity symptoms co-occur across adolescence? The role of stable and dynamic genetic and environmental influences. *European Child and Adolescent Psychiatry*, *30*(7). https://doi.org/10.1007/s00787-020-01515-6

Watson, H. J., Yilmaz, Z., Thornton, L. M., Hübel, C., Coleman, J. R. I., Gaspar, H. A., Bryois, J., Hinney, A., Leppä, V. M., Mattheisen, M., Medland, S. E., Ripke, S., Yao, S., Giusti-Rodríguez, P., Hanscombe, K. B., Purves, K. L., Adan, R. A. H., Alfredsson, L., Ando, T., … Bulik, C. M. (2019). Genome-wide association study identifies eight risk loci and implicates metabo-psychiatric origins for anorexia nervosa. *Nature Genetics*, *51*(8). https://doi.org/10.1038/s41588-019-0439-2

Wendler, D., Kington, R., Madans, J., Van Wye, G., Christ-Schmidt, H., Pratt, L. A., Brawley, O. W., Gross, C. P., & Emanuel, E. (2006). Are racial and ethnic minorities less willing to participate in health research? *PLoS Medicine*, *3*(2). https://doi.org/10.1371/journal.pmed.0030019

Whose genomics? (2019). In *Nature Human Behaviour* (Vol. 3, Issue 5). https://doi.org/10.1038/s41562-019-0619-1

Willcutt, E. G., Betjemann, R. S., McGrath, L. M., Chhabildas, N. A., Olson, R. K., DeFries, J. C., & Pennington, B. F. (2010). Etiology and neuropsychology of comorbidity between RD and ADHD: The case for multiple-deficit models. *Cortex*, *46*(10). https://doi.org/10.1016/j.cortex.2010.06.009

Willcutt, E. G., McGrath, L. M., Pennington, B. F., Keenan, J. M., DeFries, J. C., Olson, R. K., & Wadsworth, S. J. (2019). Understanding Comorbidity Between Specific Learning

Disabilities. In *New Directions for Child and Adolescent Development* (Vol. 2019, Issue 165). https://doi.org/10.1002/cad.20291

Willcutt, E. G., Pennington, B. F., & DeFries, J. C. (2000a). Etiology of inattention and hyperactivity/impulsivity in a community sample of twins with learning difficulties. *Journal of Abnormal Child Psychology*, *28*(2). https://doi.org/10.1023/A:1005170730653

Willcutt, E. G., Pennington, B. F., & DeFries, J. C. (2000b). Twin study of the etiology of comorbidity between reading disability and attention-deficit/hyperactivity disorder. *American Journal of Medical Genetics - Neuropsychiatric Genetics*, *96*(3). https://doi.org/10.1002/1096-8628(20000612)96:3<293::AID-AJMG12>3.0.CO;2-C

Willcutt, E. G., Pennington, B. F., Olson, R. K., & DeFries, J. C. (2007). Understanding comorbidity: A twin study of reading disability and attention-deficit/hyperactivity disorder. *American Journal of Medical Genetics, Part B: Neuropsychiatric Genetics*, *144*(6). https://doi.org/10.1002/ajmg.b.30310

Wong, C. C. Y., Meaburn, E. L., Ronald, A., Price, T. S., Jeffries, A. R., Schalkwyk, L. C., Plomin, R., & Mill, J. (2014). Methylomic analysis of monozygotic twins discordant for autism spectrum disorder and related behavioural traits. *Molecular Psychiatry*, *19*(4). https://doi.org/10.1038/mp.2013.41

Wong, S. W. L., Chow, B. W.-Y., Ho, C. S.-H., Waye, M. M. Y., & Bishop, D. V. M. (2014). Genetic and environmental overlap between Chinese and English reading-related skills in Chinese children. *Developmental Psychology*, *50*(11), 2539.

Wood, A. C., Kuntsi, J., Asherson, P., & Saudino, K. J. (2008). Actigraph data are reliable, with functional reliability increasing with aggregation. *Behavior Research Methods*, *40*(3). https://doi.org/10.3758/BRM.40.3.873

Wood, A. C., Rijsdijk, F., Asherson, P., & Kuntsi, J. (2009). Hyperactive-impulsive symptom scores and oppositional behaviours reflect alternate manifestations of a single liability. *Behavior Genetics*, *39*(5). https://doi.org/10.1007/s10519-009-9290-z

Wood, A. C., Rijsdijk, F., Asherson, P., & Kuntsi, J. (2011). Inferring causation from cross-sectional data: Examination of the causal relationship between hyperactivity-impulsivity and novelty seeking. *Frontiers in Genetics*, *2*(MAR). https://doi.org/10.3389/fgene.2011.00006

Woodward, L. J., & Fergusson, D. M. (2001). Life course outcomes of young people with anxiety disorders in adolescence. *Journal of the American Academy of Child and Adolescent Psychiatry*, *40*(9). https://doi.org/10.1097/00004583-200109000-00018

Wray, N. R., Lin, T., Austin, J., McGrath, J. J., Hickie, I. B., Murray, G. K., & Visscher, P. M. (2021). From Basic Science to Clinical Application of Polygenic Risk Scores: A Primer. In *JAMA Psychiatry* (Vol. 78, Issue 1). https://doi.org/10.1001/jamapsychiatry.2020.3049

Wray, N. R., Ripke, S., Mattheisen, M., Trzaskowski, M., Byrne, E. M., Abdellaoui, A., Adams, M. J., Agerbo, E., Air, T. M., Andlauer, T. M. F., Bacanu, S. A., Bækvad-Hansen, M., Beekman, A. F. T., Bigdeli, T. B., Binder, E. B., Blackwood, D. R. H., Bryois, J., Buttenschøn, H. N., Bybjerg-Grauholm, J., … Sullivan, P. F. (2018). Genome-wide association analyses identify 44 risk variants and refine the genetic architecture of major depression. *Nature Genetics*, *50*(5). https://doi.org/10.1038/s41588-018-0090-3

Wright, J., Small, N., Raynor, P., Tuffnell, D., Bhopal, R., Cameron, N., Fairley, L., A Lawlor, D., Parslow, R., Petherick, E. S., Pickett, K. E., Waiblinger, D., & West, J. (2013). Cohort profile: The born in bradford multi-ethnic family cohort study. *International Journal of Epidemiology*, *42*(4). https://doi.org/10.1093/ije/dys112

Yang, J., Lee, S. H., Goddard, M. E., & Visscher, P. M. (2011). GCTA: A tool for genome-wide complex trait analysis. *American Journal of Human Genetics*, *88*(1). https://doi.org/10.1016/j.ajhg.2010.11.011

Yang, J., Zeng, J., Goddard, M. E., Wray, N. R., & Visscher, P. M. (2017). Concepts, estimation and interpretation of SNP-based heritability. In *Nature Genetics* (Vol. 49, Issue 9). https://doi.org/10.1038/ng.3941

Yang, Z., Wu, H., Lee, P. H., Tsetsos, F., Davis, L. K., Yu, D., Lee, S. H., Dalsgaard, S., Haavik, J., Barta, C., Zayats, T., Eapen, V., Wray, N. R., Devlin, B., Daly, M., Neale, B., Børglum, A. D., Crowley, J. J., Scharf, J., … Paschou, P. (2021). Investigating Shared Genetic Basis Across Tourette Syndrome and Comorbid Neurodevelopmental Disorders Along the Impulsivity-Compulsivity Spectrum. *Biological Psychiatry*, *90*(5). https://doi.org/10.1016/j.biopsych.2020.12.028

Yarkoni, T., & Westfall, J. (2017). Choosing Prediction Over Explanation in Psychology: Lessons From Machine Learning. *Perspectives on Psychological Science*, *12*(6). https://doi.org/10.1177/1745691617693393

Yengo, L., Vedantam, S., Marouli, E., Sidorenko, J., Bartell, E., Sakaue, S., Graff, M., Eliasen, A. U., Jiang, Y., Raghavan, S., Miao, J., Arias, J. D., Graham, S. E., Mukamel, R. E., Spracklen, C. N., Yin, X., Chen, S. H., Ferreira, T., Highland, H. H., … Hirschhorn, J. N. (2022). A saturated map of common genetic variants associated with human height. *Nature*, *610*(7933). https://doi.org/10.1038/s41586-022-05275-y

Yip, B. H. K., Bai, D., Mahjani, B., Klei, L., Pawitan, Y., Hultman, C. M., Grice, D. E., Roeder, K., Buxbaum, J. D., Devlin, B., Reichenberg, A., & Sandin, S. (2018). Heritable Variation, With Little or No Maternal Effect, Accounts for Recurrence Risk to Autism Spectrum Disorder in Sweden. *Biological Psychiatry*, *83*(7). https://doi.org/10.1016/j.biopsych.2017.09.007

Yu, D., Sul, J. H., Tsetsos, F., Nawaz, M. S., Huang, A. Y., Zelaya, I., Illmann, C., Osiecki, L., Darrow, S. M., Hirschtritt, M. E., Greenberg, E., Muller-Vahl, K. R., Stuhrmann, M., Dion, Y., Rouleau, G. A., Aschauer, H., Stamenkovic, M., Schlögelhofer, M., Sandor, P., … Worbe, Y. (2019). Interrogating the genetic determinants of Tourette's syndrome and other tiC disorders through genome-wide association studies. *American Journal of Psychiatry*, *176*(3). https://doi.org/10.1176/appi.ajp.2018.18070857

Zeng, J., De Vlaming, R., Wu, Y., Robinson, M. R., Lloyd-Jones, L. R., Yengo, L., Yap, C. X., Xue, A., Sidorenko, J., McRae, A. F., Powell, J. E., Montgomery, G. W., Metspalu, A., Esko, T., Gibson, G., Wray, N. R., Visscher, P. M., & Yang, J. (2018). Signatures of negative selection in the genetic architecture of human complex traits. *Nature Genetics*, *50*(5). https://doi.org/10.1038/s41588-018-0101-4

Zheng, Y., Pingault, J. B., Unger, J. B., & Rijsdijk, F. (2020). Genetic and environmental influences on attention-deficit/hyperactivity disorder symptoms in Chinese adolescents: a longitudinal twin study. *European Child and Adolescent Psychiatry*, *29*(2). https://doi.org/10.1007/s00787-019-01346-0

Zou, H., & Hastie, T. (2005). Regularization and variable selection via the elastic net. *Journal of the Royal Statistical Society. Series B: Statistical Methodology*, *67*(2). https://doi.org/10.1111/j.1467-9868.2005.00503.x

Zumberge, A., Baker, L. A., & Manis, F. R. (2007). Focus on words: A twin study of reading and inattention. *Behavior Genetics*, *37*(2). https://doi.org/10.1007/s10519-006-9134-z

Zwicker, J. G., Missiuna, C., Harris, S. R., & Boyd, L. A. (2012). Developmental coordination disorder: A review and update. In *European Journal of Paediatric Neurology* (Vol. 16, Issue 6). https://doi.org/10.1016/j.ejpn.2012.05.005

# Appendices

## Appendix 1

## Supplementary Notes

Supplementary Note 1: Meta-analytic results for shared and nonshared environmental factors.

*Shared and nonshared environmental influences on NDDs*

*Shared environment ($c^2$)*

We identified 127 studies that reported information on shared environmental influences on NDDs, only a little over half (53.6%) of all studies that reported on $h^2$ also reported on $c^2$. Out of the total 127 studies, 65 studies focused on specific learning disorders, 48 on ADHD, 15 on communication disorders, 14 on ASD, 3 on motor disorders, and 0 studies included $c^2$ estimates for intellectual disabilities, the only two studies that had examined the aetiology of intellectual disabilities had reported a model only including genetic and nonshared environmental factors (AE) as the best fitting model (see Method and Supplementary Note 3). The contribution of shared environmental influences to all NDD categories was modest ($c^2$ = 0.17, SE= 0.02), ranging from weak ($c^2$ = 0.10, SE= 0.02) for ADHD to moderate ($c^2$ = 0.36, SE= 0.06) for communication disorders (Figure 2. 3 in the main text and Supplementary Table 1).

*Nonshared environment ($e^2$)*

We identified 195 family-based studies (82.2% of the total) that reported on the nonshared environmental contribution to NDDs, out of which 107 studies focused on ADHD, 67 on specific learning disorders, 28 on ASD, 18 on communication disorders, 6 on motor disorders and 2 studies on intellectual disabilities. Nonshared environmental influences on all NDDs were moderate ($e^2$ = 0.29, SE= 0.02), but ranged from weak ($e^2$ = 0.10, SE= 0.16) for intellectual disabilities to moderate ($e^2$ = 0.38, SE= 0.11) for motor disorders. Nonshared environmental estimates did not differ significantly across all NDDs (Figure 2. 3 in the main text and Supplementary Table 1).

*Shared and nonshared environmental overlap between NDDs*

*Shared environmental correlations (rC)*

Since several studies only reported the most parsimonious, best-fitting, model (see Supplementary Note 3), meta-analytic estimates of rC could be derived from 16 studies (43.2% of the total number; Supplementary Table 3). A first meta-analysis of all NDD categories jointly, yielded a significant and substantial grand estimate for the shared environmental co-occurrence between different NDDs (rC= 0.63, SE= 0.32), although estimates varied substantially between studies, as indicated by the large meta-analytic standard error.

*Nonshared environmental correlations (rE)*

A total of 22 studies (59.5%) reported on the nonshared environmental co-occurrence between NDDs, this was largely due to the fact that different studies adopted different family-based designs, some of which do not provide nonshared environmental estimates[1] (see Supplementary Note 3). The grand estimate for the transdiagnostic rE was 0.17, SE= 0.5. When we considered NDD categories separately, nonshared environmental correlations could only be estimated between ASD & ADHD (5 studies, rE = 0.22, SE= 0.13), and between ADHD & specific learning disorders (9 studies, rE = 0.11, SE= 0.05; Figure 2. 4 in the main text and Supplementary Table 3)

*Shared and nonshared environmental overlap between NDDs and DICCs*

*Shared environmental correlations (rC)*

Out of 15 studies that reported genetic correlations between NDDs and DICCs, 11 also reported shared environmental correlations (73.3%). These included 4 studies looking at the co-occurrence between ADHD & oppositional defiant disorder, 3 studies looking at the co-occurrence between ADHD & conduct disorder, and 3 studies looking at the co-occurrence between ASD & conduct disorder. A strong meta-analytic shared environmental correlation was found between all NDDs and DICCs (0.88, SE= 0.34). The grand shared environmental overlap was consistently estimated as very high for all co-occurring disorders for which we identified sufficient studies: rC= 0.96 (SE= 0.57) between ADHD & oppositional defiant disorder, rC= 0.94 (SE= 0.71) between ADHD & conduct disorder, and rC= 0.88 (SE= 0.57) between ASD & conduct disorder (Figure 2. 4 in the main text and Supplementary Table 5).

*Nonshared environmental correlations (rE)*

Thirteen out of 15 studies that reported on the genetic overlap between NDDs and DICCs also reported nonshared environmental correlations (86.7%). These 13 studies consisted of 5 studies targeting the co-occurrence between ADHD & conduct disorder, 5 studies that between ADHD & oppositional defiant disorder, and 3 studies the co-occurrence between ASD & conduct disorder. The nonshared environmental overlap across all NDD and DICC pairs was moderate (rE = 0.39, SE= 0.14), but differed between specific pairs of disorders. The strongest correlation (rE = 0.54, SE= 0.25) was found between ADHD & oppositional defiant disorder and was markedly higher if compared to the overlap between ADHD & conduct disorder (rE = 0.11, SE= 0.08) and between ASD & conduct disorder (0.07, SE= 0.08) (Figure 2. 4 in the main text and Supplementary Table 5).

*Sex differences*

*Sex differences in environmental aetiology of NDDs*

Across all NDDs, family-based shared and nonshared environmental influences were not significantly different between males ($c^2$= 0.35, SE= 0.09; $e^2$= 0.31, SE= 0.05) and females ($c^2$= 0.28, SE= 0.08; $e^2$= 0.33, SE= 0.04). Distributions of sex-specific family-based variance components for all NDDs, except for motor disorders for which a sufficient number of studies (>1) was not identified, are presented in Figure 2. 5 in the main text and Supplementary Table 16)

*Sex differences in environmental overlap between NDDs*

Sex-specific shared environmental correlations could not be estimated, whereas nonshared environmental correlations were estimated at 0.09 (SE= 0.08) in males and 0.10 (SE= 0.11) in females (Supplementary Table 17). Sex-specific grand estimates of environmental correlations between specific disorders are not reported because of the limited number of studies identified. The only exception was the co-occurrence between ASD & ADHD in males, where 2 studies were identified (rE = 0.20, SE= 0.14; Supplementary Table 17). Due to the lack of available studies, the shared environmental overlap could not be calculated.

*Sex differences in environmental overlap between NDDs and DICCs*

We could only meta-analyse the co-occurrence between ADHD & conduct disorder in females. We found a meta-analytic nonshared environmental correlation of 0.06 (SE= 0.12; Supplementary Table 18).

*Developmental trends trajectories*

*Age-related differences in environmental aetiology of NDDs*

Across all NDDs, grand shared and nonshared environmental influences were observed to decrease from childhood ($c^2$= 0.21, SE= 0.04; $e^2$= 0.27, SE= 0.03) to middle childhood ($c^2$= 0.12, SE= 0.03; $e^2$= 0.25, SE= 0.02) followed by a later increase in adolescence ($c^2$= 0.17, SE= 0.03; $e^2$= 0.36, SE= 0.03). This trend was consistent across some specific NDDs, such as ASD and ADHD, but not for others. For example, for communication disorders and specific learning disorders genetic and shared environmental variance decreased while nonshared environmental variance increased developmentally (Figure 2. 6A in the main text and Supplementary Table 19).

*Age-related differences in environmental overlap between NDDs, as well as between NDDs and DICCs*

Overall, we could not explore developmental trends in genetic and environmental correlations due to a lack of available studies, the only exceptions were grand estimates for adolescence (see Supplementary Tables 28-30).

*Categorical versus continuous measurement of NDDs*

We found no significant differences in shared and nonshared environmental influences between measurement methods (Supplementary Figure 22 and Supplementary Table 25). Furthermore, shared and nonshared environmental genetic overlap could not be compared across co-occurrences between NDDs, and between NDDs and DICCs, due to insufficient number of identified studies (Supplementary Figure 22 and Supplementary Tables 26 and 27).

*Geographical differences*

*Geographical differences in environmental aetiology of NDDs*

Grand shared environmental influences ranged between 0.30 (SE= 0.13) in Chinese cohorts and 0.07 (SE= 0.04) in Swedish cohorts (Figure 2. 7A in the main text and Supplementary Table 19), whereas nonshared environmental influences were highest in Canada (0.38, SE= 0.07), if compared to the lowest grand estimate of nonshared environmental influence (0.17, SE= 0.05) obtained for Australian cohorts (Figure 2. 7A in the main text and Supplementary Table 22).

*Geographical differences in environmental overlap between NDDs*

The highest meta-analytic estimate of shared environmental correlation was estimated in United Kingdom-based samples (0.91, SE= 0.29), while the lowest in United States-based studies (0.07, SE= 0.21; Figure 2. 7B in the main text and Supplementary Table 23). The strongest grand estimate of nonshared environmental correlation was found in Swedish samples (0.36, SE= 0.12) while the lowest in Australian samples (0.03, SE= 0.09; Figure 2. 7B in the main text and Supplementary Table 23).

*Geographical differences in environmental overlap between NDDs and DICCs*

Studies yielded consistently strong estimates of shared environmental correlation across the United Kingdom, United Stated and Sweden (0.97, SE= 0.57; 0.85, SE= 0.56; and 0.89, SE= 0.55; Supplementary Figure 28 and Supplementary Table 24). Grand nonshared environmental correlations could only be calculated for United Kingdom and United States-based studies and were estimated at 0.49 (SE= 0.44) and 0.24 (SE= 0.09), respectively (Supplementary Figure 28 and Supplementary Table 24).

*Ancestral differences*

*Ancestry-related differences in the environmental aetiology of NDDs*

Meta-analytic shared environmental influences remained relatively stable across sample ancestral composition (mean of $c^2$= 0.24) with only a slight drop observed when the sample included 100% of participants of European ancestry ($c^2$= 0.19, SE= 0.04; Supplementary Figure 27 and Supplementary Table 25). However, estimates differed for specific disorders. The decrease in shared environmental influences in fully European descent samples was especially evident for ADHD, where the estimates dropped from a mean of 0.17 for more diverse categories to 0.04 (SE= 0.09) for 100% European ancestry samples. A similar pattern was observed for specific learning disorders, with estimates dropping from a mean of 0.26 to 0.16 (SE= 0.04) (Supplementary Figure 27 and Supplementary Table 25).

All NDDs were subject to subtle changes in nonshared environmental influences depending on the ancestral composition of the samples, with the exception of motor disorders for which only studies using 100% European ancestry samples were found. Across all NDDs, the meta-analytic estimate for nonshared environmental influences decreased as the percentage of participants of European ancestry in the sample increased: from 0.44 (SE= 0.08) for samples where participants of European ancestry were in the minority, to 0.32 (SE= 0.13) for samples

where they were between 50 and 74% to 0.25 (SE =0.03) for samples between 75 and 99% European ancestry) to 0.32 (SE= 0.05) for 100% European ancestry samples. This same trend was observed for ADHD (from 0.54, SE= 0.09 to 0.39, SE= 0.06) and specific learning disorders (0.28, SE= 0.06 to 0.19, SE= 0.06, although the estimate increased again for samples 100% of European descent, 0.30, SE= 0.07; Supplementary Figure 27 and Supplementary Table 25). For communication disorders, $e^2$ increased from 0.16 (SE= 0.11) for samples 75-99% European ancestry to 0.24 (SE= 0.06) for samples where all participants were of European ancestry.

*Ancestry-related differences in environmental overlap between NDDs*

Differences in sources of co-occurrence between NDDs could not be estimated for shared and nonshared environmental overlap. Estimates for samples comprising only individuals of European ancestry are presented in Supplementary Table 26.

*Ancestry-related differences in environmental overlap between NDDs and DICCs*

We were able to estimate the meta-analytic shared environmental overlap between NDDs and DICCs, as 4 out of 5 studies reporting on genetic correlations also reported on shared environmental correlations. The grand shared environmental overlap remained stable across samples ancestral composition (0.88, SE= 0.87 and 0.89, SE= 0.85, respectively; Supplementary Table 27).

Supplementary Note 2: Meta-analytic results for NDDs phenotypic sub-categories.

Where the number of studies identified was sufficiently large, we were able to stratify sources of variance and co-occurrence by specific phenotypic sub-categories to reflect within-category differences. Supplementary Figure 2 presents family and SNP-based heritability, shared and nonshared environmental influences on sub-categories of NDDs, whereas Supplementary Figure 3 shows family-based genetic, shared and nonshared environmental overlap between sub-categories of NDDs, as well as between sub-categories of NDDs and DICCs. All estimates with standard errors are presented in Supplementary Tables 2-5.

For example, within intellectual disabilities, we estimated heritability of learning disability (0.86, SE= 0.43), which constitutes one of the sub-categories. Within communication disorders, we distinguished 5 specific phenotypes, out of which specific language impairment had the highest meta-analytic heritability (0.87, SE= 0.60), whereas the lowest grand heritability estimate was estimated for stuttering (0.58, SE= 0.17). All ADHD-related specific phenotypes were highly heritable, ranging from 0.76 (SE= 0.07) for impulsivity to 0.65 (SE= 0.05) for inattention. For ASD, the highest grand heritability was found for restrictive and repetitive behaviours and interests (0.83, SE= 0.49), whereas the lowest was found for social impairments (0.67, SE= 0.05). Within motor disorders, we identified 4 specific sub-categories. The highest grand heritability estimate was found for motor coordination (0.82, SE= 0.08) and the weakest for tic disorders (0.56, SE= 0.17).

Specific learning disorders were divided into three primary sub-categories, i.e., dyslexia, dysgraphia, and dyscalculia-related phenotypes with heritabilities ranging from 0.62 (SE= 0.04) for dyslexia (and/or the continuously measured phenotype of reading ability) to 0.56 (SE= 0.18) for dysgraphia (and/or the continuously measured phenotype of writing ability), and 0.55 (SE= 0.04) for dyscalculia (and/or the continuously measured phenotype of mathematics ability). The three subcategories of dyslexia, dysgraphia, and dyscalculia were further divided into secondary sub-categories comprising specific reading, writing and mathematics-related phenotypes. Within the dyslexia sub-category, the highest meta-analytic heritability was estimated for decoding (0.69, SE= 0.14), while the lowest for vocabulary (0.25, SE= 0.14). Within the dysgraphia-related phenotype, writing ability had a grand heritability estimate of 0.56 (SE= 0.17). Within the Dyscalculia sub-category, we identified 4

further specific phenotypes, out of which broadly defined mathematics ability was most heritable, with a meta-analytic estimate of 0.57 (SE= 0.04), with the lowest grand heritability obtained for mathematics problem solving (0.36, SE= 0.18).

Stratified estimates for specific phenotypes could also be calculated for a few homotypic and heterotypic co-occurrent disorders. The co-occurrence between ASD & ADHD was divided into 4 sub-categories, out of which the highest meta-analytic genetic correlation was obtained between broadly defined ASD & ADHD (0.71, SE= 0.27), while the lowest was estimated between restrictive and repetitive behaviours and interests & inattention (0.16, SE= 0.11; see Supplementary Table 4).

We could only distinguish only one specific phenotype sub-category for the co-occurrence between ADHD & motor disorders, namely the association between ADHD & developmental coordination disorder for which grand genetic correlation of 0.91 (SE= 0.80) was found. The co-occurrence between ADHD & specific learning disorders was stratified into 6 phenotypic sub-categories, with the overlap ranging between 0.19 (SE= 0.22) for ADHD & reading ability and -0.32 (SE= 0.11) for inattention & mathematic ability. The co-occurrence between specific language impairment and dyslexia was the only specific phenotype sub-category identified for the co-occurrence between communication disorders & specific learning disorders and yielded grand genetic overlap of 0.66 (0.15), whereas the co-occurrence between subtypes of specific learning disorders was stratified into dyslexia and dyscalculia and quantitatively measured reading ability and mathematics ability, both of which yielded comparable meta-analytic genetic overlaps: 0.56 (SE= 0.07) and 0.55 (SE= 0.08), respectively.

When considering the genetic overlap between NDDs and DICCs, stratification was only possible for the co-occurrence between ADHD & oppositional defiant disorder, where the grand genetic overlap between hyperactivity & oppositional defiant disorder traits was stronger (0.80, SE=0.57) if compared to the genetic overlap between inattention & oppositional defiant disorder traits (0.52, SE= 0.10).

Supplementary Note 3: Description of moderators.

*Age*

The age group moderator was created based on age range of the study, or the mean age when the age range was not reported, and consisted of six levels, three separate categories and three groups cutting across age categories: childhood (ages 4-7), middle childhood (ages 8-10), adolescence (ages 11-24), childhood & middle childhood (ages 4-10), middle childhood & adolescence (ages 8-24) and childhood & adolescence (ages 4-24). The same age categories were used across all methods.

*Design*

The design covariate consisted of different categories, depending on whether the study had employed family or SNP-based methods. For family-based studies, 8 types of designs were identified: classical twin study, categorical threshold twin study, DFextremes twin study, classical twin and sibling study, categorical threshold twin and sibling study, DFextremes twin and sibling study, classical sibling study and categorical threshold sibling study. We identified two types of designs for SNP-based studies: those using genome-wide (GREML) and summary-level data (LDSC).

*Model*

When meta-analysing family-based studies we also controlled for type of model, i.e., full model (twin or twin and sibling studies reporting A, C and E estimates), DFextremes full model (DFextremes studies reporting A, C and E estimates), best model (twin or twin and sibling studies reporting best-fitting parsimonious models, that is either AE, CE or E only models), DFextremes best model (DFextremes studies reporting best-fitting parsimonious models, that is either AE, CE or E only models), A only model (twin or twin and sibling studies reporting heritability estimates only, without providing estimates of C and E), DFextremes A only model (DFextremes studies reporting heritability estimates only, without providing estimates of C and E).

*Rater*

Eight types of raters were identified with the meta-analytic dataset, referring to both family and SNP-based studies. NDD and DICC symptoms were rated by either parents, teachers, self-reports, or researchers, with several studies reporting cross-rater measures assessed by

parents & teachers and parents & self-reports. In addition, specific learning disorders and communication disorders symptoms were often assessed using reading, writing, mathematical and language ability tests, hence test was also included as an additional level of this covariate. A further level, diagnosis, was also incorporated to reflect clinical diagnosis of NDDs and DICCs.

*Measurement scale*

Measurement scale moderator involved two levels, continuous reflecting quantitatively measured symptoms and categorical reflecting binary diagnoses and clinical cut-offs.

*Ancestry*

From studies that reported on the ancestral composition of the sample used in analyses we recorded the percentage of participants of European ancestry. We created the %European ancestry and created a moderator with four levels: less than 50%, more than 50% but less than 75%, more than 75% but less than 100% and 100%.

*Number of covariates*

Behaviour genetic studies often include covariates in the models or regress covariates out prior to analyses. It is a common procedure to control for age and sex in both family and SNP-based studies, and additionally controlling for batch effects and population stratification in molecular genetics studies[2,3]. To determine the impact of including covariates on estimate heterogeneity, we created a moderator by adding up the number of covariates used in each study. This resulted in a moderator including 5 levels: 0 to 4 covariates included.

*Measure*

Further heterogeneity between studies may arise from differences in the measurement instruments used to assess NDDs and DICCs. Diagnostic and assessment tools tend to be specific to the disorder being measured, therefore we created a moderator variable indexing the specific measurement instrument used to assess each NDD category, with levels varying within and between conditions.

*Country*

The last moderator involved the country where each cohort was based. We distinguished eight levels of this moderator: Australia, Canada, China, Netherlands, Norway, Sweden, United Kingdom, and United States.

Supplementary Note 4: Categorical versus continuous measurement of NDDs.

*Family-based studies*

Categorical phenotypes were measured by 28 family-based studies, whereas 215 studies reported estimates for continuous phenotypes. Higher grand heritability was estimated for categorically measured NDDs (0.77, SE= 0.07), compared to NDDs measured on a continuum (0.64, SE= 0.03) (Supplementary Figure 26; Supplementary Table 28). No significant differences in shared and nonshared environmental influences were present between measurement methods.

Disparities in family-based genetic overlap was found across co-occurrences between NDDs, with grand genetic correlation of 0.56 (SE= 0.32) estimated from studies using categorical phenotypes and 0.31 (SE= 0.12) estimated from studies using quantitative measures (Supplementary Figure 26 and Supplementary Table 29). Shared and nonshared environmental genetic overlap could not be compared across co-occurrences between NDDs due to insufficient number of identified studies. Similarly, sources of co-occurrence could not be compared between measurement scales for the co-occurrence between NDDs and DICCs as less than 2 studies investigated categorically defined phenotypes (Supplementary Figure 26 and Supplementary Table 30).

*SNP-based studies*

Categorically and quantitatively defined NDDs were measured by 12 and 17 SNP-based studies, respectively. Just as family-based heritability, SNP heritability across NDDs differed between measures: categorical phenotypes yielded lower heritability (0.17, SE= 0.03) estimates if compared to quantitatively measured symptom scores (0.25, SE= 0.06; Supplementary Figure 26 and Supplementary Table 28).

Supplementary Note 5: Meta-analytic results for different levels of sample diversity.

*Family-based heritability ($h^2$)*

Given the general lack of diversity in participants' ancestry, we could only examine this issue by calculating how samples differed between each other in terms of their percentage of participants of European ancestry. A related issue was also that less than half of the studies reported information on the ancestral composition of their sample (97 out of the 236 studies).

Across all NDDs, heritability was observed to increase with increasing percentage of participants of European ancestry, from 0.46 (SE= 0.07) when they constituted less than half of the sample to 0.66 (SE= 0.06) when 100% of the sample was of European ancestry (Supplementary figure 27; Supplementary Table 25). This trend was particularly observed for ADHD, where the heritability increased from 0.41 (SE= 0.12) in samples where European ancestry participants were the minority (less than 50%) to 0.67 (SE= 0.04) in samples where European ancestry participants were the totality. On the other hand, genetic influences on communication disorders and specific learning disorders remained stable across ancestral compositions: For communication disorders, heritability estimates ranged between 0.59 (SE= 0.27) in samples less than 75-99% of European ancestry to 0.56 (SE= 0.09) in samples 100% of European descent. For Specific learning disorders, heritability was 0.54 (SE= 0.16) in samples where European ancestry participants were in the minority vs. 0.61 (SE= 0.04) in samples 100% of European ancestry.

*SNP heritability (SNP $h^2$)*

We did not identify SNP-based studies that used samples other than 100% European ancestry in populations of children and adolescents.

*Ancestry-related differences in genetic overlap between NDDs*

Differences in sources of co-occurrence between NDDs could only be estimated for the genetic overlap between all NDDs, where a total of 6 studies were identified. Two studies (one focusing on the co-occurrence between ADHD & specific learning disorders, and the other on the co-occurrence between subtypes of specific learning disorders) reported estimates for sample where participants were between 75% and 99% of European ancestry, while 4 studies (2 on the co-occurrence between ADHD & specific learning disorders, and 2 on the co-occurrence between subtypes of specific learning disorders) included samples

where 100% of the participants were of European descent. The meta-analytic genetic overlap between NDDs decreased, albeit not significantly, from 0.63 (SE= 0.44) in samples where 75-99% of European ancestry to 0.54 (SE= 0.10) in samples entirely of European ancestry (Supplementary Table 26).

SNP-based studies (6 in total) addressing the co-occurrence between NDDs were exclusively conducted in combined samples from the United Kingdom and Denmark (Supplementary Table 26).

*Ancestry-related differences in genetic overlap between NDDs and DICCs*

Estimating the sources of co-occurrence between NDDs and DICCs by percentage of sample diversity was similarly challenging as we could identify only 5 studies that included the relevant information. Out of the total number of studies, 3 involved samples of between 75% and 99% participants of European ancestry and focused on examining the genetic overlap between ADHD & conduct disorder and ADHD & oppositional defiant disorder, while 2 involved samples of 100% European descent and examined the genetic correlations between ADHD & oppositional defiant disorder and ADHD & disruptive behaviour. The meta-analytic genetic overlap between NDDs and DICCs increased, albeit not significantly, from 0.57 (SE= 0.25) in samples involving less than 100% of European ancestry participants to 0.71 (SE= 0.31) in 100% European ancestry samples (Supplementary Table 27).

Supplementary Note 6: Heterogeneity assessment.

Across all NDDs we found that 74% of the total variance in family-based heritability was due to heterogeneity, out of which 53% could be attributed to between-cluster and 22% to within-cluster heterogeneity, where clusters refer to cohorts and individual studies (Supplementary figure 4; Supplementary table 7). The lowest $I^2$ statistic was estimated for motor disorders (36%, with equal contribution of between and within-cluster heterogeneity of 18% each), while the highest one for ASD (86%, where 78% was attributed to between-cluster and 8% to within-cluster heterogeneity). When considering SNP heritability, the proportion of total variance accounted for by heterogeneity was very low across disorders (6-8%, most of which was represented by between-cluster heterogeneity). Total variance in shared environmental influences across NDDs was moderate (18%) and almost exclusively attributable to within-cluster heterogeneity. The highest proportion of variance in shared environmental influences accounted for by heterogeneity was found for ASD (41%) and was accounted for solely by within-cluster heterogeneity, while the lowest was found for specific learning disorders and motor disorders, for which variance explained by heterogeneity was less than 0.001%. A similar degree of heterogeneity was estimated for nonshared environmental factors, where the variance explained across NDDs was 38% (21% and 17% attributed to between and within-cluster heterogeneity, respectively) and ranged from 43% (accounted solely by within-cluster heterogeneity) for ADHD to less than 0.001% for intellectual disabilities.

Overall, genetic correlations between NDDs were estimated as 89%, with 34% attributed to between-cluster and 55% to within-cluster heterogeneity (Supplementary figure 4; Supplementary table 8). The largest proportion of total variance accounted for by heterogeneity was estimated for the co-occurrence between ADHD & motor disorders (99%, with equal contribution of between and within-cluster heterogeneity of 49%), whereas the lowest one was estimated for the co-occurrence between communication disorders & motor disorders and communication disorders & specific learning disorders (<0.001% each). Heterogeneity in SNP-based genetic overlap across co-occurrences between NDDs accounted for 49% of the total variance, with 33% attributed to between-cluster and 15% to within-cluster heterogeneity. Between ASD & ADHD, 24% of the total variance was explained by heterogeneity, all of which was accounted for by between-cluster heterogeneity.

Variance in shared environmental overlap across co-occurrences between NDDs accounted for by heterogeneity was estimated as 95%, with 36% attributed to between-cluster and 59% to within-cluster heterogeneity and for the only pair of NDDs where meta-analysis of shared environmental correlations was possible, i.e., ADHD & specific learning disorders, we found 53% of the total variance to be explained by heterogeneity with 6% attributed to between-cluster and 47% to within-cluster heterogeneity. Variance in nonshared environmental overlap across NDDs was modest (24%, all accounted for by between-cluster heterogeneity) and ranged from 62% (all accounted for by between-cluster heterogeneity) for the co-occurrence between ASD & ADHD to less than 0.001% for the co-occurrence between ADHD & specific learning disorders.

Finally, 93% of the total variance in genetic overlap across co-occurrences between NDDs and DICCs was accounted for by heterogeneity, with 55% attributed to between-cluster and 38% to within-cluster heterogeneity (Supplementary Figure 4 and Supplementary Table 9). The variance explained by heterogeneity was high for co-occurrence between ADHD & conduct disorder (92%, with equal contribution of between and within-cluster heterogeneity, 46% each) and between ADHD & oppositional defiant disorder (84%, with equal contribution of between and within-cluster heterogeneity, 42% each), but much lower between ASD & conduct disorder (less than 0.001%). In case of shared environmental overlap between NDDs and DICCs, 95% of the variance was due to heterogeneity and was solely accounted for by within-cluster heterogeneity. The highest proportion of variance in shared environmental correlations explained by heterogeneity was estimated for co-occurrence between ADHD & conduct disorder (96%, with equal contribution of between and within-cluster heterogeneity, 48% each), whereas the lowest was estimated between ASD & conduct disorder (67%, all accounted for by within-cluster heterogeneity). Total variance in nonshared environmental overlap was high across all co-occurrences between NDDs and DICCs (91%, all accounted for by within-cluster heterogeneity), as well as between ADHD & oppositional defiant disorder (92%, equally accounted for by between and within-cluster heterogeneity, 46% each), whereas less than 0.001% of variance in nonshared environmental overlap between ADHD & conduct disorder and ASD & conduct disorder was explained by heterogeneity.

Supplementary Note 7: Publication bias.

Publication bias refers to the higher probability of studies reporting statistically significant findings being accepted for publication. In an unbiased scenario, we would expect to find as many studies reporting significant results, as those not rejecting the null hypothesis. The publication bias can be reflected by the linear relationship between the estimate and standard error[4]. Supplementary Figures 8-14 include funnel plots of studies that reported estimates of heritability, shared and nonshared environmental influences on NDDs. Supplementary Table 13 presents the results of Egger's regressions for all NDDs, apart from intellectual disabilities where the number of parameters to be estimated was larger than the number of studies. A significant risk of publication bias ($z= -3.95$, beta= 0.73 (95% CIs: 0.69, .78), $p< 0.001$) for family-based heritability was found across all NDDs, largely driven by ADHD and specific learning disorders. The overall relationship between shared environmental influences and their standard errors was significant across all NDDs, suggesting the greater likelihood of reporting significant estimates in larger studies. This relationship was not significant for specific NDDs. Publication bias was also found for nonshared environmental influences across all NDDs, which was likely driven by nonshared environmental influences on ADHD. Risk of publication bias was not observed for SNP heritability.

Supplementary Figures 15-20 include funnel plots of studies that reported estimates of genetic, shared and nonshared environmental overlap between NDDs. Supplementary Table 14 presents the results of Egger's regressions across all comorbidities between NDDs, as well as for comorbidities between ASD & ADHD and ADHD & specific learning disorders. For the remaining comorbidities between NDDs the number of parameters to be estimated was larger than the number of studies identified. Risk of publication bias was not significant for family-based genetic and environmental correlations nor for SNP-based genetic correlations.

Supplementary Figures 21-24 include funnel plots of studies that reported estimates for the genetic, shared and nonshared environmental overlap between NDDs and DICCs. Supplementary Table 15 presents the results of Egger's regressions across all comorbidities between NDDs and DICCs, as well as for comorbidities between ADHD & conduct disorder and ADHD & oppositional defiant disorder and ASD & antisocial personality disorder. We found a significant relationship between environmental influences and standard errors, i.e.,

publication bias, for shared environmental correlation between all NDDs and all DICCs, and, when considering specific disorder categories, between ADHD & conduct disorder.

Supplementary Note 8: Deviations from the PROSPERO pre-registered protocol.

The protocol for the current meta-analysis was registered with the international prospective register of systematic reviews (PROSPERO) and can be accessed at the following link: https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=230158. Although we followed the preregistered plan step-by-step, some deviations from the plan were made based on the availability of software and evidence. Below we describe our deviations from the preregistered protocol.

(1) As opposed to the first (primary) literature search which followed the procedure described in the protocol, in the second (confirmatory) literature search we included an additional set of terms to identify studies that measured Specific Learning Disorder and Communication Disorder on a quantitative scale. For details, see Supplementary Note 11.
(2) In the protocol we indicated that study screening would be documented on an excel spreadsheet. Instead, we used Covidence (https://www.covidence.org/), a software that automatically enables the double-blinded screening of title and abstract, as well as full-text screening and study selection, without the need for external recording of decisions.
(3) Finally, while all 296 papers were assessed for publication reporting bias (see Supplementary Note 7, Supplementary Tables 13-15, and Supplementary Figures 8-24), the first 82 papers that were extracted (27.7% of the total) were also assessed for study quality using the checklist provided by Kmet et al. (2020)(see Supplementary Note 13 and Supplementary Figure 25).

Supplementary Note 9: PRISMA 2020 Checklist.

PRISMA 2020 Checklist

| Section and Topic | Item # | Checklist item | Location where item is reported |
|---|---|---|---|
| TITLE | | | |
| Title | 1 | Identify the report as a systematic review. | Title |
| ABSTRACT | | | |
| Abstract | 2 | See the PRISMA 2020 for Abstracts checklist. | Supplementary Material |
| INTRODUCTION | | | |
| Rationale | 3 | Describe the rationale for the review in the context of existing knowledge. | Introduction |
| Objectives | 4 | Provide an explicit statement of the objective(s) or question(s) the review addresses. | Introduction |
| METHOD | | | |
| Eligibility criteria | 5 | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses. | Method |
| Information sources | 6 | Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | Method |
| Search strategy | 7 | Present the full search strategies for all databases, registers and websites, including any filters and limits used. | Method |
| Selection process | 8 | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process. | Method |
| Data collection process | 9 | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process. | Method |
| Data items | 10a | List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect. | Method |
| | 10b | List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information. | Method |

| | | | |
|---|---|---|---|
| Study risk of bias assessment | 11 | Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process. | Method |
| Effect measures | 12 | Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results. | Method |
| Synthesis methods | 13a | Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)). | Method |
| | 13b | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions. | Method |
| | 13c | Describe any methods used to tabulate or visually display results of individual studies and syntheses. | Method |
| | 13d | Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used. | Method |
| | 13e | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression). | Method |
| | 13f | Describe any sensitivity analyses conducted to assess robustness of the synthesized results. | Method |
| Reporting bias assessment | 14 | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases). | Method |
| Certainty assessment | 15 | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome. | Method |
| RESULTS | | | |
| Study selection | 16a | Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram. | Results |
| | 16b | Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded. | Results |
| Study characteristics | 17 | Cite each included study and present its characteristics. | Supplementary Material |
| Risk of bias in studies | 18 | Present assessments of risk of bias for each included study. | Supplementary Material |
| Results of individual studies | 19 | For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots. | Results |
| Results of syntheses | 20a | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies. | Results & Supplementary Material |
| | 20b | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | Results |

| | | | |
|---|---|---|---|
| | 20c | Present results of all investigations of possible causes of heterogeneity among study results. | Supplementary Material |
| | 20d | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results. | Supplementary Material |
| Reporting biases | 21 | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed. | Supplementary Material |
| Certainty of evidence | 22 | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed. | Supplementary Material |
| DISCUSSION | | | |
| Discussion | 23a | Provide a general interpretation of the results in the context of other evidence. | Discussion |
| | 23b | Discuss any limitations of the evidence included in the review. | Discussion |
| | 23c | Discuss any limitations of the review processes used. | Supplementary Material |
| | 23d | Discuss implications of the results for practice, policy, and future research. | Discussion |
| OTHER INFORMATION | | | |
| Registration and protocol | 24a | Provide registration information for the review, including register name and registration number, or state that the review was not registered. | Method |
| | 24b | Indicate where the review protocol can be accessed, or state that a protocol was not prepared. | Method |
| | 24c | Describe and explain any amendments to information provided at registration or in the protocol. | Supplementary Material |
| Support | 25 | Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review. | Acknowledgements |
| Competing interests | 26 | Declare any competing interests of review authors. | Competing interests |
| Availability of data, code and other materials | 27 | Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review. | Method |

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi:
10.1136/bmj.n71 For more information, visit: http://www.prisma-statement.org/

Supplementary Note 10: PRISMA 2020 for Abstracts Checklist.

| Section and Topic | Item # | Checklist item | Reported (Yes/No) |
|---|---|---|---|
| TITLE | | | |
| Title | 1 | Identify the report as a systematic review. | Yes |
| BACKGROUND | | | |
| Objectives | 2 | Provide an explicit statement of the main objective(s) or question(s) the review addresses. | Yes |
| METHOD | | | |
| Eligibility criteria | 3 | Specify the inclusion and exclusion criteria for the review. | Yes |
| Information sources | 4 | Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched. | Yes |
| Risk of bias | 5 | Specify the methods used to assess risk of bias in the included studies. | Yes |
| Synthesis of results | 6 | Specify the methods used to present and synthesise results. | Yes |
| RESULTS | | | |
| Included studies | 7 | Give the total number of included studies and participants and summarise relevant characteristics of studies. | Yes |
| Synthesis of results | 8 | Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured). | Yes |
| DISCUSSION | | | |
| Limitations of evidence | 9 | Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision). | Yes |
| Interpretation | 10 | Provide a general interpretation of the results and important implications. | Yes |
| OTHER | | | |
| Funding | 11 | Specify the primary source of funding for the review. | No |

| | | | |
|---|---|---|---|
| Registration | 12 | Provide the register name and registration number. | No |

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

Supplementary Note 11: Indexes, timespans, search strategy and key words.

Searches were conducted with the aid of Covidence (https://www.covidence.org/) and using the following sources:

1) Web of Science.
Core Collection Indexes and timespans:
•Science Citation Index Expanded (SCI-Expanded) -- 1900-present
•Social Sciences Citation Index (SSCI) -- 1900-present
•Arts & Humanities Citation Index (A&HCI) -- 1975-present
•Emerging Sources Citation Index (ESCI) -- 2015-present
•Conference Proceedings Citation Index - Science (CPCI-S) -- 1990-present •Conference Proceedings Citation Index - Social Sciences & Humanities (CPCI SSH) -- 1990-present

2) Ovid platform.
Indexes and timespans:
• Embase (1974 - present)
• Ovid MEDLINE(R), including Epub Ahead of Print and In-Process & Other Non- Indexed Citations (1946 - present)
• LWW Health Library: Speech, Language & Hearing Collection
• Global Health (1973 - present)
• PsycINFO (1806 - present)

To identify studies focusing on the phenotypes of interest, we used the following key terms in the first (primary) search:

((heritab* OR genetic* OR twin* OR genom* OR sibling*) AND (Neurodevelopmental OR "Intellectual* Disabilit*" OR "Learning* Disabilit*" OR "Intellectual* Developmental* Disorder*" OR "Global* Developmental* Delay" OR "Communication Disorder*" OR "Language Disorder*" OR "Speech* Sound* Disorder*" OR "Childhood-Onset* Fluency* Disorder*" OR Stutter* OR "Social Communication Disorder*" OR "Pragmatic Communication Disorder*" OR Autis* OR ASD OR "Attention-Deficit*" OR Hyperactiv* OR Hyperkinetic OR Inattent* OR ADHD OR "Specific Learning Disorder*" OR SLD OR Dyslex* OR Dysgraph* OR Dyscalcul* OR "Motor Disorder*" OR "Developmental

Coordination Disorder*" OR Dysprax* OR "Stereotypic Movement Disorder*" OR "Tic* Disorder*" OR "Tourett* Disorder*" OR Disruptive OR "Impulse control" OR "Oppositional Defiant Disorder*" OR ODD OR "Intermittent* Explosive* Disorder*" OR "Conduct* disorder" OR Antisocial* OR APD OR Pyromani* OR Kleptomani* OR "behavio* problem*" OR Deliquen* OR Externalizing))

In the second (confirmatory) search, we decided to include an additional set of terms to capture studies focusing on Specific Learning Disorder and Communication Disorder measured on a continuum (i.e., reading, mathematics, writing, language) that had not been identified by the diagnosis-related search terms (i.e., dyslexia, dyscalculia, dysgraphia, language disorder). The following confirmatory search terms were used:
((heritab* OR genetic* OR twin* OR genom* OR sibling*) AND (Neurodevelopmental OR "Intellectual* Disabilit*" OR "Learning* Disabilit*" OR "Intellectual* Developmental* Disorder*" OR "Global* Developmental* Delay" OR "Communication Disorder*" OR "Language Disorder*" OR "Speech* Sound* Disorder*" OR "Childhood-Onset* Fluency* Disorder*" OR Stutter* OR "Social Communication Disorder*" OR "Pragmatic Communication Disorder*" OR Autis* OR ASD OR "Attention-Deficit*" OR Hyperactiv* OR Hyperkinetic OR Inattent* OR ADHD OR "Specific Learning Disorder*" OR SLD OR Dyslex* OR Dysgraph* OR Dyscalcul* OR Reading OR Math* OR Writing OR Language OR "Motor Disorder*" OR "Developmental Coordination Disorder*" OR Dysprax* OR "Stereotypic Movement Disorder*" OR "Tic* Disorder*" OR "Tourett* Disorder*" OR Disruptive OR "Impulse control" OR "Oppositional Defiant Disorder*" OR ODD OR "Intermittent* Explosive* Disorder*" OR "Conduct* disorder" OR Antisocial* OR APD OR Pyromani* OR Kleptomani* OR "behavio* problem*" OR Deliquen* OR Externalizing))

Supplementary Note 12: Description of SNP-based methods targeted by the meta-analysis.

*Genome-wide complex trait analysis and restricted maximum likelihood (GCTA; REML)*
The genome-wide complex trait analysis (GCTA) software employs restricted maximum likelihood method (REML) that allows for the estimation of the variance in a trait that is captured by single nucleotide polymorphisms (SNPs) assessed on SNP arrays commonly used in GWAS (J. Yang et al., 2011). This method estimates SNP heritability from DNA in unrelated individuals. The first step is to calculate a genetic relatedness matrix by weighting genetic similarities between all possible pairs of individuals by the allele frequencies across all SNPs on the SNP array. The matrix of pair-by-pair genetic similarity is compared to the matrix of pair-by-pair phenotypic similarity using residual maximum likelihood estimation to obtain the proportion of phenotypic variation accounted for by genetic variation. GCTA can also be used to quantify the degree of shared genetic variance (genetic covariance) between two phenotypes, two disorders for example (J. Yang et al., 2011).

*Linkage disequilibrium score regression (LDSC)*
LDSC quantifies the proportion of variance in a trait explained by common genetic variants (i.e., SNP heritability), as well as the proportion of shared genetic variance between traits (i.e., genetic covariance), using GWAS summary statistics (Bulik-Sullivan et al., 2015). LDSC applies regression to calculate the association between SNP test statistics obtained from GWAS results, and linkage disequilibrium (LD) scores, therefore allowing us to dissect the true polygenic signal (i.e., the contribution of multiple genetic variants of small effect to variability in a trait or disorder) from confounding signal, including for example false positive associations due to population stratification (Bulik-Sullivan et al., 2015).

*Summary-data-based BayeS (SBayeS)*
SBayeS is a Bayesian approach to estimating SNP heritability using GWA summary statistics (Zeng et al., 2018). SBayeS employs an array of linear mixed models using GWA data to estimate SNP heritability, as well as polygenicity and the relationship between variant effect sizes and minor allele frequencies (Zeng et al., 2018).

Supplementary Note 13: Quality scoring checklist.

Quality scoring of the studies included in the present meta-analysis was conducted in line with the framework proposed by (Kmet et al., 2020). Namely, we used the following checklist:

1. Question/objective sufficiently described?
2. Study design evident and appropriate?
3. Method of subject/comparison group selection or source of information/input variables described and appropriate?
4. Subject (and comparison group, if applicable) characteristics sufficiently described?
5. Outcome and (if applicable) exposure measure(s) well defined and robust to measurement / misclassification bias? Means of assessment reported?
6. Analytic methods described/justified and appropriate?
7. Some estimate of variance is reported for the main results?
8. Results reported in sufficient detail?
9. Conclusions supported by the results?

Items were scored based on the scale developed by Kmet et. al. (2020), where: 0= NO, 1= PARTIAL and 2= YES. Quality scoring was conducted by a primary reviewer and checked by a secondary reviewer. Following completion of the checklist, we calculated the mean total score obtained by each reviewer to ensure inter-rater agreement. Reviewer discrepancies were identified and resolved through discussion.

Supplementary Figure 25 shows our findings for the first 82 studies that were extracted (27.7% of the total). 93.8% of studies showed a low risk of bias across all 9 quality checklist items, and the remaining 6.2% showed moderate risk. Therefore, given the generally low bias, we did not repeat the analyses excluding low-quality studies.

Supplementary Note 14: Requesting missing data from study authors.

The first author of Partitioning the heritability of Tourette syndrome and obsessive compulsive disorder reveals differences in genetic architecture (L. K. Davis et al., 2013) was contacted via e-mail about the age range of the sample. Response was received that the age range of the sample was not restricted and consisted of both children and adults. Therefore, the study was not included in the meta-analysis.

We contacted authors of two other studies via ResearchGate, however we did not receive a response.

Supplementary Note 15: Aggregation sensitivity analyses.

We explored multiple aggregation techniques, that is aggregating non-independent effect sizes by study, by cohort, as well as by country. Furthermore, we checked whether estimates differed when setting different correlation thresholds (r= 0.3, r= 0.5 and r= 0.9) for aggregating between effect sizes. Grand estimates across all NDDs and co-occurring disorders resulting from various aggregation methods are presented in Supplementary Figure 30. Grand estimates were not significantly different across aggregation methods and correlation thresholds, therefore we proceeded with aggregating by study and set a fixed correlation between related effect sizes of r= 0.5 for all downstream analyses.

Supplementary Note 16: Certainty assessment.

We evaluated our confidence in the body of research included in the present meta-analysis based on a number of key factors: (a) the sample size of each study, (b) the consistency of findings across studies, (c) study quality and risk of publication bias.

(a) Because differences in sample size can introduce an imbalance in the power to estimate effects reliably across studies, in our meta-analysis we weighted each estimate by the standard errors. Estimates reported by studies conducted in larger samples had smaller standard errors and were therefore given more weight if compared to studies conducted in smaller samples.
(b) The consistency of findings across studies was assessed by visually examining forest plots. Overall, we did not find significant differences between estimates.
(c) Study quality and risk of bias were assessed in line with the framework proposed by Kmet et al. (2020) (see Supplementary Note 13 and Supplementary Figure 25). We applied Egger's regression and inspected funnel plots to examine the impact of publication bias on our results, the outcomes of these analyses are reported in Supplementary Note 7 and Supplementary Tables 13-15 and Supplementary Figures 8-24.

Based on these criteria, we place confidence in the results of the current meta-analysis that shows that: 1) NDDs in childhood and adolescence are highly heritable; 2) that the pattern of co-occurrence between NDDs is complex, and while some NDDs are closely related, others show little genetic overlap; and 3) NDDs show a moderate-to-strong genetic overlap with DICCs.

Supplementary Note 17: Discussion of limitations of the review process used.

The review process of the current meta-analysis does not come without limitations. A first limitations is our sole focus on childhood and adolescence. A second limitation relates to our choice of focusing on specific co-occurring conditions, DICCs, without considering other neurological disorders that have been found to co-occur with NDDs, such as epilepsy, cerebral palsy, sleep, or psychiatric disorders. The inclusion of a wider range of co-occurring conditions could have resulted in a more detailed characterization of aetiological overlaps between NDDs and other conditions.

A third limitation is that the current meta-analysis only focused on single-generation studies, i.e., twin and sibling studies and excluded multi-generational family designs, such as children-of-twins and in-vitro fertilization studies. Future studies focusing on multi-generational designs could provide valuable insights into the role that parental genotypes and correlated environmental influences play in offspring's NDDs and their co-occurring conditions.

# Supplementary Tables

Supplementary Table 1. Heritability, shared and nonshared environmental influences on NDDs.

| NDDs | Family $h^2$ (SE) | N | Family $c^2$ (SE) | N | Family $e^2$ (SE) | N | SNP $h^2$ (SE) | N |
|---|---|---|---|---|---|---|---|---|
| NDDs combined | 0.66 (0.03) | 236 | 0.17 (0.02) | 127 | 0.29 (0.02) | 195 | 0.19 (0.03) | 29 |
| Intellectual disabilities | 0.86 (0.44) | 2 | - | - | 0.1 (0.16) | 2 | - | - |
| Communication disorders | 0.64 (0.19) | 23 | 0.35 (0.06) | 15 | 0.21 (0.04) | 18 | 0.32 (0.14) | 4 |
| ASD | 0.76 (0.11) | 36 | 0.13 (0.05) | 14 | 0.27 (0.03) | 28 | 0.14 (0.04) | 15 |
| ADHD | 0.67 (0.04) | 121 | 0.11 (0.02) | 48 | 0.3 (0.02) | 107 | 0.20 (0.04) | 14 |
| Specific learning disorders | 0.62 (0.04) | 89 | 0.19 (0.02) | 65 | 0.24 (0.02) | 67 | 0.30 (0.08) | 9 |
| Motor disorders | 0.74 (0.08) | 6 | 0.13 (0.11) | 3 | 0.38 (0.11) | 6 | - | - |
| Note. $H^2$= heritability; $c^2$= shared environmental influences; $e^2$= nonshared environmental influences; N= number of studies identified; SE= standard error. | | | | | | | | |

Supplementary Table 2. Heritability, shared and nonshared environmental influences on NDDs, stratified by specific phenotypic sub-categories.

| Specific phenotypes from family-based studies | | | | | | | Specific phenotypes from SNP-based studies | | |
|---|---|---|---|---|---|---|---|---|---|
| NDDs | Family $h^2$ (SE) | N | Family $c^2$ (SE) | N | Family $e^2$ (SE) | N | NDDs | SNP $h^2$ (SE) | N |
| Intellectual disabilities | | | | | | | | | |
| Learning disability | 0.86 (0.44) | 2 | - | - | 0.1 (0.16) | 2 | - | - | - |
| Communication disorders | | | | | | | | | |
| Language ability | 0.65 (0.2) | 20 | 0.36 (0.07) | 13 | 0.21 (0.04) | 15 | Language ability | 0.32 (0.14) | 4 |
| Specific language impairment | 0.87 (0.6) | 2 | - | - | - | - | - | - | - |
| Speech | 0.8 (0.17) | 2 | - | - | 0.2 (0.15) | 2 | - | - | - |
| Stuttering | 0.58 (0.17) | 2 | - | - | 0.21 (0.12) | 2 | - | - | - |
| Syntax | 0.65 (0.37) | 2 | - | - | 0.49 (0.24) | 2 | - | - | - |
| ASD | | | | | | | | | |
| ASD | 0.79 (0.14) | 26 | 0.06 (0.04) | 12 | 0.26 (0.03) | 19 | ASD | 0.13 (0.04) | 10 |
| CIs | 0.76 (0.09) | 8 | - | - | 0.27 (0.06) | 5 | Sis | 0.2 (0.09) | 6 |
| RRBIs | 0.83 (0.49) | 10 | 0.24 (0.24) | 2 | 0.35 (0.09) | 6 | - | - | - |
| Sis | 0.67 (0.05) | 15 | 0.31 (0.22) | 3 | 0.3 (0.05) | 11 | - | - | - |
| Strict autism | 0.51 (0.28) | 2 | - | - | - | - | - | - | - |
| ADHD | | | | | | | | | |
| ADHD | 0.7 (0.05) | 54 | 0.12 (0.03) | 22 | 0.3 (0.03) | 47 | ADHD | 0.21 (0.04) | 11 |
| Hyperactivity | 0.66 (0.16) | 2 | - | - | 0.38 (0.11) | 2 | Hyperactivity/Impulsivity | 0.13 (0.11) | 5 |
| Impulsivity | 0.76 (0.07) | 2 | - | - | 0.24 (0.08) | 2 | Inattention | 0.27 (0.17) | 4 |
| Hyperactivity/Impulsivity | 0.69 (0.06) | 63 | 0.16 (0.06) | 24 | 0.27 (0.03) | 56 | - | - | - |
| Inattention | 0.65 (0.05) | 65 | 0.08 (0.03) | 26 | 0.28 (0.02) | 58 | - | - | - |
| Specific learning disorders | | | | | | | | | |
| Dyslexia | 0.62 (0.04) | 76 | 0.19 (0.02) | 55 | 0.23 (0.02) | 55 | - | - | - |
| Dysgraphia | 0.56 (0.18) | 3 | 0.08 (0.08) | 3 | 0.38 (0.12) | 3 | - | - | - |
| Dyscalculia | 0.55 (0.04) | 30 | 0.19 (0.04) | 24 | 0.27 (0.02) | 25 | - | - | - |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Decoding | 0.69 (0.14) | 7 | 0.17 (0.1) | 6 | 0.15 (0.06) | 6 | - | - | - |
| Grammar | 0.55 (0.1) | 2 | 0.3 (0.24) | 2 | 0.26 (0.1) | 2 | - | - | - |
| Nonword reading | 0.67 (0.13) | 3 | - | - | - | - | - | - | - |
| Orthographic skills | 0.49 (0.15) | 4 | 0.46 (0.18) | 2 | - | - | - | - | - |
| Phonological skills | 0.59 (0.09) | 13 | 0.2 (0.08) | 11 | 0.23 (0.06) | 10 | - | - | - |
| Rapid naming | 0.6 (0.12) | 7 | 0.17 (0.13) | 5 | 0.25 (0.08) | 5 | - | - | - |
| Reading ability | 0.62 (0.04) | 51 | 0.19 (0.03) | 33 | 0.23 (0.03) | 34 | - | - | - |
| Reading comprehension | 0.56 (0.07) | 11 | 0.19 (0.07) | 10 | 0.26 (0.05) | 10 | - | - | - |
| Reading fluency | 0.64 (0.13) | 5 | 0.16 (0.09) | 4 | 0.25 (0.06) | 4 | - | - | - |
| Spelling | 0.62 (0.11) | 8 | 0.14 (0.08) | 6 | 0.23 (0.06) | 6 | - | - | - |
| Vocabulary | 0.25 (0.14) | 4 | 0.57 (0.15) | 4 | 0.18 (0.07) | 4 | - | - | - |
| Word reading | 0.65 (0.08) | 16 | 0.22 (0.06) | 13 | 0.12 (0.04) | 13 | - | - | - |
| Writing ability | 0.56 (0.18) | 3 | 0.08 (0.08) | 3 | 0.38 (0.12) | 3 | - | - | - |
| Calculations | 0.39 (0.13) | 3 | - | - | 0.55 (0.23) | 2 | - | - | - |
| Mathematic ability | 0.57 (0.04) | 27 | 0.19 (0.04) | 22 | 0.25 (0.02) | 22 | - | - | - |
| Mathematic fluency | 0.52 (0.14) | 5 | 0.21 (0.14) | 4 | 0.27 (0.09) | 4 | - | - | - |
| Mathematic problems solving | 0.36 (0.19) | 2 | 0.28 (0.19) | 2 | 0.36 (0.13) | 2 | - | - | - |
| Motor disorders | | | | | | | | | |
| Coordination | 0.82 (0.07) | 2 | - | - | 0.38 (0.26) | 2 | - | - | - |
| DCD | 0.69 (0.13) | 2 | 0.12 (0.15) | 2 | 0.43 (0.2) | 3 | - | - | - |
| Motor control | 0.68 (0.12) | 2 | - | - | 0.41 (0.33) | 2 | - | - | - |
| Tics | 0.56 (0.17) | 2 | - | - | 0.44 (0.16) | 2 | - | - | - |

Note. $H^2$= heritability; $c^2$= shared environmental influences; $e^2$= nonshared environmental influences; N= number of studies identified;
SE= standard error; Sis= social impairments; CIs= communication impairments; RRBIs= restrictive, repetitive behaviours and interests; DCD= developmental coordination disorder.

Supplementary Table 3. Genetic, shared and nonshared environmental correlations between NDDs.

| NDDs | Family rA (SE) | N | Family rC (SE) | N | Family rE (SE) | N | SNP rG (SE) | N |
|---|---|---|---|---|---|---|---|---|
| NDDs combined | 0.36 (0.12) | 37 | 0.63 (0.33) | 16 | 0.17 (0.05) | 22 | 0.39 (0.19) | 6 |
| ASD & ADHD | 0.67 (0.3) | 6 | - | - | 0.22 (0.13) | 5 | 0.26 (0.14) | 5 |
| ADHD & motor disorders | 0.9 (0.82) | 2 | - | - | - | - | - | - |
| ADHD & specific learning disorders | 0.07 (0.12) | 18 | 0.32 (0.14) | 7 | 0.11 (0.04) | 9 | - | - |
| Communication disorders & motor disorders | 0.33 (0.16) | 2 | - | - | - | - | - | - |
| Communication disorders & specific learning disorders | 0.66 (0.15) | 2 | - | - | - | - | - | - |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; N= number of studies identified; SE= standard error. | | | | | | | | |

Supplementary Table 4. Genetic, shared and nonshared environmental correlations between NDDs, stratified by specific phenotypic sub-categories.

| NDDs | Family rA (SE) | N | Family rC (SE) | N | Family rE (SE) | N |
|---|---|---|---|---|---|---|
| ASD & ADHD | | | | | | |
| ASD & ADHD | 0.71 (0.27) | 4 | - | - | 0.27 (0.11) | 3 |
| Hyperactivity & Sis | 0.22 (0.19) | 2 | - | - | 0.02 (0.08) | 2 |
| Inattention & RRBIs | 0.16 (0.11) | 2 | - | - | 0.09 (0.11) | 2 |
| Inattention & Sis | 0.27 (0.24) | 2 | - | - | 0.03 (0.08) | 2 |
| ADHD & motor disorders | | | | | | |
| ADHD & DCD | 0.91 (0.8) | 2 | - | - | - | - |
| ADHD & specific learning disorders | | | | | | |
| ADHD & Dyslexia | 0.07 (0.12) | 17 | 0.32 (0.15) | 7 | 0.11 (0.04) | 9 |
| ADHD & Dyscalculia | -0.29 (0.11) | 2 | - | - | 0.09 (0.1) | 2 |
| ADHD & Reading ability | 0.19 (0.22) | 6 | 0.12 (0.11) | 3 | 0.1 (0.08) | 3 |
| Hyperactivity & Reading ability | 0.11 (0.08) | 11 | 0.66 (0.19) | 4 | 0.03 (0.05) | 6 |
| Inattention & Reading ability | 0.07 (0.16) | 13 | 0.43 (0.26) | 5 | 0.16 (0.06) | 7 |
| inattention & Maths ability | -0.32 (0.11) | 2 | - | - | 0.15 (0.1) | 2 |
| Communication disorders & specific learning disorders | | | | | | |
| Specific language disorder & dyslexia | 0.66 (0.15) | 2 | - | - | - | - |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; N= number of studies identified; SE= standard error; Sis= social impairments; RRBIs= restrictive, repetitive behaviours and interests; DCD= developmental coordination disorder. | | | | | | |

Supplementary Table 5. Genetic, shared and nonshared environmental correlations between NDDs and DICCs.

| NDDs and DICCs | Family rA (SE) | N | Family rC (SE) | N | Family rE (SE) | N |
|---|---|---|---|---|---|---|
| NDDs and DICCs combined | 0.62 (0.19) | 15 | 0.88 (0.34) | 11 | 0.38 (0.14) | 13 |
| ADHD & conduct disorder | 0.66 (0.36) | 6 | 0.94 (0.71) | 3 | 0.11 (0.08) | 5 |
| ADHD & oppositional defiant disorder | 0.66 (0.18) | 6 | 0.96 (0.57) | 4 | 0.54 (0.25) | 5 |
| ASD & conduct disorder | 0.35 (0.10) | 3 | 0.88 (0.57) | 3 | 0.07 (0.08) | 3 |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; N= number of studies identified; SE= standard error. | | | | | | |

Supplementary Table 6. Genetic, shared and nonshared environmental correlations between NDDs and DICCs, stratified by specific phenotypic sub-categories.

| NDDs and DICCs | Family rA (SE) | N | Family rC (SE) | N | Family rE (SE) | N |
|---|---|---|---|---|---|---|
| ADHD & oppositional defiant disorder | | | | | | |
| ADHD & oppositional defiant disorder | 0.58 (0.2) | 5 | 0.95 (0.68) | 3 | 0.29 (0.1) | 4 |
| Hyperactivity & oppositional defiant disorder | 0.8 (0.57) | 2 | 0.87 (0.86) | 2 | 0.87 (0.74) | 2 |
| Inattention & oppositional defiant disorder | 0.52 (0.1) | 2 | - | - | 0.49 (0.11) | 2 |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; N= number of studies identified; SE= standard error. | | | | | | |

Supplementary Table 7. Proportion of variance in heritability, shared and nonshared environmental influences on NDDs accounted for by heterogeneity.

| NDDs | Family $h^2$ | | | Family $c^2$ | | | Family $e^2$ | | | SNP $h^2$ | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $I^2_t$ | $I^2_b$ | $I^2_w$ | $I^2_t$ | $I^2_b$ | $I^2_w$ | $I^2_t$ | $I^2_b$ | $I^2_w$ | $I^2_t$ | $I^2_b$ | $I^2_w$ |
| NDDs combined | 0.75 | 0.53 | 0.21 | 0.18 | <0.001 | 0.18 | 0.38 | 0.21 | 0.17 | <0.001 | <0.001 | <0.001 |
| Intellectual disabilities | 0.84 | 0.42 | 0.42 | - | - | - | <0.001 | <0.001 | <0.001 | - | - | - |
| Communication disorders | 0.82 | 0.74 | 0.09 | 0.21 | <0.001 | 0.21 | 0.09 | <0.001 | 0.9 | <0.001 | <0.001 | <0.001 |
| ASD | 0.86 | 0.78 | 0.07 | 0.41 | <0.001 | 0.41 | 0.11 | <0.001 | 0.11 | <0.001 | <0.001 | <0.001 |
| ADHD | 0.78 | 0.54 | 0.24 | 0.03 | 0.03 | <0.001 | 0.43 | <0.001 | 0.43 | <0.001 | <0.001 | <0.001 |
| Specific learning disorders | 0.47 | 0.33 | 0.14 | <0.001 | <0.001 | <0.001 | 0.05 | 0.05 | <0.001 | <0.001 | <0.001 | <0.001 |
| Motor disorders | 0.36 | 0.18 | 0.18 | <0.001 | <0.001 | <0.001 | 0.37 | 0.18 | 0.18 | - | - | - |

Note. $H^2$= heritability; $c^2$= shared environmental influences; $e^2$= nonshared environmental influences; $I^2_t$= total variance accounted for by heterogeneity; $I^2_b$= between-cluster heterogeneity; $I^2_w$= within-cluster heterogeneity.

Supplementary Table 8. Proportion of variance in genetic, shared and nonshared environmental correlations between NDDs accounted for by heterogeneity.

| NDDs | Family rA | | | Family rC | | | Family rE | | | SNP rG | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $I^2_t$ | $I^2_b$ | $I^2_w$ | $I^2_t$ | $I^2_b$ | $I^2_w$ | $I^2_t$ | $I^2_b$ | $I^2_w$ | $I^2_t$ | $I^2_b$ | $I^2_w$ |
| NDDs combined | 0.89 | 0.34 | 0.55 | 0.95 | 0.36 | 0.59 | 0.24 | 0.24 | <0.001 | 0.49 | 0.33 | 0.16 |
| ASD & ADHD | 0.94 | 0.65 | 0.29 | - | - | - | 0.62 | 0.62 | <0.001 | 0.24 | <0.001 | 0.24 |
| ADHD & motor disorders | 0.99 | 0.49 | 0.49 | - | - | - | - | - | - | - | - | - |
| ADHD & specific learning disorders | 0.79 | 0.17 | 0.62 | 0.53 | 0.06 | 0.47 | <0.001 | <0.001 | <0.001 | - | - | - |
| Communication disorders & motor disorders | <0.001 | <0.001 | <0.001 | - | - | - | - | - | - | - | - | - |
| Communication disorders & specific learning disorders | <0.001 | <0.001 | <0.001 | - | - | - | - | - | - | - | - | - |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; $I^2_t$= total variance accounted for by heterogeneity; $I^2_b$= between-cluster heterogeneity; $I^2_w$= within-cluster heterogeneity. | | | | | | | | | | | | |

Supplementary Table 9. Proportion of variance in genetic, shared and nonshared environmental correlations between NDDs and DICCs accounted for by heterogeneity.

| NDDs and DICCs | Family rA | | | Family rC | | | Family rE | | |
|---|---|---|---|---|---|---|---|---|---|
| | $I^2_t$ | $I^2_b$ | $I^2_w$ | $I^2_t$ | $I^2_b$ | $I^2_w$ | $I^2_t$ | $I^2_b$ | $I^2_w$ |
| NDDs and DICCs combined | 0.93 | 0.55 | 0.38 | 95 | 0 | 95 | 91 | 0 | 91 |
| ADHD & conduct disorder | 0.93 | 0.46 | 0.46 | 96 | 48 | 48 | <0.001 | <0.001 | <0.001 |
| ADHD & oppositional defiant disorder | 0.83 | 0.42 | 0.42 | 94 | 47 | 47 | 93 | 46 | 46 |
| ASD & conduct disorder | <0.001 | <0.001 | <0.001 | 67 | <0.001 | 67 | <0.001 | <0.001 | <0.001 |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; $I^2_t$= total variance accounted for by heterogeneity; $I^2_b$= between-cluster heterogeneity; $I^2_w$= within-cluster heterogeneity. | | | | | | | | | |

Supplementary Table 10. Proportion of variance in heritability, shared and nonshared environmental influences on NDDs accounted for by heterogeneity, following exclusion of studies identified as outliers.

| NDDs | Family $h^2$ | | Family $c^2$ | | Family $e^2$ | | SNP $h^2$ | |
|---|---|---|---|---|---|---|---|---|
| | $I^2_t$ | $N_r$ | $I^2_t$ | $N_r$ | $I^2_t$ | $N_r$ | $I^2_t$ | $N_r$ |
| NDDs combined | 0.64 | 85 | 0.53 | 71 | 0.64 | 69 | 0.69 | 25 |
| Intellectual disabilities | - | - | - | - | - | - | - | - |
| Communication disorders | 0.84 | 16 | 0.76 | 14 | 0.82 | 11 | - | - |
| ASD | 0.95 | 19 | 0.43 | 9 | 0.89 | 18 | 0.77 | 12 |
| ADHD | 0.86 | 45 | 0.56 | 29 | 0.69 | 47 | 0.75 | 12 |
| Specific learning disorders | 0.52 | 49 | 0.63 | 44 | 0.69 | 27 | - | - |
| Motor disorders | 0.91 | 6 | - | - | 0.92 | 5 | - | - |

Note. $H^2$= heritability; $c^2$= shared environmental influences; $e^2$= nonshared environmental influences; $N_r$= number of studies remaining after exclusion of outliers; $I^2_t$= total variance accounted for by heterogeneity; -= no outliers detected.

Supplementary Table 11. Proportion of variance in genetic, shared and nonshared environmental correlations between NDDs accounted for by heterogeneity, following exclusion of studies identified as outliers.

| NDDs | Family rA | | Family rC | | Family rE | | SNP rG | |
|---|---|---|---|---|---|---|---|---|
| | $I^2_t$ | $N_r$ | $I^2_t$ | $N_r$ | $I^2_t$ | $N_r$ | $I^2_t$ | $N_r$ |
| NDDs combined | 0.94 | 20 | 0.98 | 6 | 0.94 | 14 | - | - |
| ASD & ADHD | 0.99 | 5 | 0.99 | 4 | 0.94 | 5 | - | - |
| ADHD & motor disorders | - | - | - | - | - | - | - | - |
| ADHD & specific learning disorders | 0.82 | 6 | 0.91 | 6 | 0.75 | 7 | - | - |
| Communication disorders & motor disorders | - | - | - | - | - | - | - | - |
| Communication disorders & specific learning disorders | - | - | - | - | - | - | - | - |

Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; $N_r$= number of studies remaining after exclusion of outliers; $I^2_t$= total variance accounted for by heterogeneity; -= no outliers detected.

Supplementary Table 12. Proportion of variance in genetic, shared and nonshared environmental correlations between NDDs and DICCs accounted for by heterogeneity, following exclusion of studies identified as outliers.

| NDDs and DICCs | Family rA | | Family rC | | Family rE | |
|---|---|---|---|---|---|---|
| | $I^2_t$ | $N_r$ | $I^2_t$ | $N_r$ | $I^2_t$ | $N_r$ |
| NDDs and DICCs combined | 0.96 | 10 | 0.90 | 6 | 0.92 | 9 |
| ADHD & conduct disorder | 0.73 | 6 | - | - | 0.74 | 5 |
| ADHD & oppositional defiant disorder | - | - | - | - | 0.88 | 4 |
| ASD & conduct disorder | - | - | - | - | - | - |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; $N_r$= number of studies remaining after exclusion of outliers; $I^2_t$= total variance accounted for by heterogeneity; -= no outliers detected. | | | | | | |

Supplementary Table 13. Results of Egger's regression for studies addressing heritability and environmental influences on NDDs.

| NDDs | Family $h^2$ | | | Family $c^2$ | | | Family $e^2$ | | | SNP $h^2$ | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Z | P | Estimate (95% CIs) | Z | P | Estimate (95% CIs) | Z | P | Estimate (95% CIs) | Z | P | Estimate (95% CIs) |
| NDDs combined | 0.0 | <0.001 | 0.73 (0.69-0.78) | 3.82 | <0.001 | 0.03 (-0.04-0.1) | 3.76 | <0.001 | 0.17 (0.11-0.22) | 1.59 | 0.11 | 0.09 (-0.05-0.22) |
| Communication disorders | 0.71 | 0.48 | 0.43 (0.23-0.63) | -1.8 | 0.07 | 0.6 (0.33-0.88) | 1.62 | 0.1 | 0.05 (-0.14-0.25) | 1.62 | 0.1 | 0.05 (-0.14-0.25) |
| ASD | 0.14 | 0.89 | 0.68 (0.57-0.79) | 1.65 | 0.1 | -0.01 (-0.15-0.14) | 0.65 | 0.52 | 0.23 (0.13-0.33) | 1.49 | 0.14 | 0.01 (-0.18-0.2) |
| ADHD | -2.58 | 0.01 | 0.75 (0.69-0.81) | 1.83 | 0.07 | 0.01 (-0.09-0.11) | 3.43 | <0.001 | 0.17 (0.09-0.24) | -0.17 | 0.87 | 0.22 (0.01-0.42) |
| Specific learning disorders | -5.03 | <0.001 | 0.75 (0.69-0.81) | 1.52 | 0.13 | 0.08 (-0.06-0.22) | 1.62 | 0.1 | 0.16 (0.06-0.27) | -0.25 | 0.81 | 0.38 (-0.34-1.11) |
| Motor disorders | -1.19 | 0.23 | 0.83 (0.71-0.95) | 0.27 | 0.78 | 0.04 (-0.62-0.71) | 0.81 | 0.42 | 0.09 (-0.56-0.74) | - | - | - |

Note. $H^2$= heritability; $c^2$= shared environmental influences; $e^2$= nonshared environmental influences; CIs= confidence intervals; Estimate= the limit estimate; -= number of parameters to be estimated was larger than the number of observations; Z= z-value of the test statistic; P= p-value.

Supplementary Table 14. Results of Egger's regression for studies addressing genetic and environmental overlap between NDDs.

| NDDs | Family rA | | | Family rC | | | Family rE | | | SNP rG | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Z | P | Estimate (95% CIs) | Z | P | Estimate (95% CIs) | Z | P | Estimate (95% CIs) | Z | P | Estimate (95% CIs) |
| NDDs combined | -0.97 | 0.33 | 0.42 (0.16-0.68) | 1.84 | 0.07 | 0.09 (-0.36-0.54) | 1.65 | 0.1 | <0.001 (-0.2-0.2) | 1.07 | 0.28 | -0.38 (-1.61-0.85) |
| ASD & ADHD | -0.49 | 0.62 | 0.68 (-0.03-1.39) | - | - | - | 0.73 | 0.47 | 0.01 (-0.5-0.52) | 0.47 | 0.64 | -0.14 (-1.71-1.44) |
| ADHD & specific learning disorders | -0.02 | 0.99 | 0.08 (-0.31-0.47) | 1.17 | 0.24 | -0.02 (-0.46-0.42) | 1.15 | 0.25 | -0.04 (-0.32-0.23) | - | - | - |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; CIs= confidence intervals; Estimate= the limit estimate; -= number of parameters to be estimated was larger than the number of observations; Z= z-value of the test statistic; P= p-value. | | | | | | | | | | | | |

Supplementary Table 15. Results of Egger's regression for studies addressing genetic and environmental overlap between NDDs and DICCs.

| NDDs and DICCs | Family rA | | | Family rC | | | Family rE | | |
|---|---|---|---|---|---|---|---|---|---|
| | Z | P | Estimate (95% CIs) | Z | P | Estimate (95% CIs) | Z | P | Estimate (95% CIs) |
| NDDs and DICCs combined | -0.79 | 0.43 | 0.63 (0.26, 1) | 3.62 | <0.001 | -0.17 (-0.42, 0.07) | 0.78 | 0.44 | 0.12 (-0.11, 0.35) |
| ADHD & conduct disorder | 0.32 | 0.75 | 0.38 (-0.28, 1.04) | 2.88 | <0.001 | -0.43 (-0.95, 0.09) | 1.1 | 0.27 | -0.15 (-0.64, 0.34) |
| ADHD & oppositional defiant disorder | -0.66 | 0.51 | 0.73 (0.32, 1.14) | 1.46 | 0.14 | 0.06 (-0.78, 0.89) | -0.79 | 0.43 | 0.63 (0.14, 1.12) |
| ASD & conduct disorder | 0.52 | 0.60 | -0.06 (-1.61, 1.49) | 0.45 | 0.65 | -0.24 (-4.32, 3.84) | 0.85 | 0.40 | -0.16 (-0.71, 0.38) |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; CIs= confidence intervals; Estimate= the limit estimate; Z= z-value of the test statistic; P= p-value. | | | | | | | | | |

Supplementary Table 16. Sex-specific heritability, shared and nonshared environmental influences on NDDs.

| NDDs | Males | | Females | | Males | | Females | | Males | | Females | | Males | | Females | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Family $h^2$ (SE) | N | Family $h^2$ (SE) | N | Family $c^2$ (SE) | N | Family $c^2$ (SE) | N | Family $e^2$ (SE) | N | Family $e^2$ (SE) | N | SNP $h^2$ (SE) | N | SNP $h^2$ (SE) | N |
| NDDs combined | 0.65 (0.06) | 68 | 0.67 (0.06) | 67 | 0.35 (0.08) | 36 | 0.28 (0.08) | 34 | 0.31 (0.04) | 63 | 0.33 (0.04) | 61 | 0.19 (0.07) | 2 | 0.09 (0.10) | 2 |
| Intellectual disabilities | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| Communication disorders | 0.64 (0.33) | 4 | 0.67 (0.42) | 4 | 0.35 (0.14) | 3 | 0.35 (0.16) | 3 | 0.28 (0.14) | 4 | 0.29 (0.14) | 4 | - | - | - | - |
| ASD | 0.64 (0.16) | 21 | 0.68 (0.09) | 23 | 0.46 (0.20) | 12 | 0.30 (0.14) | 12 | 0.28 (0.06) | 19 | 0.24 (0.02) | 21 | - | - | - | - |
| ADHD | 0.68 (0.08) | 38 | 0.71 (0.08) | 38 | 0.38 (0.17) | 14 | 0.13 (0.07) | 12 | 0.32 (0.06) | 36 | 0.34 (0.06) | 35 | 0.20 (0.08) | 2 | 0.13 (0.11) | 2 |
| Specific learning disorders | 0.61 (0.08) | 9 | 0.61 (0.09) | 9 | 0.21 (0.07) | 8 | 0.18 (0.06) | 8 | 0.30 (0.07) | 8 | 0.34 (0.08) | 8 | - | - | - | - |
| Motor disorders | 0.59 (0.36) | 2 | 0.58 (0.34) | 2 | -. | - | -. | - | 0.24 (0.09) | 2 | 0.27 (0.08) | 2 | - | - | - | - |

Note. $H^2$= heritability; $c^2$= shared environmental influences; $e^2$= nonshared environmental influences; N= number of studies identified;
SE= standard error.

Supplementary Table 17. Sex-specific genetic, shared and nonshared environmental correlations between NDDs.

| NDDs | Males | | Females | | Males | | Females | | Males | | Females | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Family rA (SE) | N | Family rA (SE) | N | Family rC (SE) | N | Family rC (SE) | N | Family rE (SE) | N | Family rE (SE) | N |
| NDDs combined | 0.86 (0.58) | 4 | 0.25 (0.36) | 2 | - | - | - | - | 0.09 (0.08) | 3 | 0.10 (0.11) | 2 |
| ASD & ADHD | 0.79 (0.42) | 2 | - | - | - | - | - | - | 0.20 (0.14) | 2 | - | - |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; N= number of studies identified; SE= standard error. | | | | | | | | | | | | |

Supplementary Table 18. Sex-specific genetic, shared and nonshared environmental correlations between NDDs and DICCs.

| NDDs and DICCs | Males | | Females | | Males | | Females | | Males | | Females | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Family rA (SE) | N | Family rA (SE) | N | Family rC (SE) | N | Family rC (SE) | N | Family rE (SE) | N | Family rE (SE) | N |
| NDDs and DICCs combined | - | - | 0.75 (0.58) | 2 | - | - | - | - | - | - | 0.06 (0.12) | 2 |
| ADHD & conduct disorder | - | - | 0.75 (0.58) | 2 | - | - | - | - | - | - | 0.06 (0.12) | 2 |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; N= number of studies identified; SE= standard error. | | | | | | | | | | | | |

Supplementary Table 19. Heritability, shared and nonshared environmental influences on NDDs, stratified by age categories.

| NDDs | Family $h^2$ (SE) | N | Family $c^2$ (SE) | N | Family $e^2$ (SE) | N | SNP $h^2$ (SE) | N |
|---|---|---|---|---|---|---|---|---|
| NDDs combined | | | | | | | | |
| Childhood (4-7y) | 0.63 (0.03) | 54 | 0.21 (0.04) | 36 | 0.27 (0.03) | 51 | 0.24 (0.11) | 6 |
| Middle childhood (8-10y) | 0.68 (0.04) | 54 | 0.12 (0.03) | 33 | 0.25 (0.02) | 51 | 0.26 (0.08) | 7 |
| Adolescence (11-24y) | 0.62 (0.04) | 79 | 0.17 (0.03) | 47 | 0.35 (0.03) | 72 | 0.23 (0.07) | 13 |
| Childhood & middle childhood (4-10y) | 0.67 (0.06) | 14 | 0.33 (0.08) | 7 | 0.21 (0.05) | 11 | - | - |
| Childhood & adolescence (4-24y) | 0.72 (0.07) | 40 | 0.20 (0.05) | 19 | 0.20 (0.03) | 31 | 0.17 (0.03) | 11 |
| Middle childhood & adolescence (8-24y) | 0.69 (0.04) | 50 | 0.14 (0.04) | 19 | 0.28 (0.03) | 31 | - | - |
| Communication disorders | | | | | | | | |
| Childhood (4-7y) | 0.56 (0.08) | 15 | 0.41 (0.07) | 12 | 0.21 (0.05) | 14 | - | - |
| Adolescence (11-24y) | 0.45 (0.07) | 7 | 0.26 (0.08) | 5 | 0.27 (0.06) | 5 | 0.32 (0.16) | 3 |
| Childhood & middle childhood (4-10y) | 0.92 (0.75) | 2 | - | - | - | - | - | - |
| ASD | | | | | | | | |
| Childhood (4-7y) | 0.69 (0.16) | 3 | - | - | 0.31 (0.08) | 3 | - | - |
| Middle childhood (8-10y) | 0.88 (0.40) | 11 | 0.13 (0.07) | 5 | 0.22 (0.05) | 9 | 0.26 (0.12) | 4 |
| Adolescence (11-24y) | 0.61 (0.07) | 9 | 0.31 (0.17) | 4 | 0.28 (0.07) | 7 | 0.16 (0.09) | 7 |
| Childhood & adolescence (4-24y) | 0.79 (0.17) | 5 | 0.02 (0.05) | 3 | 0.21 (0.13) | 4 | 0.13 (0.05) | 7 |
| Middle childhood & adolescence (8-24y) | 0.75 (0.07) | 10 | 0.13 (0.08) | 3 | 0.29 (0.04) | 8 | - | - |
| ADHD | | | | | | | | |
| Childhood (4-7y) | 0.64 (0.05) | 21 | 0.07 (0.06) | 7 | 0.33 (0.04) | 19 | 0.10 (0.17) | 2 |
| Middle childhood (8-10y) | 0.65 (0.07) | 28 | 0.07 (0.04) | 12 | 0.30 (0.04) | 28 | 0.19 (0.12) | 3 |
| Adolescence (11-24y) | 0.64 (0.05) | 44 | 0.23 (0.08) | 17 | 0.37 (0.03) | 39 | 0.09 (0.13) | 3 |
| Childhood & middle childhood (4-10y) | 0.68 (0.10) | 7 | 0.39 (0.13) | 2 | 0.27 (0.07) | 6 | - | - |
| Childhood & adolescence (4-24y) | 0.73 (0.08) | 24 | 0.19 (0.06) | 10 | 0.20 (0.04) | 20 | 0.21 (0.05) | 7 |
| Middle childhood & adolescence (8-24y) | 0.73 (0.06) | 19 | 0.04 (0.07) | 4 | 0.30 (0.04) | 15 | - | - |
| Specific learning disorders | | | | | | | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Childhood (4-7y) | 0.63 (0.05) | 18 | 0.18 (0.04) | 18 | 0.21 (0.03) | 18 | 0.29 (0.14) | 3 |
| Middle childhood (8-10y) | 0.62 (0.06) | 20 | 0.17 (0.04) | 18 | 0.26 (0.03) | 19 | - | - |
| Adolescence (11-24y) | 0.57 (0.03) | 33 | 0.17 (0.03) | 27 | 0.30 (0.03) | 29 | 0.31 (0.09) | 8 |
| Childhood & middle childhood (4-10y) | 0.59 (0.10) | 6 | 0.24 (0.13) | 5 | 0.24 (0.07) | 6 | - | - |
| Childhood & adolescence (4-24y) | 0.61 (0.10) | 11 | 0.22 (0.06) | 8 | 0.20 (0.05) | 8 | - | - |
| Middle childhood & adolescence (8-24y) | 0.65 (0.06) | 26 | 0.22 (0.06) | 13 | 0.18 (0.04) | 12 | - | - |
| Motor disorders | | | | | | | | |
| Childhood & adolescence (4-24y) | 0.73 (0.09) | 4 | 0.21 (0.15) | 2 | 0.20 (0.12) | 3 | - | - |
| Note. $H^2$= heritability; $c^2$= shared environmental influences; $e^2$= nonshared environmental influences; N= number of studies identified; SE= standard error. | | | | | | | | |

Supplementary Table 20. Genetic, shared and nonshared environmental correlations between NDDs, stratified by age categories.

| NDDs | Family rA (SE) | N | Family rC (SE) | N | Family rE (SE) | N | SNP rG (SE) | N |
|---|---|---|---|---|---|---|---|---|
| NDDs combined | | | | | | | | |
| Adolescence (11-24y) | 0.40 (0.23) | 11 | 0.80 (0.37) | 8 | 0.18 (0.05) | 10 | 0.73 (0.29) | 2 |
| Childhood & middle childhood (4-10y) | -0.17 (0.30) | 4 | - | - | 0.12 (0.10) | 3 | - | - |
| Childhood & adolescence (4-24y) | 0.16 (0.13) | 8 | - | 3 | 0.04 (0.07) | 4 | - | - |
| ASD & ADHD | | | | | | | | |
| Adolescence (11-24y) | 0.66 (0.49) | 3 | 0.15 (0.07) | 3 | 0.15 (0.07) | 3 | - | - |
| ADHD & specific learning disorders | | | | | | | | |
| Adolescence (11-24y) | -0.12 (0.16) | 5 | 0.26 (0.11) | 4 | 0.12 (0.06) | 4 | - | - |
| Childhood & middle childhood (4-10y) | -0.12 (0.36) | 3 | - | - | 0.12 (0.10) | 3 | - | - |
| Childhood & adolescence (4-24y) | -0.07 (0.20) | 3 | - | - | 0.05 (0.09) | 2 | - | - |
| Communication disorders & motor disorders | | | | | | | | |
| Childhood & adolescence (4-24y) | 0.33 (0.16) | 2 | - | - | - | - | - | - |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; N= number of studies identified; SE= standard error. | | | | | | | | |

Supplementary Table 21. Genetic, shared and nonshared environmental correlations between NDDs and DICCs, stratified by age categories.

| NDDs and DICCs | Family rA (SE) | N | Family rC (SE) | N | Family rE (SE) | N |
|---|---|---|---|---|---|---|
| NDDs and DICCs combined | | | | | | |
| Adolescence (11-24y) | 0.73 (.29) | 3 | 0.70 (0.63) | 2 | 0.82 (0.64) | 2 |
| Childhood & adolescence (4-24y) | 0.83 (0.61) | 3 | 0.09 (0.56) | 2 | 0.27 (0.08) | 3 |
| ADHD & conduct disorder | | | | | | |
| Childhood & adolescence (4-24y) | 0.90 (0.81) | 2 | - | - | 0.15 (0.18) | 2 |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; N= number of studies identified; SE= standard error. | | | | | | |

Supplementary Table 22. Heritability, shared and nonshared environmental influences on NDDs, stratified by countries.

| NDDs | Family $h^2$ (SE) | N | Family $c^2$ (SE) | N | Family $e^2$ (SE) | N | SNP $h^2$ (SE) | N |
|---|---|---|---|---|---|---|---|---|
| NDDs combined | | | | | | | | |
| Australia | 0.76 (0.17) | 11 | 0.21 (0.07) | 9 | 0.17 (0.05) | 8 | - | - |
| Australia & United States & Norway & Sweden | 0.74 (0.13) | 2 | 0.05 (0.11) | 2 | 0.24 (0.09) | 2 | - | - |
| Canada | 0.43 (0.09) | 7 | 0.18 (0.09) | 6 | 0.38 (0.07) | 6 | - | - |
| China | 0.5 (0.15) | 4 | 0.3 (0.13) | 3 | 0.29 (0.12) | 4 | - | - |
| Netherlands | 0.52 (0.26) | 19 | 0.12 (0.12) | 5 | 0.37 (0.13) | 17 | 0.47 (0.22) | 3 |
| Norway | 0.53 (0.09) | 2 | 0.25 (0.23) | 2 | 0.28 (0.14) | 2 | - | - |
| Sweden | 0.74 (0.05) | 24 | 0.07 (0.04) | 9 | 0.28 (0.03) | 22 | - | - |
| United Kingdom | 0.7 (0.06) | 96 | 0.18 (0.02) | 53 | 0.27 (0.02) | 85 | 0.22 (0.06) | 14 |
| United States | 0.61 (0.04) | 77 | 0.22 (0.03) | 44 | 0.32 (0.04) | 53 | - | - |
| Intellectual disabilities | | | | | | | | |
| Sweden | 0.86 (0.44) | 2 | - | - | 0.1 (0.16) | 2 | - | - |
| Communication disorders | | | | | | | | |
| Canada | 0.32 (0.2) | 2 | 0.38 (0.18) | 2 | 0.35 (0.12) | 2 | - | - |
| Netherlands | 0.45 (0.19) | 2 | - | - | 0.3 (0.18) | 2 | - | - |
| United Kingdom | 0.77 (0.41) | 17 | 0.35 (0.07) | 11 | 0.2 (0.04) | 13 | 0.32 (0.14) | 4 |
| United States | 0.71 (0.38) | 2 | - | - | - | - | - | - |
| ASD | | | | | | | | |
| Netherlands | 0.5 (0.17) | 2 | - | - | 0.52 (0.16) | 2 | - | - |
| Sweden | 0.74 (0.05) | 10 | 0.09 (0.06) | 5 | 0.28 (0.04) | 9 | - | - |
| United Kingdom | 0.8 (0.24) | 20 | 0.19 (0.08) | 8 | 0.24 (0.04) | 15 | 0.18 (0.08) | 7 |
| United States | 0.8 (0.5) | 3 | - | - | - | - | - | - |
| ADHD | | | | | | | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Australia | 0.83 (0.31) | 7 | 0.26 (0.11) | 6 | 0.11 (0.05) | 5 | - | - |
| Australia & United States & Norway & Sweden | 0.73 (0.14) | 2 | 0.03 (0.12) | 2 | 0.26 (0.1) | 2 | - | - |
| Canada | 0.45 (0.16) | 3 | - | - | 0.38 (0.19) | 2 | - | - |
| China | 0.49 (0.33) | 2 | 0.26 (0.17) | 2 | 0.31 (0.24) | 2 | - | - |
| Netherlands | 0.52 (0.27) | 15 | 0.05 (0.08) | 4 | 0.28 (0.03) | 12 | 0.42 (0.24) | 2 |
| Sweden | 0.75 (0.07) | 18 | 0.04 (0.06) | 6 | 0.27 (0.04) | 17 | - | - |
| United Kingdom | 0.71 (0.03) | 42 | 0.2 (0.11) | 14 | 0.29 (0.02) | 39 | 0.08 (0.11) | 4 |
| United States | 0.62 (0.06) | 30 | 0.12 (0.06) | 12 | 0.38 (0.05) | 25 | - | - |
| Specific learning disorders | | | | | | | | |
| Australia | 0.72 (0.11) | 5 | 0.09 (0.07) | 4 | 0.23 (0.06) | 4 | - | - |
| Canada | 0.53 (0.13) | 4 | 0.1 (0.11) | 4 | 0.39 (0.09) | 4 | - | - |
| Netherlands | 0.59 (0.19) | 2 | - | - | 0.33 (0.13) | 2 | - | - |
| United Kingdom | 0.59 (0.03) | 33 | 0.17 (0.03) | 26 | 0.29 (0.02) | 29 | 0.31 (0.08) | 8 |
| United States | 0.57 (0.05) | 47 | 0.24 (0.04) | 33 | 0.21 (0.03) | 30 | - | - |
| Motor disorders | | | | | | | | |
| Sweden | 0.69 (0.12) | 4 | 0.06 (0.17) | 2 | 0.36 (0.12) | 4 | - | - |
| Note. $H^2$= heritability; $c^2$= shared environmental influences; $e^2$= nonshared environmental influences; N= number of studies identified; SE= standard error. | | | | | | | | |

Supplementary Table 23. Genetic, shared and nonshared environmental correlations between NDDs, stratified by countries.

| NDDs | Family rA (SE) | N | Family rC (SE) | N | Family rE (SE) | N | SNP rG (SE) | N |
|---|---|---|---|---|---|---|---|---|
| NDDs combined | | | | | | | | |
| Australia | 0.27 (0.08) | 2 | 0.1 (0.09) | 2 | 0.02 (0.08) | 2 | - | - |
| Canada | -0.44 (0.24) | 2 | 0.19 (0.2) | 2 | 0.16 (0.15) | 2 | - | - |
| Sweden | 0.8 (0.26) | 3 | - | - | 0.36 (0.12) | 2 | - | - |
| United Kingdom | 0.37 (0.1) | 18 | 0.91 (0.29) | 10 | 0.16 (0.04) | 14 | 0.74 (0.28) | 2 |
| United States | 0.44 (0.07) | 11 | 0.07 (0.2) | 2 | - | - | - | - |
| ASD & ADHD | | | | | | | | |
| Sweden | 0.8 (0.25) | 3 | - | - | 0.36 (0.12) | 2 | - | - |
| United Kingdom | 0.28 (0.09) | 3 | - | - | 0.1 (0.07) | 3 | - | - |
| ADHD & specific learning disorders | | | | | | | | |
| Canada | -0.44 (0.24) | 2 | 0.19 (0.2) | 2 | 0.16 (0.15) | 2 | - | - |
| United Kingdom | 0.06 (0.16) | 6 | 0.48 (0.2) | 3 | 0.13 (0.05) | 5 | - | - |
| United States | 0.39 (0.09) | 8 | - | - | - | - | - | - |
| Communication disorders & specific learning disorders | | | | | | | | |
| United Kingdom | 0.66 (0.15) | 2 | - | - | - | - | - | - |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; N= number of studies identified; SE= standard error. | | | | | | | | |

Supplementary Table 24. Genetic, shared and nonshared environmental correlations between NDDs and DICCs, stratified by countries.

| NDDs and DICCs | Family rA (SE) | N | Family rC (SE) | N | Family rE (SE) | N |
|---|---|---|---|---|---|---|
| NDDs and DICCs combined | | | | | | |
| Sweden | 0.68 (0.41) | 3 | 0.89 (0.55) | 2 | 0.68 (0.64) | 3 |
| United Kingdom | 0.58 (0.29) | 3 | 0.97 (0.57) | 3 | 0.49 (0.44) | 3 |
| United States | 0.42 (0.15) | 6 | 0.85 (0.55) | 5 | 0.24 (0.09) | 4 |
| ADHD & conduct disorder | | | | | | |
| United States | 0.41 (0.17) | 3 | 0.99 (0.28) | 2 | 0.12 (0.14) | 2 |
| ADHD & oppositional defiant disorder | | | | | | |
| United States | 0.59 (0.32) | 3 | 0.99 (0.57) | 2 | 0.25 (0.14) | 2 |
| ASD & conduct disorder | | | | | | |
| United Kingdom | 0.33 (0.13) | 2 | 0.93 (0.77) | 2 | 0.04 (0.08) | 2 |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; N= number of studies identified; SE= standard error. | | | | | | |

Supplementary Table 25. Heritability, shared and nonshared environmental influences on NDDs, stratified by the percentage of individuals of European ancestry.

| NDDs | Family $h^2$ (SE) | N | Family $c^2$ (SE) | N | Family $e^2$ (SE) | N | SNP $h^2$ (SE) | N |
|---|---|---|---|---|---|---|---|---|
| NDDs combined | | | | | | | | |
| Less than 50% | 0.46 (0.07) | 7 | 0.24 (0.08) | 6 | 0.43 (0.08) | 7 | - | - |
| 50-74% | 0.47 (0.08) | 12 | 0.24 (0.08) | 9 | 0.32 (0.13) | 9 | - | - |
| 75-99% | 0.71 (0.07) | 37 | 0.24 (0.06) | 15 | 0.25 (0.03) | 32 | - | - |
| 100% | 0.66 (0.06) | 41 | 0.19 (0.04) | 29 | 0.32 (0.05) | 40 | 0.19 (0.03) | 29 |
| Communication disorders | | | | | | | | |
| 75-99% | 0.59 (0.27) | 3 | 0.36 (0.15) | 3 | 0.16 (0.11) | 3 | - | - |
| 100% | 0.56 (0.09) | 11 | 0.33 (0.1) | 8 | 0.24 (0.06) | 10 | 0.32 (0.14) | 4 |
| ASD | | | | | | | | |
| 75-99% | 0.91 (0.57) | 9 | - | - | 0.29 (0.06) | 6 | - | - |
| ADHD | | | | | | | | |
| Less than 50% | 0.41 (0.12) | 3 | 0.17 (0.15) | 2 | 0.54 (0.09) | 3 | - | - |
| 50-74% | 0.49 (0.11) | 5 | 0.18 (0.13) | 3 | 0.35 (0.19) | 4 | - | - |
| 75-99% | 0.73 (0.06) | 20 | 0.17 (0.07) | 6 | 0.27 (0.04) | 19 | - | - |
| 100% | 0.67 (0.04) | 11 | 0.04 (0.09) | 3 | 0.39 (0.05) | 10 | 0.2 (0.04) | 14 |
| Specific learning disorders | | | | | | | | |
| Less than 50% | 0.54 (0.16) | 5 | 0.25 (0.09) | 5 | 0.28 (0.06) | 5 | - | - |
| 50-74% | 0.52 (0.1) | 7 | 0.24 (0.1) | 6 | 0.24 (0.06) | 6 | - | - |
| 75-99% | 0.55 (0.09) | 7 | 0.29 (0.12) | 6 | 0.19 (0.06) | 6 | - | - |
| 100% | 0.61 (0.04) | 22 | 0.16 (0.04) | 19 | 0.3 (0.07) | 21 | 0.3 (0.08) | 9 |
| Motor disorders | | | | | | | | |
| 100% | 0.8 (0.05) | 2 | - | - | 0.47 (0.27) | 2 | - | - |
| Note. $H^2$= heritability; $c^2$= shared environmental influences; $e^2$= nonshared environmental influences; N= number of studies identified; SE= standard error. | | | | | | | | |

Supplementary Table 26. Genetic, shared and nonshared environmental correlations between NDDs, stratified by the percentage of individuals of European ancestry.

| NDDs | Family rA (SE) | N | Family rC (SE) | N | Family rE (SE) | N | SNP rG (SE) | N |
|---|---|---|---|---|---|---|---|---|
| NDDs combined | | | | | | | | |
| 75-99% | 0.63 (0.44) | 2 | - | - | - | - | - | - |
| 100% | 0.54 (0.1) | 4 | 0.93 (0.18) | 2 | 0.24 (0.09) | 4 | 0.39 (0.19) | 6 |
| ASD & ADHD | | | | | | | | |
| 100% | - | - | - | - | - | - | 0.26 (0.14) | 5 |
| ADHD & specific learning disorders | | | | | | | | |
| 100% | 0.48 (0.13) | 2 | - | - | 0.26 (0.15) | 2 | - | - |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; N= number of studies identified; SE= standard error. | | | | | | | | |

Supplementary Table 27. Genetic, shared and nonshared environmental correlations between NDDs and DICCs, stratified by the percentage of individuals of European ancestry.

| NDDs and DICCs | Family rA (SE) | N | Family rC (SE) | N | Family rE (SE) | N |
|---|---|---|---|---|---|---|
| NDDs and DICCs combined | | | | | | |
| 75-99% | 0.57 (0.25) | 3 | 0.88 (0.87) | 2 | - | - |
| 100% | 0.71 (0.31) | 2 | 0.89 (0.85) | 2 | 0.74 (0.49) | 2 |
| ADHD & conduct disorder | | | | | | |
| 75-99% | 0.41 (0.22) | 2 | - | - | - | - |
| ADHD & oppositional defiant disorder | | | | | | |
| 75-99% | 0.61 (0.48) | 2 | - | - | - | - |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; N= number of studies identified; SE= standard error. | | | | | | |

Supplementary Table 28. Heritability, shared and nonshared environmental influences on NDDs, stratified by measurement scales.

| NDDs | Family $h^2$ (SE) | N | Family $c^2$ (SE) | N | Family $e^2$ (SE) | N | SNP $h^2$ (SE) | N |
|---|---|---|---|---|---|---|---|---|
| NDDs combined | | | | | | | | |
| Categorical | 0.77 (0.07) | 28 | 0.19 (0.08) | 12 | 0.28 (0.06) | 25 | 0.17 (0.03) | 12 |
| Continuous | 0.64 (0.03) | 215 | 0.16 (0.02) | 116 | 0.28 (0.01) | 175 | 0.25 (0.06) | 17 |
| Intellectual disabilities | | | | | | | | |
| Categorical | 0.86 (0.44) | 2 | - | - | 0.1 (0.16) | 2 | - | - |
| Communication disorders | | | | | | | | |
| Categorical | 0.67 (0.24) | 6 | 0.47 (0.12) | 4 | 0.13 (0.06) | 5 | - | - |
| Continuous | 0.65 (0.2) | 19 | 0.3 (0.06) | 12 | 0.25 (0.05) | 14 | 0.32 (0.14) | 4 |
| ASD | | | | | | | | |
| Categorical | 0.83 (0.08) | 11 | 0.03 (0.08) | 5 | 0.18 (0.06) | 9 | 0.13 (0.05) | 7 |
| Continuous | 0.72 (0.15) | 29 | 0.18 (0.07) | 9 | 0.27 (0.03) | 23 | 0.2 (0.08) | 8 |
| ADHD | | | | | | | | |
| Categorical | 0.79 (0.1) | 13 | 0.05 (0.08) | 5 | 0.26 (0.07) | 12 | 0.21 (0.04) | 8 |
| Continuous | 0.66 (0.04) | 109 | 0.11 (0.03) | 43 | 0.31 (0.02) | 96 | 0.16 (0.1) | 6 |
| Specific learning disorders | | | | | | | | |
| Continuous | 0.62 (0.04) | 89 | 0.19 (0.02) | 65 | 0.24 (0.02) | 67 | 0.31 (0.08) | 8 |
| Motor disorders | | | | | | | | |
| Categorical | 0.72 (0.08) | 5 | 0.13 (0.11) | 3 | 0.38 (0.12) | 6 | - | - |
| Continuous | 0.69 (0.2) | 3 | - | - | - | - | - | - |
| Note. $H^2$= heritability; $c^2$= shared environmental influences; $e^2$= nonshared environmental influences; N= number of studies identified; SE= standard error. | | | | | | | | |

Supplementary Table 29. Genetic, shared and nonshared environmental correlations between NDDs, stratified by measurement scales.

| NDDs co-occurrences | Family rA (SE) | N | Family rC (SE) | N | Family rE (SE) | N | SNP rG (SE) | N |
|---|---|---|---|---|---|---|---|---|
| NDDs combined | | | | | | | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Categorical | 0.56 (0.32) | 3 | - | - | - | - | - | - |
| Continuous | 0.31 (0.12) | 34 | 0.67 (0.33) | 15 | 0.18 (0.05) | 21 | 0.74 (0.28) | 2 |
| ASD & ADHD | | | | | | | | |
| Continuous | 0.56 (0.34) | 5 | - | - | 0.22 (0.13) | 5 | - | - |
| ADHD & motor disorders | | | | | | | | |
| Categorical | 0.9 (0.82) | 2 | - | - | - | - | - | - |
| ADHD & specific learning disorders | | | | | | | | |
| Continuous | 0.06 (0.12) | 17 | 0.32 (0.14) | 7 | 0.11 (0.04) | 9 | - | - |
| Communication disorders & specific learning disorders | | | | | | | | |
| Continuous | 0.66 (0.15) | 2 | - | - | - | - | - | - |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; N= number of studies identified; SE= standard error. | | | | | | | | |

Supplementary Table 30. Genetic, shared and nonshared environmental correlations between NDDs and DICCs, stratified by measurement scales.

| Co-occurrences between NDDs and DICCs | Family rA (SE) | N | Family rC (SE) | N | Family rE (SE) | N |
|---|---|---|---|---|---|---|
| NDDs and DICCs combined | | | | | | |
| Continuous | 0.62 (0.19) | 15 | 0.88 (0.34) | 11 | 0.38 (0.14) | 13 |
| ADHD & conduct disorder | | | | | | |
| Continuous | 0.66 (0.36) | 6 | 0.94 (0.71) | 3 | 0.11 (0.08) | 5 |
| ADHD & oppositional defiant disorder | | | | | | |
| Continuous | 0.66 (0.18) | 6 | 0.96 (0.57) | 4 | 0.54 (0.25) | 5 |
| ASD & conduct disorder | | | | | | |
| Continuous | 0.35 (0.10) | 3 | 0.88 (0.57) | 3 | 0.07 (0.08) | 3 |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; N= number of studies identified; SE= standard error. | | | | | | |

Supplementary Table 31. Overview of family-based studies using samples of males and females combined. Co-occurrences between disorders annotated with an asterisk (*) indicate pairs of disorders for which meta-analysis could not be performed.

| Reference | Cohort | Age category | Country |
|---|---|---|---|
| Heritability and environmental influences on intellectual disabilities | | | |
| (Du Rietz et al., 2021b) | Medical Birth Register, Multi-Generation Register | Childhood & Adolescence | Sweden |
| (M. J. Taylor et al., 2019b) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood & Adolescence | Sweden |
| Heritability and environmental influences on communication disorders | | | |
| (Bishop & Hayiou-Thomas, 2008) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (Cheesman et al., 2017) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Dethorne et al., 2006) | Western reserve twin project (WRTP) | Childhood | United States |
| (Hayiou-Thomas et al., 2012) | Twins Early Development Study (TEDS) | Childhood & Middle Childhood | United Kingdom |
| (Hayiou-Thomas et al., 2014) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (Hohnen & Stevenson, 1999) | Twin study in London | Childhood | United Kingdom |
| (Tomblin & Buckwalter, 1998) | Twin study in Iowa | Childhood | United States |
| (Trzaskowski, Dale, et al., 2013) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Van Beijsterveldt et al., 2010) | Netherlands twin register (NTR) | Childhood | Netherlands |
| (Bishop, 2002) | Twin study in the United Kingdom | Childhood & Adolescence | United Kingdom |
| (Bishop, 2005) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (Bishop, Adams, et al., 2006) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (Bishop, Laws, et al., 2006) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |

| | | | |
|---|---|---|---|
| (Bishop et al., 1996) | Twin study in the United Kingdom | Childhood & Middle Childhood | United Kingdom |
| (Dale et al., 2018) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Dionne et al., 2011) | The Quebec Newborn Twin Study (QNTS) | Childhood | Canada |
| (Dworzynski et al., 2007) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (Hoekstra et al., 2009) | Netherlands twin register (NTR) | Middle Childhood & Adolescence | Netherlands |
| (Mimeau et al., 2018) | The Quebec Newborn Twin Study (QNTS) | Childhood | Canada |
| (Price et al., 2004) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (Tosto et al., 2017) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (Trzaskowski, Davis, et al., 2013) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Viding et al., 2004) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| Heritability and environmental influences on ASD | | | |
| (Bailey et al., 2013) | The twin study of Folstein & Rutter | Childhood & Adolescence | United Kingdom |
| (Cheesman et al., 2017) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Deng et al., 2015) | Twin study in China | Childhood & Adolescence | China |
| (Du Rietz et al., 2021b) | Medical Birth Register, Multi-Generation Register | Childhood & Adolescence | Sweden |
| (Dworzynski et al., 2008) | Twins Early Development Study (TEDS) | Childhood & Middle Childhood | United Kingdom |
| (Dworzynski et al., 2009) | Twins Early Development Study (TEDS) | Middle Childhood & Adolescence | United Kingdom |
| (Frazier et al., 2014) | Interactive Autism Network (IAN) | Middle Childhood | United States |
| (Hallett et al., 2009) | Twins Early Development Study | Middle Childhood | United Kingdom |

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| | (TEDS) | | |
| (Hoekstra et al., 2007) | Netherlands twin register (NTR) | Adolescence | Netherlands |
| (Jones et al., 2009) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Lichtenstein et al., 2010) | Swedish Twin Register | Middle Childhood | Sweden |
| (Lundström et al., 2012) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood & Adolescence | Sweden |
| (Pinto et al., 2016) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Polderman et al., 2006) | Netherlands twin register (NTR) | Childhood | Netherlands |
| (E. B. Robinson et al., 2011) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (E. B. Robinson et al., 2012) | Twins Early Development Study (TEDS) | Middle Childhood & Adolescence | United Kingdom |
| (Ronald, Happé, Bolton, et al., 2006) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Ronald, Happé, Price, et al., 2006) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Ronald et al., 2014) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood & Adolescence | Sweden |
| (Ronald et al., 2008) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Scherff et al., 2014) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Scourfield et al., 2004) | The Cardiff Study of All Wales and Northwest of England Twins (CaStANET) | Childhood & Adolescence | United Kingdom |
| (M. J. Taylor et al., 2018) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood & Adolescence | Sweden |
| (M. J. Taylor et al., 2019b) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood & Adolescence | Sweden |

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| (M. J. Taylor et al., 2020) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood & Adolescence | Sweden |
| (M. J. Taylor et al., 2015) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Tick et al., 2016) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Towers et al., 2000) | The Nonshared Environment in Adolescent Development (NEAD) | Adolescence | United States |
| (Trzaskowski, Dale, et al., 2013) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Yip et al., 2018) | Swedish Medical Register, Multi-Generation Register | Childhood | Sweden |
| (Hallmayer et al., 2011) | California Autism Twins Study | Adolescence | United States |
| (Lundström et al., 2011) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood & Adolescence | Sweden |
| (Taniai et al., 2008) | Nagoya North District Care Center for Disabled Children, Nagoya Child Welfare Center, and Nagoya West District Care Center for Disabled Children | Childhood & Adolescence | Japan |
| (Lundström et al., 2010) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood & Adolescence | Sweden |
| (Colvert et al., 2015) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Ronald et al., 2005) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| Heritability and environmental influences on ADHD | | | |
| (Boomsma et al., 2021) | The Young Netherlands Twin Register (YNTR) | Middle Childhood | Netherlands |
| (Brikell et al., 2016) | Twin Study of Child and Adolescent Development (TCHAD) | Middle Childhood | Sweden |
| (Brooker et al., 2020) | Wisconsin Twin Panel | Adolescence | United States |

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| (Burt et al., 2001) | The Minnesota Twin Family Study (MTFS) | Middle Childhood & Adolescence | United States |
| (Burt et al., 2012) | The Michigan State University Twin Registry | Childhood & Middle Childhood | United States |
| (Chang et al., 2012) | Twin Study of Child and Adolescent Development (TCHAD) | Middle Childhood & Adolescence | Sweden |
| (Chang et al., 2013) | Twin Study of Child and Adolescent Development (TCHAD) | Middle Childhood | Sweden |
| (Cheesman et al., 2017) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (T. J. Chen et al., 2016) | Chinese Child and Adolescent Twin Register | Childhood & Adolescence | China |
| (Cheung et al., 2014) | Twins Early Development Study (TEDS) | Childhood & Middle Childhood | United Kingdom |
| (Coolidge et al., 2000) | Twin study in Colorado | Middle Childhood | United States |
| (Curran et al., 2003) | The Childhood Hyperactivity and Inattention Project (CHIP) | Childhood & Adolescence | United Kingdom |
| (de Zeeuw et al., 2015) | Netherlands twin register (NTR) | Childhood | Netherlands |
| (Derks et al., 2008) | Netherlands twin register (NTR) | Childhood | Netherlands |
| (Derks et al., 2007) | Netherlands twin register (NTR) | Childhood | Netherlands |
| (Derks et al., 2006) | Netherlands twin register (NTR) | Childhood | Netherlands |
| (Dick et al., 2005) | The Finnish Twin Cohort Study | Adolescence | Finland |
| (Dolan et al., 2020) | Netherlands twin register (NTR) | Adolescence | Netherlands |
| (Du Rietz et al., 2021b) | Medical Birth Register, Multi-Generation Register | Childhood & Adolescence | Sweden |
| (Ebejer et al., 2010) | Australian Twin Register, Colorado Birth Registry, and Medical Birth Registries in Norway and Sweden | Childhood | Australia, United States, Norway, Sweden |
| (Ebejer et al., 2015) | The Brisbane Longitudinal Twin Study | Middle Childhood & Adolescence | Australia |
| (Edelbrock et al., 1995) | Western reserve twin project (WRTP) | Childhood & Adolescence | United States |

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| (Gould et al., 2018) | National Assessment Program in Numeracy and Literacy (NAPLAN) | Childhood & Adolescence | Australia |
| (Greven, Asherson, et al., 2011) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Greven, Harlaar, et al., 2011) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Greven et al., 2014) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Greven et al., 2012) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Greven, Rijsdijk, et al., 2011) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Hay et al., 2007) | The Australian Twin ADHD Project (ATAP) | Childhood & Middle Childhood | Australia |
| (Heutink et al., 2006) | Netherlands twin register (NTR) | Childhood | Netherlands |
| (Hudziak et al., 2005) | Netherlands twin register (NTR) | Childhood | Netherlands |
| (Y.-M. Hur, 2014) | The South Korean Twin Registry (SKTR) | Childhood | South Korea |
| (Jaffee et al., 2012) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Johnson et al., 2005) | The Minnesota Twin Family Study (MTFS) | Adolescence | United States |
| (Kan et al., 2013) | Netherlands twin register (NTR) | Childhood & Middle Childhood | Netherlands |
| (Kan et al., 2014) | Netherlands twin register (NTR) | Adolescence | Netherlands |
| (Kuja-Halkola et al., 2015) | Twin Study of Child and Adolescent Development (TCHAD) | Middle Childhood | Sweden |
| (Kuntsi & Stevenson, 2001) | Twin study in Southern England | Childhood & Adolescence | United Kingdom |
| (Kuntsi et al., 2014) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Kuntsi et al., 2000) | Twins Early Development Study (TEDS) | Childhood & Adolescence | United Kingdom |

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| (Kuntsi et al., 2005) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (H. Larsson et al., 2012) | Swedish Twin Register | Middle Childhood & Adolescence | Sweden |
| (H. Larsson et al., 2011) | Twin Study of Child and Adolescent Development (TCHAD) | Middle Childhood & Adolescence | Sweden |
| (Lemery-Chalfant et al., 2008) | Wisconsin Twin Panel | Middle Childhood | United States |
| (Levy et al., 1997) | The Australian Twin ADHD Project (ATAP) | Childhood & Adolescence | Australia |
| (Lewis & Plomin, 2015) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (Lewis et al., 2014) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Lichtenstein et al., 2010) | Swedish Twin Register | Middle Childhood | Sweden |
| (Lifford et al., 2009) | The Cardiff Study of All Wales and Northwest of England Twins (CaStANET), South Wales Family Study (SWFS) | Adolescence | United Kingdom |
| (Little et al., 2016) | Florida Twin Project on Behavior and Environment (FTP-BE) | Adolescence | United States |
| (LoParo & Waldman, 2014) | Twin study in Georgia | Middle Childhood | United States |
| (N. C. Martin, Piek, et al., 2006) | The Australian Twin ADHD Project (ATAP) | Childhood & Adolescence | Australia |
| (McLoughlin et al., 2007) | Twins Early Development Study (TEDS) | Childhood & Middle Childhood | United Kingdom |
| (Merwood et al., 2013) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Michelini et al., 2015) | The Genesis 12-19 (G1219) Study | Adolescence | United Kingdom |
| (Mikolajewski et al., 2013) | The Florida Twin Project on Reading (FTP-R) | Childhood & Adolescence | United States |
| (Molenaar et al., 2015) | Netherlands twin register (NTR) | Childhood | Netherlands |
| (Moruzzi et al., 2014) | Twin study in Italy | Middle Childhood & Adolescence | Italy |

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| (Nikolas et al., 2015) | The Michigan State University Twin Registry (MSUTR) | Childhood & Adolescence | United States |
| (Niv et al., 2012) | Southern California Twin Project | Adolescence | United States |
| (Paloyelis et al., 2010b) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Peng et al., 2016) | Missouri Twin Study | Adolescence | United States |
| (Pingault et al., 2015) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Pinto et al., 2016) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Plourde et al., 2015) | The Quebec Newborn Twin Study (QNTS) | Childhood & Middle Childhood | Canada |
| (Plourde et al., 2017) | The Quebec Newborn Twin Study (QNTS) | Adolescence | Canada |
| (Polderman, Huizink, et al., 2011) | Netherlands twin register (NTR) | Childhood | Netherlands |
| (Polderman et al., 2006) | Netherlands twin register (NTR) | Childhood | Netherlands |
| (Polderman, Van Dongen, et al., 2011) | Netherlands twin register (NTR) | Adolescence | Netherlands |
| (Price et al., 2005) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (Quinn et al., 2016) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood & Adolescence | Sweden |
| (Ronald et al., 2014) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood & Adolescence | Sweden |
| (Ronald et al., 2008) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Rosenberg et al., 2012) | Colorado Learning Disabilities Research Center | Middle Childhood & Adolescence | United States |
| (Rydell et al., 2017) | Preschool Twin Study in Sweden (PETSS) | Childhood | Sweden |
| (Saudino & Plomin, 2007) | Twins Early Development Study | Childhood | United Kingdom |

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| | (TEDS) | | |
| (Saunders et al., 2019) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood & Adolescence | Sweden |
| (Siebelink et al., 2019) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Simonoff et al., 1998) | Virginia twin study of adolescent behavioral development (VTSABD) | Adolescence | United States |
| (Stern et al., 2020) | E-RISK | Childhood | United Kingdom |
| (Stevenson, 1992) | Twin study in London | Adolescence | United Kingdom |
| (Stevenson et al., 1993) | Twin study in London | Adolescence | United Kingdom |
| (M. J. Taylor et al., 2019b) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood & Adolescence | Sweden |
| (J. Taylor et al., 2013) | The Florida Twin Project on Reading (FTP-R) | Childhood & Adolescence | United States |
| (M. J. Taylor et al., 2015) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Thapar et al., 1995) | The Cardiff Births Survey (CBS) | Middle Childhood & Adolescence | United Kingdom |
| (Towers et al., 2000) | The Nonshared Environment in Adolescent Development (NEAD) | Adolescence | United States |
| (Trzaskowski, Dale, et al., 2013) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Tuvblad et al., 2009) | UoC Twin Study of Risk Factors for Antisocial Behavior | Middle Childhood | United States |
| (Tye et al., 2012) | Twins Early Development Study (TEDS), The Neurophysiological Study of Activity and Attention in Twins (NEAAT) | Middle Childhood & Adolescence | United Kingdom |
| (Vendlinski et al., 2014) | Wisconsin Twin Panel | Childhood | United States |
| (Waszczuk et al., 2021) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Willcutt et al., 2007) | Colorado Twin Register, Autstralian | Childhood | Australia, United States, Norway, |

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| | Twin Register, Medical Birth Register | | Sweden |
| (Willcutt et al., 2010) | Colorado Learning Disabilities Research Center | Middle Childhood & Adolescence | United States |
| (Wood et al., 2009) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Wood et al., 2011) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Wood et al., 2008) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Zheng et al., 2020) | Qingdao Twin Registry (QTR) | Adolescence | China |
| (Zumberge et al., 2007) | The Southern California Twin register | Middle Childhood | United States |
| (Burt et al., 2005) | The Minnesota Twin Family Study (MTFS) | Middle Childhood & Adolescence | United States |
| (Q. Chen et al., 2017) | Medical Birth Register, The Swedish Twin Register, The Multi-Generation Register | Childhood & Adolescence | Sweden |
| (Crosbie et al., 2013) | Ontario Science Centre (OSC) | Childhood | Canada |
| (Eilertsen et al., 2019) | The Norwegian mother and child cohort study (MoBa) | Childhood | Norway |
| (Fedko et al., 2017) | Netherlands twin register (NTR) | Middle Childhood | Netherlands |
| (Haberstick et al., 2008) | National Longitudinal Study of Adolescent Health | Childhood & Adolescence | United States |
| (Lundström et al., 2011) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood & Adolescence | Sweden |
| (N. C. Martin, Levy, et al., 2006) | The Australian Twin ADHD Project (ATAP) | Childhood & Adolescence | Australia |
| (Merwood et al., 2013) | Twin Study of Child and Adolescent Development (TCHAD) | Adolescence | Sweden |
| (Mogensen et al., 2011) | Twin Study of Child and Adolescent Development (TCHAD) | Adolescence | Sweden |
| (Nadder et al., 1998) | Virginia twin study of adolescent | Childhood & Adolescence | United States |

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| | behavioral development (VTSABD) | | |
| (Rhee et al., 1999) | Australian Twin Register | Childhood & Adolescence | Australia |
| (Rimfeld et al., 2022) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Singh & Waldman, 2010) | Georgia Twin Register | Childhood & Adolescence | United States |
| (Willcutt et al., 2000a) | Colorado Learning Disabilities Research Center | Middle Childhood & Adolescence | United States |
| (Willcutt et al., 2007) | Colorado Learning Disabilities Research Center | Middle Childhood & Adolescence | United States |
| (Merwood et al., 2014) | The Cardiff Study of All Wales and Northwest of England Twins (CaStANET) | Childhood & Adolescence | United Kingdom |
| (Thapar et al., 2000) | The Greater Manchester Twin Register | Childhood & Adolescence | United Kingdom |
| (Ehringer et al., 2006) | Colorado Twin Register | Adolescence | United States |
| (Smith et al., 2011) | Center for AntisocialDrug Dependence (CADD) | Adolescence | United States |
| (Thapar et al., 2001) | The Greater Manchester Twin Register | Childhood & Adolescence | United Kingdom |
| (N. Martin et al., 2002) | Twin study in South Wales | Childhood & Adolescence | United Kingdom |
| Heritability and environmental influences on specific learning disorders | | | |
| (Alarcón et al., 1997) | Colorado Learning Disabilities Research Center | Middle Childhood & Adolescence | United States |
| (Bishop, 2001) | Local United Kingdom sample | Childhood & Adolescence | United Kingdom |
| (Cheesman et al., 2017) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Cheung et al., 2014) | Twins Early Development Study (TEDS) | Childhood & Middle Childhood | United Kingdom |
| (C. J. Davis et al., 2001) | Colorado Twin Study of Reading Disability | Middle Childhood & Adolescence | United States |
| (O. S. P. Davis et al., 2008) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |

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| (O. S. P. Davis et al., 2014) | Twins Early Development Study (TEDS), Avon Longitudinal Study of Parents and Children (ALSPAC) | Adolescence | United Kingdom |
| (DeFries & Alarcón, 1996) | Colorado Learning Disabilities Research Center | Middle Childhood & Adolescence | United States |
| (DeFries et al., 1999) | Colorado Learning Disabilities Research Center | Middle Childhood & Adolescence | United States |
| (Ebejer et al., 2010) | Australian Twin Register, Colorado Birth Registry, Medical Birth Registries in Norway and Sweden | Middle Childhood | Australia, United States, Norway, Sweden |
| (Erbeli et al., 2018) | The Florida Twin Project on Reading (FTP-R) | Childhood & Adolescence | United States |
| (Erbeli et al., 2019) | Florida Twin Project on Behavior and Environment (FTP-BE) | M(Gayán & Olson, 2001)d States | |
| (Gayán & Olson, 2001) | Colorado Learning Disabilities Research Center | Middle Childhood & Adolescence | United States |
| (Greven, Harlaar, et al., 2011) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Greven et al., 2014) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Greven et al., 2012) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Harlaar et al., 2012) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Harlaar et al., 2014) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (S. A. Hart et al., 2009) | Western reserve twin project (WRTP) | Childhood & Middle Childhood | United States |
| (Hensler et al., 2010) | The Florida Twin Project on Reading (FTP-R) | Childhood | United States |
| (Hohnen & Stevenson, 1999) | Twin study in London | Childhood | United Kingdom |
| (Kovas et al., 2007) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |

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| (Little et al., 2016) | Florida Twin Project on Behavior and Environment (FTP-BE) | Adolescence | United States |
| (Marlow et al., 2001) | Twin study in Reading | Childhood & Adolescence | United Kingdom |
| (Newsome et al., 2014) | The Early Childhood Longitudinal Study (ECLS) | Childhood | United States |
| (Olson et al., 1991) | Colorado Reading Project | Childhood & Adolescence | United States |
| (Paloyelis et al., 2010b) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Petrill et al., 2007) | Western reserve twin project (WRTP) | Childhood & Middle Childhood | United States |
| (Plourde et al., 2015) | The Quebec Newborn Twin Study (QNTS) | Childhood & Middle Childhood | Canada |
| (Plourde et al., 2017) | The Quebec Newborn Twin Study (QNTS) | Adolescence | Canada |
| (Polderman, Huizink, et al., 2011) | Netherlands twin register (NTR) | Middle Childhood | Netherlands |
| (Rosenberg et al., 2012) | Colorado Learning Disabilities Research Center | Middle Childhood & Adolescence | United States |
| (Samuelsson et al., 2007) | Colorado Twin Register | Childhood | Australia |
| (M. J. Taylor et al., 2019b) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood & Adolescence | Sweden |
| (Tosto et al., 2014) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Trzaskowski, Dale, et al., 2013) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Wadsworth et al., 2015) | Colorado Learning Disabilities Research Center | Childhood & Adolescence | United States |
| (Wadsworth et al., 2016) | Longitudinal Twin Study of Early Reading Development | Middle Childhood & Adolescence | United States |
| (Wadsworth et al., 2010) | Colorado Reading Project, Colorado Learning Disabilities Research Center | Middle Childhood & Adolescence | United States |
| (Wadsworth et al., 2000) | Colorado Reading Project, Colorado Learning Disabilities Research Center | Middle Childhood & Adolescence | United States |

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| (Willcutt et al., 2010) | Colorado Learning Disabilities Research Center | Middle Childhood & Adolescence | United States |
| (Willcutt et al., 2019) | Colorado Learning Disabilities Research Center | Middle Childhood & Adolescence | United States |
| (Willcutt et al., 2000b) | Colorado Learning Disabilities Research Center | Middle Childhood & Adolescence | United States |
| (Zumberge et al., 2007) | The Southern California Twin register | Middle Childhood | United States |
| (Astrom et al., 2011) | Colorado Learning Disabilities Research Center | Middle Childhood | United States |
| (Betjemann et al., 2010) | Colorado Learning Disabilities Research Center | Middle Childhood & Adolescence | United States |
| (Bishop et al., 2004) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (Castles et al., 1999) | Colorado Learning Disabilities Research Center | Middle Childhood & Adolescence | United States |
| (Christopher et al., 2013) | International Longitudinal Twin Study (ILTS) | Childhood | United States |
| (Daucourt et al., 2020) | Florida Twin Project on Behavior and Environment (FTP-BE) | Childhood & Adolescence | United States |
| (Defries et al., 1987) | Colorado Reading Project | Adolescence | United States |
| (Erbeli et al., 2018) | The Florida Twin Project on Reading (FTP-R) | Childhood | United States |
| (Friend et al., 2009) | Colorado Twin Register | Childhood | United States |
| (Friend et al., 2007) | Colorado Learning Disabilities Research Center | Middle Childhood | United States |
| (Garon-Carrier et al., 2017) | The Quebec Newborn Twin Study (QNTS) | Childhood | Canada |
| (Gayán & Olson, 2003) | Colorado Learning Disabilities Research Center | Middle Childhood & Adolescence | United States |
| (Gillis et al., 1992) | Colorado Reading Project | Childhood & Adolescence | United States |
| (Grasby & Coventry, 2016) | Australian Twin Register | Middle Childhood | Australia |

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| (Harlaar et al., 2007) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (S. A. Hart et al., 2013) | The Florida Twin Project on Reading (FTP-R) | Childhood | United States |
| (Hawke et al., 2008) | Colorado Reading Project, Colorado Learning Disabilities Research Center | Middle Childhood & Adolescence | United States |
| (Knopik et al., 2002) | Colorado Learning Disabilities Research Center | Middle Childhood & Adolescence | United States |
| (Knopik et al., 1997) | Colorado Learning Disabilities Research Center | Middle Childhood & Adolescence | United States |
| (Kovas et al., 2013) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (Kovas et al., 2007) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Lazaroo et al., 2019) | Brisbane Longitudinal Twin Study | Adolescence | Australia |
| (Logan et al., 2013) | Western reserve twin project (WRTP) | Childhood & Adolescence | United States |
| (Malanchini et al., 2017) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Malanchini et al., 2020) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Malanchini et al., 2019) | Texas Twin Project | Middle Childhood & Adolescence | United States |
| (N. C. Martin, Levy, et al., 2006) | The Australian Twin ADHD Project (ATAP) | Childhood & Adolescence | Australia |
| (Oliver et al., 2007) | Twins Early Development Study (TEDS) | Childhood & Middle Childhood | United Kingdom |
| (Petrill et al., 2010) | Western reserve twin project (WRTP) | Childhood & Middle Childhood | United States |
| (Rimfeld, Malanchini, et al., 2018) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (Rimfeld, Malanchini, Hannigan, et al., 2019) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |

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| (Rimfeld et al., 2016) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Rimfeld et al., 2015) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Shakeshaft et al., 2013) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Swagerman et al., 2017) | Netherlands twin register (NTR) | Middle Childhood | Netherlands |
| (J. Taylor & Schatschneider, 2010) | The Florida Twin Project on Reading (FTP-R) | Childhood | United States |
| (J. Taylor et al., 2020) | The Florida Twin Project on Reading (FTP-R) | Adolescence | United States |
| (Tosto et al., 2017) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (Tosto et al., 2019) | Western reserve twin project (WRTP) | Middle Childhood & Adolescence | United States |
| (Tosto et al., 2013) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Trzaskowski, Dale, et al., 2013) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Wadsworth et al., 2012) | Colorado Reading Project | Middle Childhood & Adolescence | United States |
| (Willcutt et al., 2007) | Colorado Learning Disabilities Research Center | Middle Childhood & Adolescence | United States |
| (S. W. L. Wong et al., 2014) | Chinese Twin Study of Reading Development | Childhood & Adolescence | China |
| (Keenan et al., 2006) | Colorado Learning Disabilities Research Center | Middle Childhood & Adolescence | United States |
| Heritability and environmental influences on motor disorders | | | |
| (Du Rietz et al., 2021b) | Medical Birth Register, Multi-Generation Register | Childhood & Adolescence | Sweden |
| (Lichtenstein et al., 2010) | Swedish Twin Register | Middle Childhood | Sweden |
| (N. C. Martin, Piek, et al., 2006) | The Australian Twin ADHD Project (ATAP) | Childhood & Adolescence | Australia |

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|---|---|---|---|
| (Molenaar et al., 2015) | Netherlands twin register (NTR) | Childhood | Netherlands |
| (M. J. Taylor et al., 2019b) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood & Adolescence | Sweden |
| (Bishop, 2002) | Twin study in the United Kingdom | Childhood & Adolescence | United Kingdom |
| (Mataix-Cols et al., 2015) | Multi-Generation Register, National Patient Register | Childhood & Adolescence | Sweden |
| (Fliers et al., 2009) | International Multicenter ADHD Genetics Study | Adolescence | Netherlands |
| Genetic and environmental overlap between ASD & ADHD | | | |
| (Lichtenstein et al., 2010) | Swedish Twin Register | Middle childhood & Adolescence | Sweden |
| (Lundström et al., 2011) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle childhood & Adolescence | Sweden |
| (Pinto et al., 2016) | Twins Early Development Study (TEDS) | Middle childhood | United Kingdom |
| (Ronald et al., 2014) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle childhood | Sweden |
| (M. J. Taylor et al., 2013) | Twins Early Development Study (TEDS) | Middle childhood | United Kingdom |
| (M. J. Taylor et al., 2015) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| Genetic and environmental overlap between ADHD & motor disorders | | | |
| (Lichtenstein et al., 2010) | Swedish Twin Register | Middle childhood & Adolescence | Sweden |
| (N. C. Martin, Piek, et al., 2006) | The Australian Twin ADHD Project (ATAP) | Childhood & Adolescence | Australia |
| Genetic and environmental overlap between ADHD & specific learning disorders | | | |
| (Cheung et al., 2014) | Twins Early Development Study (TEDS) | Childhood & Middle Childhood | United Kingdom |
| (Greven, Harlaar, et al., 2011) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Greven et al., 2014) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |

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| (Greven et al., 2012) | Twins Early Development Study (TEDS) | Middle childhood | United Kingdom |
| (Lichtenstein et al., 2010) | Swedish Twin Register | Middle childhood & Adolescence | Sweden |
| (Light et al., 1995) | Colorado Reading Project | Middle childhood & Adolescence | United States |
| (Paloyelis et al., 2010b) | Twins Early Development Study (TEDS) | Middle childhood | United Kingdom |
| (Plourde et al., 2015) | The Quebec Newborn Twin Study (QNTS) | Childhood & Middle Childhood | Canada |
| (Plourde et al., 2017) | The Quebec Newborn Twin Study (QNTS) | Adolescence | Canada |
| (Polderman, Huizink, et al., 2011) | Netherlands twin register (NTR) | Childhood & Middle Childhood | Netherlands |
| (Rosenberg et al., 2012) | Colorado Learning Disabilities Research Center | Middle childhood & Adolescence | United States |
| (Stevenson et al., 1993) | Twin study in London | Adolescence | United Kingdom |
| (Wadsworth et al., 2015) | Colorado Learning Disabilities Research Center | Childhood & Adolescence | United States |
| (Wadsworth et al., 2016) | Longitudinal Twin Study of Early Reading Development | Middle childhood & Adolescence | United States |
| (Willcutt et al., 2010) | Colorado Learning Disabilities Research Center | Middle childhood & Adolescence | United States |
| (Willcutt et al., 2000b) | Colorado Learning Disabilities Research Center | Middle childhood & Adolescence | United States |
| (Willcutt et al., 2007) | Colorado Learning Disabilities Research Center | Middle childhood & Adolescence | United States |
| (N. C. Martin, Levy, et al., 2006) | The Australian Twin ADHD Project (ATAP) | Childhood & Adolescence | Australia |
| Genetic and environmental overlap between ASD & communication disorders* | | | |
| (Dworzynski et al., 2008) | Twins Early Development Study (TEDS) | Childhood & Middle Childhood | United Kingdom |
| Genetic and environmental overlap between ASD & motor disorders* | | | |
| (Lichtenstein et al., 2010) | Swedish Twin Register | Middle childhood & Adolescence | Sweden |

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| Genetic and environmental overlap between ASD & specific learning disorders* | | | |
| (Lichtenstein et al., 2010) | Swedish Twin Register | Middle childhood & Adolescence | Sweden |
| Genetic and environmental overlap between motor disorders & specific learning disorders* | | | |
| (Lichtenstein et al., 2010) | Swedish Twin Register | Middle childhood & Adolescence | Sweden |
| Genetic and environmental overlap between communication disorders & motor disorders | | | |
| (Bishop, 2002) | Twin study in the United Kingdom | Childhood & Adolescence | United Kingdom |
| (Ooki, 2005) | Twin study in Japan | Childhood & Adolescence | Japan |
| Genetic and environmental overlap between communication disorders & specific learning disorders | | | |
| (Bishop, 2001) | Local United Kingdom sample | Childhood & Adolescence | United Kingdom |
| (Tosto et al., 2017) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| Genetic and environmental overlap between subtypes of specific learning disorders | | | |
| (O. S. P. Davis et al., 2008) | Twins Early Development Study (TEDS) | Middle childhood | United Kingdom |
| (O. S. P. Davis et al., 2014) | Twins Early Development Study (TEDS), Avon Longitudinal Study of Parents and Children (ALSPAC) | Adolescence | United Kingdom |
| (Greven et al., 2014) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Harlaar et al., 2012) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Willcutt et al., 2019) | Colorado Learning Disabilities Research Center | Middle childhood & Adolescence | United States |
| (Gillis et al., 1992) | Colorado Reading Project | Childhood & Adolescence | United States |
| (Knopik et al., 1997) | Colorado Learning Disabilities Research Center | Middle childhood & Adolescence | United States |
| (Kovas et al., 2007) | Twins Early Development Study (TEDS) | Middle childhood | United Kingdom |
| (Oliver et al., 2007) | Twins Early Development Study (TEDS) | Childhood & Middle childhood | United Kingdom |

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| Genetic and environmental overlap between ADHD & conduct disorder | | | |
| (Burt et al., 2001) | The Minnesota Twin Family Study (MTFS) | Middle childhood & Adolescence | United States |
| (Dick et al., 2005) | The Finnish Twin Cohort Study | Adolescence | Finland |
| (Tuvblad et al., 2009) | The Southern California Twin register | Middle childhood | United States |
| (Y. M. Hur, 2015) | The South Korean Twin Registry (SKTR) | Childhood & Adolescence | South Korea |
| (N. C. Martin, Levy, et al., 2006) | The Australian Twin ADHD Project (ATAP) | Childhood & Adolescence | Australia |
| (Coolidge et al., 2000) | Twin study in Colorado | Middle childhood | United States |
| Genetic and environmental overlap between ADHD & oppositional defiant disorder | | | |
| (Burt et al., 2001) | The Minnesota Twin Family Study (MTFS) | Middle childhood & Adolescence | United States |
| (Dick et al., 2005) | The Finnish Twin Cohort Study | Adolescence | Finland |
| (Tuvblad et al., 2009) | The Southern California Twin register | Middle childhood | United States |
| (Wood et al., 2009) | Twins Early Development Study (TEDS) | Middle childhood | United Kingdom |
| (N. C. Martin, Levy, et al., 2006) | The Australian Twin ADHD Project (ATAP) | Childhood & Adolescence | Australia |
| (Coolidge et al., 2000) | Twin study in Colorado | Middle childhood | United States |
| Genetic and environmental overlap between ASD & conduct disorder | | | |
| (Jones et al., 2009) | Twins Early Development Study (TEDS) | Middle childhood | United Kingdom |
| (O'Nions et al., 2015) | Twins Early Development Study (TEDS) | Middle childhood | United Kingdom |
| Genetic and environmental overlap between ASD & conduct disorder* | | | |
| (Lundström et al., 2011) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle childhood & Adolescence | Sweden |
| Genetic and environmental overlap between specific learning disorders & disruptive behaviour* | | | |
| (Newsome et al., 2014) | The Early Childhood Longitudinal | Childhood | United States |

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| | Study (ECLS) | | |

Supplementary Table 32. Overview of family-based studies using male samples. Co-occurrences between disorders annotated with an asterisk (*) indicate pairs of disorders for which meta-analysis could not be performed.

| Reference | Cohort | Age category | Country |
|---|---|---|---|
| Heritability and environmental influences on communication disorders | | | |
| (Spinath et al., 2004) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (M. J. Taylor et al., 2014) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Ooki, 2005) | Twin study in Japan | Childhood & Adolescence | Japan |
| (Viding et al., 2004) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| Heritability and environmental influences on ASD | | | |
| (Cheesman et al., 2017) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Constantino & Todd, 2003) | Missouri Twin Study | Adolescence | United States |
| (Frazier et al., 2014) | Interactive Autism Network (IAN) | Middle Childhood | United States |
| (Hallett et al., 2012) | Twins Early Development Study (TEDS) | Childhood & Middle Childhood | United Kingdom |
| (Hoekstra et al., 2010) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Holmboe et al., 2014) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (E. B. Robinson et al., 2011) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (E. B. Robinson et al., 2012) | Twins Early Development Study (TEDS) | Middle Childhood & Adolescence | United Kingdom |
| (Ronald, Happé, Bolton, et al., 2006) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Ronald et al., 2014) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood | Sweden |

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|---|---|---|---|
| (Ronald et al., 2008) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Scherff et al., 2014) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (M. J. Taylor et al., 2013) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (M. J. Taylor et al., 2014) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (M. J. Taylor et al., 2018) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood & Adolescence | Sweden |
| (M. J. Taylor et al., 2020) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood & Adolescence | Sweden |
| (M. J. Taylor et al., 2017) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood & Adolescence | Sweden |
| (Hallmayer et al., 2011) | California Autism Twins Study | Adolescence | United States |
| (Mazefsky et al., 2008) | Autism Genetic Resource Exchange (AGRE) | Childhood & Adolescence | United States |
| (Taniai et al., 2008) | Nagoya North District Care Center for Disabled Children, Nagoya Child Welfare Center, and Nagoya West District Care Center for Disabled Children | Childhood & Adolescence | Japan |
| (Ronald et al., 2005) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| Heritability and environmental influences on ADHD | | | |
| (Cheesman et al., 2017) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Cole et al., 2009) | Cardiff Study of All Wales and North England Twins | Childhood & Adolescence | United Kingdom |
| (Constantino et al., 2003) | Missouri Twin Study | Childhood & Adolescence | United States |
| (de Zeeuw et al., 2015) | Netherlands twin register (NTR) | Childhood | Netherlands |
| (Dick et al., 2005) | The Finnish Twin Cohort Study | Adolescence | Finland |

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|---|---|---|---|
| (L. J. Eaves et al., 1997) | Virginia twin study of adolescent behavioral development (VTSABD) | Middle Childhood & Adolescence | United States |
| (L. Eaves et al., 2000) | Virginia twin study of adolescent behavioral development (VTSABD) | Middle Childhood & Adolescence | United States |
| (Gregory et al., 2004) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (Greven, Rijsdijk, et al., 2011) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Hudziak et al., 2000) | Missouri Twin Study | Middle Childhood & Adolescence | United States |
| (Jaffee et al., 2012) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Kuntsi et al., 2005) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Kuo et al., 2004) | Twin study in Taipei City | Adolescence | Taiwan |
| (H. Larsson et al., 2006) | Twin Study of Child and Adolescent Development (TCHAD) | Middle Childhood | Sweden |
| (Lifford et al., 2009) | The Cardiff Study of All Wales and Northwest of England Twins (CaStANET), South Wales Family Study (SWFS) | Adolescence | United Kingdom |
| (Ronald et al., 2014) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood | Sweden |
| (Ronald et al., 2008) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Rydell et al., 2017) | Preschool Twin Study in Sw(Saudino & Plomin, 2007)weden | | |
| (Saudino & Plomin, 2007) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (M. J. Taylor et al., 2013) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Van Beijsterveldt et al., 2004) | Netherlands twin register (NTR) | Childhood | Netherlands |

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|---|---|---|---|
| (Vierikko et al., 2004) | The Finnish Twin Cohort Study | Adolescence | Finland |
| (Burt et al., 2005) | The Minnesota Twin Family Study (MTFS) | Middle Childhood & Adolescence | United States |
| (de Zeeuw et al., 2017) | Netherlands twin register (NTR) | Childhood & Adolescence | Netherlands |
| (Do et al., 2019) | Add Health | Childhood & Adolescence | United States |
| (J. O. Larsson et al., 2004) | Young Twins Study | Adolescence | Sweden |
| (Nadder et al., 2002) | Virginia twin study of adolescent behavioral development (VTSABD) | Middle Childhood & Adolescence | United States |
| (Nadder et al., 1998) | Virginia twin study of adolescent behavioral development (VTSABD) | Childhood & Adolescence | United States |
| (Rietveld et al., 2004) | Netherlands twin register (NTR) | Childhood | Netherlands |
| (Saudino et al., 2005) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (Silberg et al., 1996) | Virginia twin study of adolescent behavioral development (VTSABD) | Middle Childhood & Adolescence | United States |
| (Sherman et al., 1997) | The Minnesota Twin Family Study (MTFS) | Adolescence | United States |
| (Smith et al., 2011) | Center for Antisocial Drug Dependence (CADD) | Adolescence | United States |
| Heritability and environmental influences on specific learning disorders | | | |
| (Alarcón et al., 1995) | Colorado Learning Disabilities Research Center | Middle Childhood & Adolescence | United States |
| (T. C. Bates et al., 2004) | Study of melanocytic naevi (moles) | Adolescence | Australia |
| (L. J. Eaves et al., 1997) | Virginia twin study of adolescent behavioral development (VTSABD) | Middle Childhood & Adolescence | United States |
| (Harlaar et al., 2005) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (Reynolds et al., 1996) | Virginia twin study of adolescent behavioral development (VTSABD) | Middle Childhood | United States |
| (Tosto et al., 2014) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |

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|---|---|---|---|
| (Grasby & Coventry, 2016) | Australian Twin Register | Middle Childhood | Australia |
| (Shakeshaft et al., 2013) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Tosto et al., 2019) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| Heritability and environmental influences on motor disorders | | | |
| (Van Beijsterveldt et al., 2004) | Netherlands twin register (NTR) | Childhood | Netherlands |
| (Ooki, 2005) | Twin study in Japan | Childhood & Adolescence | Japan |
| Genetic and environmental overlap between ASD & ADHD | | | |
| (Constantino et al., 2003) | Missouri Twin Study | United States | BEST |
| (Ronald et al., 2008) | Twins Early Development Study (TEDS) | United Kingdom | BEST |
| Genetic and environmental overlap between ADHD & conduct disorder* | | | |
| (Silberg et al., 1996) | Virginia twin study of adolescent behavioral development (VTSABD) | Twin study | United States |

Supplementary Table 33. Overview of family-based studies using female samples. Co-occurrences between disorders annotated with an asterisk (*) indicate pairs of disorders for which meta-analysis could not be performed.

| Reference | Cohort | Age category | Country |
|---|---|---|---|
| Heritability and environmental influences on communication disorders | | | |
| (Spinath et al., 2004) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (M. J. Taylor et al., 2014) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Ooki, 2005) | Twin study in Japan | Childhood & Adolescence | Japan |
| (Viding et al., 2004) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| Heritability and environmental influences on ASD | | | |
| (Cheesman et al., 2017) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Constantino & Todd, 2003) | Missouri Twin Study | Adolescence | United States |
| (Constantino et al., 2003) | Missouri Twin Study | Childhood & Adolescence | United States |
| (Frazier et al., 2014) | Interactive Autism Network (IAN) | Middle Childhood | United States |
| (Hallett et al., 2012) | Twins Early Development Study (TEDS) | Childhood & Middle Childhood | United Kingdom |
| (Hoekstra et al., 2010) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Holmboe et al., 2014) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (E. B. Robinson et al., 2011) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood & Adolescence | Sweden |
| (E. B. Robinson et al., 2012) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Ronald, Happé, Bolton, et al., 2006) | Twins Early Development Study (TEDS) | Middle Childhood & Adolescence | United Kingdom |
| (Frazier et al., 2014) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Ronald et al., 2014) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood | Sweden |
| (Ronald et al., 2008) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Scherff et al., 2014) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (M. J. Taylor et al., 2013) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |

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|---|---|---|---|
| (M. J. Taylor et al., 2014) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (M. J. Taylor et al., 2018) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood & Adolescence | Sweden |
| (M. J. Taylor et al., 2020) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood & Adolescence | Sweden |
| (M. J. Taylor et al., 2017) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood & Adolescence | Sweden |
| (Hallmayer et al., 2011) | California Autism Twins Study | Adolescence | United States |
| (Mazefsky et al., 2008) | Autism Genetic Resource Exchange (AGRE) | Childhood & Adolescence | United States |
| (Taniai et al., 2008) | Nagoya North District Care Center for Disabled Children, Nagoya Child Welfare Center, and Nagoya West District Care Center for Disabled Children | Childhood & Adolescence | Japan |
| (Ronald et al., 2005) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| Heritability and environmental influences on ADHD | | | |
| (Cheesman et al., 2017) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Cole et al., 2009) | Cardiff Study of All Wales and North England Twins | Childhood & Adolescence | United Kingdom |
| (de Zeeuw et al., 2015) | Netherlands twin register (NTR) | Childhood | Netherlands |
| (Dick et al., 2005) | The Finnish Twin Cohort Study | Adolescence | Finland |
| (L. J. Eaves et al., 1997) | Virginia twin study of adolescent behavioral development (VTSABD) | Middle Childhood & Adolescence | United States |
| (L. Eaves et al., 2000) | Virginia twin study of adolescent behavioral development (VTSABD) | Middle Childhood & Adolescence | United States |
| (Gregory et al., 2004) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (Greven, Rijsdijk, et al., 2011) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Hudziak et al., 2000) | Missouri Twin Study | Middle Childhood & Adolescence | United States |
| (Jaffee et al., 2012) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Kuntsi et al., 2005) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Kuo et al., 2004) | Twin study in Taipei City | Adolescence | Taiwan |

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|---|---|---|---|
| (H. Larsson et al., 2006) | Twin Study of Child and Adolescent Development (TCHAD) | Middle Childhood | Sweden |
| (Lifford et al., 2009) | The Cardiff Study of All Wales and Northwest of England Twins (CaStANET), South Wales Family Study (SWFS) | Adolescence | United Kingdom |
| (Ronald et al., 2014) | The Child and Adolescent Twin Study in Sweden (CATSS) | Middle Childhood | Sweden |
| (Ronald et al., 2008) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Rydell et al., 2017) | Preschool Twin Study in Sweden (PETSS) | Childhood | Sweden |
| (Saudino & Plomin, 2007) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (M. J. Taylor et al., 2013) | Twins Early Development Study (TEDS) | Middle Childhood | United Kingdom |
| (Van Beijsterveldt et al., 2004) | Netherlands twin register (NTR) | Childhood | Netherlands |
| (Vierikko et al., 2004) | The Finnish Twin Cohort Study | Adolescence | Finland |
| (Burt et al., 2005) | The Minnesota Twin Family Study (MTFS) | Middle Childhood & Adolescence | United States |
| (de Zeeuw et al., 2017) | Netherlands twin register (NTR) | Childhood & Adolescence | Netherlands |
| (Do et al., 2019) | Add Health | Childhood & Adolescence | United States |
| (Knopik et al., 2009) | Missouri Adolescent Female Twin Study cohort | Adolescence | United States |
| (J. O. Larsson et al., 2004) | Young Twins Study | Adolescence | Sweden |
| (Nadder et al., 2002) | Virginia twin study of adolescent behavioral development (VTSABD) | Middle Childhood & Adolescence | United States |
| (Nadder et al., 1998) | Virginia twin study of adolescent behavioral development (VTSABD) | Childhood & Adolescence | United States |
| (Neuman et al., 2001) | Missouri Twin Study | Adolescence | United States |
| (Rietveld et al., 2004) | Netherlands twin register (NTR) | Childhood | Netherlands |
| (Saudino et al., 2005) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (Silberg et al., 1996) | Virginia twin study of adolescent behavioral development (VTSABD) | Middle Childhood & Adolescence | United States |
| (Smith et al., 2011) | Center for Antisocial Drug Dependence (CADD) | Adolescence | United States |
| Heritability and environmental influences on specific learning disorders | | | |

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|---|---|---|---|
| (Alarcón et al., 1995) | Colorado Learning Disabilities Research Center | Middle Childhood & Adolescence | United States |
| (T. C. Bates et al., 2004) | Study of melanocytic naevi (moles) | Adolescence | Australia |
| (L. J. Eaves et al., 1997) | Virginia twin study of adolescent behavioral development (VTSABD) | Middle Childhood & Adolescence | United States |
| (Harlaar et al., 2005) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (Reynolds et al., 1996) | Virginia twin study of adolescent behavioral development (VTSABD) | Middle Childhood | United States |
| (Tosto et al., 2014) | Twins Early Development Study (TED(Grasby & Coventry, 2016)gdom | | |
| (Grasby & Coventry, 2016) | Australian Twin Register | Middle Childhood | Australia |
| (Shakeshaft et al., 2013) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Tosto et al., 2019) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| Heritability and environmental influences on motor disorders | | | |
| (Van Beijsterveldt et al., 2004) | Netherlands twin register (NTR) | Childhood | Netherlands |
| (Ooki, 2005) | Twin study in Japan | Childhood & Adolescence | Japan |
| Genetic and environmental overlap between ASD & ADHD* | | | |
| (Ronald et al., 2008) | Twins Early Development Study (TEDS) | Middle childhood | United Kingdom |
| Genetic and environmental overlap between ADHD & conduct disorder | | | |
| (Silberg et al., 1996) | Virginia twin study of adolescent behavioral development (VTSABD) | Middle childhood & Adolescence | United States |
| (Knopik et al., 2009) | Missouri Adolescent Female Twin Study cohort | Adolescence | United States |

Supplementary Table 34. Overview of SNP-based studies using samples of males and females combined. Disorders annotated with an asterisk (*) indicate disorders for which meta-analysis could not be performed.

| Reference | Cohort | Age category | Country |
|---|---|---|---|
| Heritability and environmental influences on communication disorders | | | |
| (Cheesman et al., 2017) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Trzaskowski, Dale, et al., 2013) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Trzaskowski, Davis, et al., 2013) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Verhoef et al., 2021) | Avon Longitudinal Study of Parents and Children (ALSPAC) | Middle Childhood | United Kingdom |
| Heritability and environmental influences on ASD | | | |
| (Cheesman et al., 2017) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Gandal et al., 2018) | Psychiatric Genomics Consortium (PGC), iPSYCH | Childhood & Adolescence | United Kingdom, Denmark |
| (Grove et al., 2019) | Psychiatric Genomics Consortium (PGC), iPSYCH | Childhood & Adolescence | United Kingdom, Denmark |
| (Hill et al., 2016) | Psychiatric Genomics Consortium (PGC) | Childhood & Adolescence | United Kingdom |
| (S. H. Lee et al., 2013) | Psychiatric Genomics Consortium (PGC) | Childhood & Adolescence | United Kingdom |
| (Serdarevic et al., 2020) | Generation R | Childhood | Netherlands |
| (Solberg et al., 2019) | Psychiatric Genomics Consortium (PGC), iPSYCH | Childhood & Adolescence | United Kingdom, Denmark |
| (St Pourcain et al., 2014) | Avon Longitudinal Study of Parents and Children (ALSPAC) | Middle Childhood | United Kingdom |
| (St Pourcain, Eaves, et al., 2018) | Avon Longitudinal Study of Parents and Children (ALSPAC) | Middle Childhood | United Kingdom |
| (St Pourcain, Robinson, | Avon Longitudinal Study of Parents and Children (ALSPAC) | Middle Childhood | United Kingdom |

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| et al., 2018) | | | |
| (Stergiakouli et al., 2017) | Avon Longitudinal Study of Parents and Children (ALSPAC) | Middle Childhood | United Kingdom |
| (Trzaskowski, Dale, et al., 2013) | Avon Longitudinal Study of Parents and Children (ALSPAC) | Adolescence | United Kingdom |
| (Warrier & Baron-Cohen, 2018) | Avon Longitudinal Study of Parents and Children (ALSPAC) | Adolescence | United Kingdom |
| (Anney et al., 2017) | Psychiatric Genomics Consortium (PGC) | Childhood & Adolescence | United Kingdom |
| (Pettersson et al., 2019) | Psychiatric Genomics Consortium (PGC), iPSYCH | Childhood & Adolescence | United Kingdom, Denmark |
| Heritability and environmental influences on ADHD | | | |
| (Soler Artigas et al., 2020) | Psychiatric Genomics Consortium (PGC), iPSYCH | Childhood & Adolescence | United Kingdom, Denmark |
| (Cheesman et al., 2017) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Demontis et al., 2019) | Psychiatric Genomics Consortium (PGC), iPSYCH | Childhood & Adolescence | United Kingdom, Denmark |
| (Hill et al., 2016) | Psychiatric Genomics Consortium (PGC) | Childhood & Adolescence | United Kingdom |
| (S. H. Lee et al., 2013) | Psychiatric Genomics Consortium (PGC) | Childhood & Adolescence | United Kingdom |
| (J. Martin et al., 2018) | Psychiatric Genomics Consortium (PGC), iPSYCH | Childhood & Adolescence | United Kingdom, Denmark |
| (Micalizzi et al., 2021) | Philadelphia Neurodevelopmental Cohort | Middle Childhood & Adolescence | United States |
| (Middeldorp et al., 2016) | Avon Longitudinal Study of Parents and Children (ALSPAC) | Childhood | United Kingdom |
| (Pappa et al., 2015) | Generation R, Netherlands twin register (NTR) | Childhood & Middle Childhood | Netherlands |

| | | | |
|---|---|---|---|
| (Rovira et al., 2020) | Psychiatric Genomics Consortium (PGC), iPSYCH, IMpACT | Middle Childhood | United Kingdom, Denmark, United States |
| (Solberg et al., 2019) | Psychiatric Genomics Consortium (PGC), iPSYCH | Childhood & Adolescence | United Kingdom, Denmark |
| (Stergiakouli et al., 2017) | Avon Longitudinal Study of Parents and Children (ALSPAC) | Childhood | United Kingdom |
| (Trzaskowski, Dale, et al., 2013) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Pettersson et al., 2019) | Psychiatric Genomics Consortium (PGC), iPSYCH | Childhood & Adolescence | United Kingdom, Denmark |
| Heritability and environmental influences on specific learning disorders | | | |
| (Cheesman et al., 2017) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (O. S. P. Davis et al., 2014) | Twins Early Development Study (TEDS), Avon Longitudinal Study of Parents and Children (ALSPAC) | Adolescence | United Kingdom |
| (Gialluisi et al., 2021) | Study-specific multi-site cohort | Childhood & Adolescence | Multiple sites |
| (Harlaar et al., 2014) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (Trzaskowski, Dale, et al., 2013) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Rimfeld, Malanchini, et al., 2018) | Twins Early Development Study (TEDS) | Childhood | United Kingdom |
| (Rimfeld et al., 2015) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Trzaskowski, Davis, et al., 2013) | Twins Early Development Study (TEDS) | Adolescence | United Kingdom |
| (Verhoef et al., 2021) | Avon Longitudinal Study of Parents and Children (ALSPAC) | Childhood | United Kingdom |
| Genetic and environmental overlap between ASD & ADHD | | | |
| (Demontis et al., 2019) | Psychiatric Genomics Consortium (PGC), iPSYCH | Childhood & Adolescence | United Kingdom, Denmark |

| | | | |
|---|---|---|---|
| (Grove et al., 2019) | Psychiatric Genomics Consortium (PGC), iPSYCH | Childhood & Adolescence | United Kingdom, Denmark |
| (Solberg et al., 2019) | Psychiatric Genomics Consortium (PGC) | Childhood & Adolescence | United Kingdom |
| (Stergiakouli et al., 2017) | Avon Longitudinal Study of Parents and Children (ALSPAC) | Childhood & Middle Childhood | United Kingdom |
| (S. H. Lee et al., 2013) | Psychiatric Genomics Consortium (PGC) | Childhood & Adolescence | United Kingdom |

Supplementary Table 35. Overview of SNP-based studies using male samples. Disorders annotated with an asterisk (*) indicate disorders for which meta-analysis could not be performed.

| Reference | Cohort | Age category | Country |
|---|---|---|---|
| Heritability and environmental influences on ASD* | | | |
| (J. Martin et al., 2021) | Psychiatric Genomics Consortium (PGC), iPSYCH | Childhood & Adolescence | United Kingdom, Denmark |
| Heritability and environmental influences on ADHD | | | |
| (J. Martin et al., 2018) | Psychiatric Genomics Consortium (PGC), iPSYCH | Childhood & Adolescence | United Kingdom, Denmark |
| (J. Martin et al., 2021) | Psychiatric Genomics Consortium (PGC), iPSYCH | Childhood & Adolescence | United Kingdom, Denmark |

Supplementary Table 36. Overview of SNP-based studies using female samples. Disorders annotated with an asterisk (*) indicate disorders for which meta-analysis could not be performed.

| Reference | Cohort | Age category | Country |
|---|---|---|---|
| Heritability and environmental influences on ASD* | | | |
| (J. Martin et al., 2021) | Psychiatric Genomics Consortium (PGC), iPSYCH | Childhood & Adolescence | United Kingdom, Denmark |
| Heritability and environmental influences on ADHD | | | |
| (J. Martin et al., 2018) | Psychiatric Genomics Consortium (PGC), iPSYCH | Childhood & Adolescence | United Kingdom, Denmark |
| (J. Martin et al., 2021) | Psychiatric Genomics Consortium (PGC), iPSYCH | Childhood & Adolescence | United Kingdom, Denmark |

Supplementary Table 37. Heritability, shared and nonshared environmental influences on NDDs, stratified by designs.

| Family-based designs | | | | | | | SNP-based designs | | |
|---|---|---|---|---|---|---|---|---|---|
| NDDs | Family $h^2$ (SE) | N | Family $c^2$ (SE) | N | Family $e^2$ (SE) | N | | SNP $h^2$ (SE) | N |
| NDDs combined | | | | | | | | | |
| Categorical threshold sibling study | 0.67 (0.24) | 3 | - | - | 0.2 (0.11) | 2 | GCTA (REML) | 0.21 (0.05) | 19 |
| Categorical threshold twin and sibling study | 0.85 (0.19) | 2 | - | - | 0.37 (0.21) | 3 | LDSC | 0.17 (0.04) | 13 |
| DF extremes twin and sibling study | 0.83 (0.38) | 4 | 0.17 (0.13) | 4 | - | - | | | |
| Classical twin and sibling study | 0.57 (0.09) | 8 | 0.08 (0.09) | 2 | 0.45 (0.08) | 8 | | | |
| Categorical threshold twin study | 0.74 (0.07) | 23 | 0.25 (0.08) | 11 | 0.27 (0.07) | 21 | | | |
| DF extremes twin study | 0.7 (0.11) | 57 | 0.19 (0.05) | 22 | 0.27 (0.05) | 20 | | | |
| Classical twin study | 0.65 (0.03) | 157 | 0.15 (0.02) | 95 | 0.27 (0.01) | 151 | | | |
| Communication disorders | | | | | | | | | |
| Categorical threshold twin study | 0.47 (0.1) | 5 | 0.47 (0.12) | 4 | 0.13 (0.06) | 5 | GCTA (REML) | 0.32 (0.14) | 4 |
| DF extremes twin study | 0.78 (0.41) | 8 | 0.31 (0.12) | 5 | 0.22 (0.09) | 5 | LDSC | - | - |
| Classical twin study | 0.56 (0.09) | 11 | 0.29 (0.07) | 7 | 0.25 (0.06) | 8 | | | |
| ASD | | | | | | | | | |
| Categorical threshold twin study | 0.87 (0.11) | 7 | 0.09 (0.15) | 3 | 0.16 (0.07) | 6 | GCTA (REML) | 0.17 (0.07) | 9 |
| DF extremes twin study | 0.78 (0.36) | 11 | - | - | 0.33 (0.07) | 5 | LDSC | 0.13 (0.05) | 8 |
| Classical twin study | 0.68 (0.04) | 20 | 0.16 (0.07) | 8 | 0.26 (0.03) | 19 | | | |
| ADHD | | | | | | | | | |
| Categorical threshold twin and sibling study | 0.84 (0.21) | 2 | - | - | 0.13 (0.09) | 2 | GCTA (REML) | 0.17 (0.06) | 8 |
| DF extremes twin and sibling study | 0.94 (0.46) | 2 | 0.06 (0.25) | 2 | - | - | LDSC | 0.22 (0.05) | 7 |
| Classical twin and sibling study | 0.56 (0.1) | 7 | 0.08 (0.09) | 2 | 0.45 (0.08) | 7 | | | |
| Categorical threshold twin study | 0.76 (0.1) | 13 | 0.14 (0.09) | 5 | 0.28 (0.08) | 12 | | | |
| DF extremes twin study | 0.75 (0.18) | 11 | 0.04 (0.08) | 3 | 0.36 (0.14) | 2 | | | |
| Classical twin study | 0.67 (0.03) | 91 | 0.1 (0.03) | 38 | 0.29 (0.02) | 87 | | | |
| Specific learning disorders | | | | | | | | | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| DF extremes twin and sibling study | 0.5 (0.13) | 2 | 0.2 (0.15) | 2 | - | - | GCTA (REML) | 0.31 (0.08) | 8 |
| DF extremes twin study | 0.62 (0.06) | 30 | 0.21 (0.06) | 14 | 0.25 (0.06) | 9 | LDSC | - | - |
| Classical twin study | 0.62 (0.05) | 63 | 0.18 (0.02) | 55 | 0.25 (0.02) | 60 | | | |
| Motor disorders | | | | | | | | | |
| Categorical threshold twin and sibling study | - | - | - | - | 0.64 (0.18) | 2 | | | |
| Categorical threshold twin study | 0.71 (0.1) | 3 | 0.12 (0.12) | 2 | 0.25 (0.12) | 3 | | | |
| Classical twin study | 0.71 (0.23) | 2 | - | - | - | - | | | |
| Note. $H^2$= heritability; $c^2$= shared environmental influences; $e^2$= nonshared environmental influences; N= number of studies identified; SE= standard error; GCTA= genome-wide complex trait analysis; REML= restricted maximum likelihood; LDSC= linkage disequilibrium score regression. | | | | | | | | | |

Supplementary Table 38. Genetic, shared and nonshared environmental correlations between NDDs, stratified by designs.

| Family-based designs | | | | | | | SNP-based designs | | |
|---|---|---|---|---|---|---|---|---|---|
| NDDs | Family rA (SE) | N | Family rC (SE) | N | Family rE (SE) | N | | SNP rG (SE) | N |
| NDDs combined | | | | | | | | | |
| Categorical threshold twin study | 0.67 (0.49) | 2 | - | - | - | - | GCTA (REML) | 0.5 (0.36) | 3 |
| DF extremes twin study | 0.38 (0.08) | 15 | - | - | 0.13 (0.12) | 2 | LDSC | 0.26 (0.14) | 3 |
| Classical twin study | 0.31 (0.17) | 21 | 0.69 (0.37) | 15 | 0.18 (0.05) | 20 | | | |
| ASD & ADHD | | | | | | | | | |
| Classical twin study | 0.56 (0.34) | 5 | - | - | 0.22 (0.13) | 5 | GCTA (REML) | 0.36 (0.49) | 2 |
| | | | | | | | LDSC | 0.26 (0.14) | 3 |
| ADHD & motor disorders | | | | | | | | | |
| Categorical threshold twin study | 0.9 (0.82) | 2 | - | - | - | - | | - | - |
| ADHD & specific learning disorders | | | | | | | | | |
| DF extremes twin study | 0.41 (0.09) | 9 | - | - | - | - | | - | - |
| Classical twin study | -0.09 (0.12) | 9 | 0.32 (0.14) | 7 | 0.10 (0.05) | 8 | | - | - |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; N= number of studies identified; SE= standard error; GCTA= genome-wide complex trait analysis; REML= restricted maximum likelihood; LDSC= linkage disequilibrium score regression. | | | | | | | | | |

Supplementary Table 39. Genetic, shared and nonshared environmental correlations between NDDs and DICCs, stratified by designs.

| NDDs and DICCs | Family rA (SE) | N | Family rC (SE) | N | Family rE (SE) | N |
|---|---|---|---|---|---|---|
| NDDs and DICCs combined | | | | | | |
| Classical twin study | 0.62 (0.19) | 15 | 0.88 (0.34) | 11 | 0.38 (0.14) | 13 |
| ADHD & conduct disorder | | | | | | |
| Classical twin study | 0.66 (0.36) | 6 | 0.94 (0.71) | 3 | 0.11 (0.08) | 5 |
| ADHD & oppositional defiant disorder | | | | | | |
| Classical twin study | 0.66 (0.18) | 6 | 0.96 (0.57) | 4 | 0.54 (0.25) | 5 |
| ASD & conduct disorder | | | | | | |
| Classical twin study | 0.35 (0.10) | 3 | 0.88 (0.57) | 3 | 0.07 (0.08) | 3 |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; N= number of studies identified; SE= standard error; GCTA= genome-wide complex trait analysis; REML= restricted maximum likelihood; LDSC= linkage disequilibrium score regression. | | | | | | |

Supplementary Table 40. Heritability, shared and nonshared environmental influences on NDDs, stratified by models.

| NDDs | Family $h^2$ (SE) | N | Family $c^2$ (SE) | N | Family $e^2$ (SE) | N |
|---|---|---|---|---|---|---|
| NDDs combined | | | | | | |
| A only | 0.74 (0.16) | 11 | - | - | - | - |
| Best fitting | 0.7 (0.05) | 82 | - | - | 0.34 (0.02) | 81 |
| Full ACE | 0.61 (0.03) | 104 | 0.16 (0.02) | 104 | 0.22 (0.01) | 104 |
| DF extremes A only | 0.77 (0.16) | 31 | - | - | - | - |
| DF extremes best fitting | 0.72 (0.16) | 18 | 0.24 (0.07) | 12 | 0.33 (0.06) | 7 |
| DF extremes full ACE | 0.6 (0.07) | 15 | 0.17 (0.05) | 15 | 0.24 (0.05) | 15 |
| Twin correlations | 0.67 (0.07) | 14 | 0.17 (0.07) | 4 | 0.37 (0.06) | 13 |
| Communication disorders | | | | | | |
| A only | 0.55 (0.2) | 3 | - | - | - | - |
| Best fitting | 0.57 (0.22) | 4 | - | - | 0.51 (0.19) | 4 |
| Full ACE | 0.47 (0.06) | 11 | 0.37 (0.07) | 11 | 0.19 (0.04) | 11 |
| DF extremes A only | 0.94 (0.56) | 4 | - | - | - | - |
| DF extremes best fitting | 0.55 (0.2) | 3 | 0.45 (0.26) | 2 | - | - |
| DF extremes full ACE | 0.47 (0.13) | 5 | 0.3 (0.11) | 5 | 0.23 (0.09) | 5 |
| ASD | | | | | | |
| A only | 0.83 (0.38) | 4 | - | - | - | - |
| Best fitting | 0.71 (0.09) | 13 | - | - | 0.28 (0.04) | 13 |
| Full ACE | 0.72 (0.1) | 11 | 0.11 (0.06) | 11 | 0.21 (0.05) | 11 |
| DF extremes A only | 0.86 (0.45) | 3 | - | - | - | - |
| DF extremes best fitting | 0.67 (0.07) | 6 | - | - | 0.33 (0.07) | 5 |
| Twin correlations | 0.7 (0.07) | 4 | 0.16 (0.08) | 2 | 0.25 (0.11) | 4 |
| ADHD | | | | | | |
| A only | 0.7 (0.21) | 4 | - | - | - | - |
| Best fitting | 0.7 (0.05) | 61 | - | - | 0.33 (0.02) | 59 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Full ACE | 0.65 (0.04) | 43 | 0.1 (0.02) | 43 | 0.24 (0.02) | 43 |
| DF extremes A only | 0.79 (0.28) | 9 | - | - | - | - |
| DF extremes best fitting | 0.88 (0.24) | 4 | 0.08 (0.2) | 3 | - | - |
| Twin correlations | 0.67 (0.1) | 11 | 0.2 (0.13) | 2 | 0.38 (0.07) | 10 |
| Specific learning disorders | | | | | | |
| A only | 0.58 (0.09) | 4 | - | - | - | - |
| Best fitting | 0.73 (0.17) | 9 | - | - | 0.34 (0.11) | 9 |
| Full ACE | 0.6 (0.05) | 54 | 0.18 (0.02) | 54 | 0.24 (0.02) | 54 |
| DF extremes A only | 0.64 (0.09) | 16 | - | - | - | - |
| DF extremes best fitting | 0.55 (0.08) | 7 | 0.22 (0.08) | 7 | - | - |
| DF extremes full ACE | 0.63 (0.08) | 9 | 0.18 (0.07) | 9 | 0.24 (0.06) | 9 |
| Motor disorders | | | | | | |
| Best fitting | 0.77 (0.18) | 3 | - | - | 0.39 (0.14) | 4 |
| Full ACE | 0.69 (0.1) | 3 | 0.13 (0.11) | 3 | 0.24 (0.13) | 3 |
| Note. $H^2$= heritability; $c^2$= shared environmental influences; $e^2$= nonshared environmental influences; N= number of studies identified; SE= standard error. | | | | | | |

Supplementary Table 41. Genetic, shared and nonshared environmental correlations between NDDs, stratified by models.

| NDDs | Family rA (SE) | N | Family rC (SE) | N | Family rE (SE) | N |
|---|---|---|---|---|---|---|
| NDDs combined | | | | | | |
| A only | 0.68 (0.48) | 2 | - | - | - | - |
| Best fitting | 0.31 (0.24) | 8 | - | - | 0.14 (0.05) | 7 |
| Full ACE | 0.31 (0.13) | 16 | 0.67 (0.39) | 15 | 0.18 (0.06) | 16 |
| DF extremes A only | 0.37 (0.09) | 13 | - | - | - | - |
| ASD & ADHD | | | | | | |
| Best fitting | 0.68 (0.49) | 3 | - | - | 0.18 (0.09) | 3 |
| Full ACE | 0.42 (0.17) | 2 | - | - | 0.31 (0.21) | 2 |
| ADHD & specific learning disorders | | | | | | |
| Best fitting | 0.14 (0.16) | 5 | - | - | 0.11 (0.08) | 4 |
| Full ACE | -0.18 (0.21) | 6 | 0.31 (0.15) | 6 | 0.1 (0.05) | 6 |
| DF extremes A only | 0.38 (0.11) | 8 | - | - | - | - |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; N= number of studies identified; SE= standard error. | | | | | | |

Supplementary Table 42. Genetic, shared and nonshared environmental correlations between NDDs and DICCs, stratified by models.

| NDDs and DICCs | Family rA (SE) | N | Family rC (SE) | N | Family rE (SE) | N |
|---|---|---|---|---|---|---|
| NDDs and DICCs combined | | | | | | |
| Best fitting | 0.69 (0.3) | 7 | - | - | 0.15 (0.07) | 5 |
| Full ACE | 0.48 (0.14) | 10 | 0.9 (0.35) | 10 | 0.42 (0.18) | 10 |
| ADHD & conduct disorder | | | | | | |
| Best fitting | 0.78 (0.5) | 4 | - | - | 0.14 (0.13) | 3 |
| Full ACE | 0.33 (0.12) | 3 | 0.94 (0.71) | 3 | 0.07 (0.1) | 3 |
| ADHD & oppositional defiant disorder | | | | | | |
| Best fitting | 0.69 (0.24) | 3 | - | - | 0.42 (0.13) | 2 |
| Full ACE | 0.56 (0.24) | 4 | 0.96 (0.57) | 4 | 0.54 (0.3) | 4 |
| ASD & conduct disorder | | | | | | |
| Full ACE | 0.35 (0.11) | 3 | 0.88 (0.57) | 3 | 0.06 (0.08) | 3 |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; N= number of studies identified; SE= standard error. | | | | | | |

Supplementary Table 43. Heritability, shared and nonshared environmental influences on NDDs, stratified by raters.

| NDDs | Family $h^2$ (SE) | N | Family $c^2$ (SE) | N | Family $e^2$ (SE) | N | SNP $h^2$ (SE) | N |
|---|---|---|---|---|---|---|---|---|
| NDDs combined | | | | | | | | |
| Diagnosis | 0.81 (0.15) | 7 | 0.02 (0.09) | 2 | 0.3 (0.11) | 6 | 0.17 (0.04) | 11 |
| Parent | 0.7 (0.04) | 110 | 0.15 (0.03) | 48 | 0.25 (0.02) | 93 | 0.19 (0.07) | 10 |
| Parent & Self | 0.72 (0.1) | 8 | 0.09 (0.15) | 2 | 0.31 (0.06) | 8 | - | - |
| Parent & Teacher | 0.72 (0.06) | 17 | 0.04 (0.08) | 5 | 0.3 (0.04) | 14 | - | - |
| Researcher | 0.71 (0.18) | 2 | 0.02 (0.05) | 2 | 0.18 (0.16) | 2 | - | - |
| Self-report | 0.5 (0.07) | 19 | 0.12 (0.11) | 5 | 0.55 (0.05) | 17 | 0.05 (0.18) | 2 |
| Teacher | 0.65 (0.03) | 29 | 0.18 (0.07) | 12 | 0.34 (0.05) | 28 | 0.3 (0.19) | 5 |
| Cognitive test | 0.6 (0.04) | 98 | 0.21 (0.02) | 71 | 0.25 (0.02) | 73 | 0.29 (0.07) | 10 |
| Intellectual disabilities | | | | | | | | |
| Diagnosis | 0.86 (0.44) | 2 | - | - | 0.1 (0.16) | 2 | - | - |
| Communication disorders | | | | | | | | |
| Parent | 0.76 (0.22) | 7 | 0.43 (0.14) | 4 | 0.14 (0.06) | 6 | - | - |
| Teacher | 0.62 (0.11) | 2 | - | - | 0.17 (0.08) | 2 | - | - |
| Cognitive test | 0.6 (0.21) | 18 | 0.31 (0.06) | 12 | 0.25 (0.05) | 13 | 0.32 (0.14) | 4 |
| ASD | | | | | | | | |
| Diagnosis | 0.85 (0.15) | 4 | 0.01 (0.1) | 2 | 0.19 (0.11) | 3 | 0.12 (0.05) | 6 |
| Parent | 0.78 (0.21) | 27 | 0.19 (0.07) | 11 | 0.24 (0.03) | 20 | 0.2 (0.07) | 8 |
| Parent & Teacher | 0.63 (0.11) | 3 | - | - | 0.41 (0.12) | 3 | - | - |
| Self-report | 0.52 (0.12) | 2 | - | - | - | - | - | - |
| Teacher | 0.58 (0.07) | 6 | 0.04 (0.1) | 2 | 0.42 (0.07) | 5 | 0 (0.21) | 2 |
| ADHD | | | | | | | | |
| Diagnosis | 0.79 (0.24) | 4 | - | - | 0.29 (0.16) | 4 | 0.21 (0.05) | 7 |
| Parent | 0.7 (0.04) | 83 | 0.09 (0.03) | 34 | 0.23 (0.02) | 72 | 0.13 (0.1) | 5 |
| Parent & Self | 0.72 (0.1) | 8 | 0.09 (0.15) | 2 | 0.31 (0.06) | 8 | - | - |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Parent & Teacher | 0.71 (0.05) | 15 | 0.04 (0.08) | 5 | 0.29 (0.05) | 12 | - | - |
| Self-report | 0.5 (0.08) | 18 | 0.12 (0.11) | 5 | 0.56 (0.05) | 16 | 0.02 (0.18) | 2 |
| Teacher | 0.65 (0.05) | 18 | 0.16 (0.11) | 5 | 0.37 (0.04) | 17 | 0.38 (0.23) | 3 |
| Specific learning disorders | | | | | | | | |
| Parent | 0.72 (0.25) | 2 | - | - | 0.23 (0.08) | 2 | - | - |
| Teacher | 0.67 (0.05) | 5 | 0.16 (0.06) | 4 | 0.22 (0.04) | 5 | - | - |
| Cognitive test | 0.6 (0.04) | 85 | 0.19 (0.02) | 62 | 0.24 (0.02) | 63 | 0.32 (0.09) | 8 |
| Motor disorders | | | | | | | | |
| Diagnosis | 0.73 (0.15) | 3 | - | - | 0.32 (0.16) | 3 | - | - |
| Parent | 0.71 (0.11) | 4 | 0.12 (0.12) | 2 | 0.39 (0.12) | 4 | - | - |
| Note. $H^2$= heritability; $c^2$= shared environmental influences; $e^2$= nonshared environmental influences; N= number of studies identified; SE= standard error. | | | | | | | | |

Supplementary Table 44. Genetic, shared and nonshared environmental correlations between NDDs, stratified by raters.

| NDDs | Family rA (SE) | N | Family rC (SE) | N | Family rE (SE) | N | SNP rG (SE) | N |
|---|---|---|---|---|---|---|---|---|
| NDDs combined | | | | | | | | |
| Parent | 0.34 (0.16) | 15 | 0.64 (0.45) | 5 | 0.17 (0.07) | 9 | - | - |
| Parent & Teacher | 0.41 (0.07) | 8 | - | - | 0.18 (0.1) | 3 | - | - |
| Teacher | 0.08 (0.52) | 3 | 0.88 (0.57) | 3 | 0.18 (0.1) | 3 | - | - |
| Cognitive test | 0.5 (0.09) | 11 | 0.69 (0.42) | 7 | 0.17 (0.07) | 7 | 0.25 (0.14) | 5 |
| ASD & ADHD | | | | | | | | |
| Parent | 0.67 (0.3) | 5 | - | - | 0.22 (0.12) | 4 | - | - |
| ADHD & motor disorders | | | | | | | | |
| Parent | 0.9 (0.82) | 2 | - | - | - | - | - | - |
| ADHD & specific learning disorders | | | | | | | | |
| Parent | -0.03 (0.13) | 8 | 0.25 (0.12) | 3 | 0.11 (0.06) | 4 | - | - |
| Parent & Teacher | 0.43 (0.08) | 7 | - | - | 0.26 (0.15) | 2 | - | - |
| Teacher | -0.4 (0.23) | 2 | 0.69 (0.2) | 2 | 0.1 (0.08) | 2 | - | - |
| Communication disorders & specific learning disorders | | | | | | | | |
| Cognitive test | 0.66 (0.15) | 2 | - | - | - | - | - | - |

Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; N= number of studies identified; SE= standard error.

Supplementary Table 45. Genetic, shared and nonshared environmental correlations between NDDs and DICCs, stratified by raters.

| NDDs and DICCs | Family rA (SE) | N | Family rC (SE) | N | Family rE (SE) | N |
|---|---|---|---|---|---|---|
| NDDs and DICCs combined | | | | | | |
| Parent | 0.72 (0.34) | 6 | 0.93 (0.57) | 4 | 0.2 (0.09) | 5 |
| Parent & Self | 0.63 (0.5) | 2 | 0.97 (0.53) | 2 | 0.7 (0.61) | 2 |
| Parent & Teacher | 0.6 (0.28) | 3 | 0.82 (0.68) | 3 | 0.66 (0.6) | 2 |
| Self-report | 0.51 (0.25) | 2 | - | - | 0.11 (0.14) | 2 |
| ADHD & conduct disorder | | | | | | |
| Parent | 0.85 (0.61) | 3 | - | - | 0.22 (0.15) | 2 |
| ADHD & oppositional defiant disorder | | | | | | |
| Parent | 0.73 (0.32) | 2 | - | - | - | - |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; N= number of studies identified; SE= standard error. | | | | | | |

Supplementary Table 46. Heritability, shared and nonshared environmental influences on NDDs, stratified by number of covariates included in analyses.

| NDDs | Family $h^2$ (SE) | N | Family $c^2$ (SE) | N | Family $e^2$ (SE) | N | SNP $h^2$ (SE) | N |
|---|---|---|---|---|---|---|---|---|
| NDDs combined | | | | | | | | |
| 0 | 0.67 (0.04) | 56 | 0.22 (0.05) | 25 | 0.31 (0.03) | 39 | - | - |
| 1 | 0.68 (0.06) | 56 | 0.16 (0.04) | 25 | 0.27 (0.03) | 40 | 0.16 (0.07) | 2 |
| 2 | 0.64 (0.03) | 113 | 0.15 (0.02) | 69 | 0.3 (0.03) | 104 | 0.17 (0.16) | 3 |
| 3 | 0.61 (0.11) | 9 | 0.18 (0.07) | 5 | 0.31 (0.08) | 9 | 0.26 (0.06) | 14 |
| 4 | 0.73 (0.18) | 5 | 0.17 (0.08) | 3 | 0.23 (0.07) | 4 | - | - |
| Intellectual disabilities | | | | | | | | |
| 1 | 0.86 (0.44) | 2 | - | - | 0.1 (0.16) | 2 | - | - |
| Communication disorders | | | | | | | | |
| 0 | 0.47 (0.1) | 5 | 0.52 (0.11) | 3 | 0.15 (0.07) | 4 | - | - |
| 1 | 0.77 (0.24) | 7 | 0.29 (0.15) | 3 | 0.21 (0.1) | 5 | - | - |
| 2 | 0.5 (0.06) | 10 | 0.28 (0.07) | 8 | 0.26 (0.09) | 8 | - | - |
| ASD | | | | | | | | |
| 0 | 0.8 (0.19) | 11 | 0.03 (0.05) | 4 | 0.3 (0.1) | 6 | - | - |
| 1 | 0.76 (0.09) | 3 | - | - | 0.25 (0.09) | 3 | - | - |
| 2 | 0.68 (0.04) | 20 | 0.17 (0.08) | 8 | 0.26 (0.03) | 17 | - | - |
| ADHD | | | | | | | | |
| 0 | 0.68 (0.05) | 31 | 0.17 (0.07) | 12 | 0.36 (0.04) | 26 | - | - |
| 1 | 0.71 (0.09) | 25 | 0.08 (0.05) | 10 | 0.29 (0.05) | 21 | 0.17 (0.07) | 2 |
| 2 | 0.65 (0.04) | 58 | 0.09 (0.03) | 24 | 0.33 (0.04) | 54 | - | - |
| 3 | 0.66 (0.22) | 4 | - | - | 0.34 (0.17) | 4 | 0.15 (0.11) | 5 |
| 4 | 0.83 (0.16) | 3 | - | - | 0.11 (0.09) | 2 | - | - |
| Specific learning disorders | | | | | | | | |
| 0 | 0.58 (0.06) | 13 | 0.22 (0.07) | 8 | 0.21 (0.06) | 6 | - | - |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 1 | 0.66 (0.07) | 26 | 0.21 (0.06) | 14 | 0.18 (0.03) | 15 | - | - |
| 2 | 0.59 (0.03) | 46 | 0.18 (0.03) | 39 | 0.26 (0.02) | 41 | - | - |
| 3 | 0.56 (0.06) | 6 | 0.17 (0.08) | 4 | 0.32 (0.06) | 6 | 0.31 (0.09) | 7 |
| Motor disorders | | | | | | | | |
| 1 | 0.7 (0.09) | 4 | 0.21 (0.15) | 2 | 0.43 (0.17) | 4 | - | - |
| 2 | 0.8 (0.05) | 2 | - | - | - | - | - | - |
| Note. $H^2$= heritability; $c^2$= shared environmental influences; $e^2$= nonshared environmental influences; N= number of studies identified; SE= standard error. | | | | | | | | |

Supplementary Table 47. Genetic, shared and nonshared environmental correlations between NDDs, stratified by number of covariates included in analyses.

| NDDs | Family rA (SE) | N | Family rC (SE) | N | Family rE (SE) | N |
|---|---|---|---|---|---|---|
| NDDs combined | | | | | | |
| 0 | 0.35 (0.08) | 8 | - | - | - | - |
| 1 | 0.51 (0.22) | 7 | 0.1 (0.09) | 2 | 0.02 (0.08) | 2 |
| 2 | 0.3 (0.22) | 20 | 0.8 (0.35) | 13 | 0.17 (0.03) | 17 |
| 3 | 0.53 (0.11) | 2 | - | - | 0.44 (0.14) | 2 |
| ASD & ADHD | | | | | | |
| 2 | 0.68 (0.49) | 4 | - | - | 0.18 (0.09) | 4 |
| ADHD & motor disorders | | | | | | |
| 1 | 0.9 (0.82) | 2 | - | - | - | - |
| ADHD & specific learning disorders | | | | | | |
| 0 | 0.36 (0.13) | 4 | - | - | - | - |
| 1 | 0.28 (0.1) | 4 | - | - | - | - |
| 2 | -0.13 (0.13) | 9 | 0.4 (0.14) | 6 | 0.12 (0.05) | 7 |
| Communication disorders & specific learning disorders | | | | | | |
| 2 | 0.66 (0.15) | 2 | - | - | - | - |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; N= number of studies identified; SE= standard error. | | | | | | |

Supplementary Table 48. Genetic, shared and nonshared environmental correlations between NDDs and DICCs, stratified by number of covariates included in analyses.

| NDDs and DICCs | Family rA (SE) | N | Family rC (SE) | N | Family rE (SE) | N |
|---|---|---|---|---|---|---|
| NDDs and DICCs combined | | | | | | |
| 0 | 0.39 (0.13) | 6 | 0.71 (0.6) | 4 | 0.2 (0.09) | 5 |
| 1 | 0.58 (0.19) | 5 | 0.94 (0.55) | 4 | 0.44 (0.34) | 4 |
| 2 | 0.93 (0.74) | 3 | 0.93 (0.77) | 2 | 0.58 (0.41) | 3 |
| ADHD & conduct disorder | | | | | | |
| 0 | 0.43 (0.24) | 2 | - | - | 0.12 (0.16) | 2 |
| 1 | 0.37 (0.1) | 3 | 0.87 (0.86) | 2 | 0.05 (0.1) | 2 |
| ADHD & oppositional defiant disorder | | | | | | |
| 0 | 0.62 (0.25) | 2 | - | - | 0.35 (0.17) | 2 |
| 1 | 0.56 (0.29) | 3 | 0.87 (0.86) | 2 | 0.32 (0.1) | 2 |
| Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; N= number of studies identified; SE= standard error. | | | | | | |

Supplementary Table 49. Heritability, shared and nonshared environmental influences on NDDs, stratified by measurement instruments.

| Measures from family-based studies | | | | | | | Measures from SNP-based studies | | |
|---|---|---|---|---|---|---|---|---|---|
| NDDs | Family $h^2$ (SE) | N | Family $c^2$ (SE) | N | Family $e^2$ (SE) | N | | SNP $h^2$ (SE) | N |
| Intellectual disabilities | | | | | | | | | |
| ICD-9/ICD-10 | 0.86 (0.44) | 2 | - | - | 0.1 (0.16) | 2 | | | |
| Communication disorders | | | | | | | | | |
| Clinical evaluation | 0.75 (0.13) | 3 | - | - | 0.27 (0.15) | 2 | TOAL | 0.32 (0.16) | 3 |
| Goldman-Fristoe Test of Articulation | 0.58 (0.2) | 2 | 0.27 (0.2) | 2 | 0.16 (0.12) | 2 | | - | - |
| MCDI | 0.46 (0.13) | 3 | 0.53 (0.11) | 3 | 0.05 (0.05) | 3 | | - | - |
| TEGI | 0.74 (0.32) | 2 | 0.12 (0.2) | 2 | 0.19 (0.2) | 2 | | - | - |
| ASD | | | | | | | | | |
| A-TAC | 0.73 (0.06) | 8 | 0.14 (0.08) | 3 | 0.29 (0.04) | 7 | AQ | - | - |
| ADI-R & ADOS | 0.81 (0.62) | 2 | 0.28 (0.3) | 2 | - | - | CAST | 0.03 (0.18) | 2 |
| AQ | 0.51 (0.1) | 3 | - | - | 0.2 (0.17) | 2 | ICD-9/ICD-10 | 0.12 (0.05) | 7 |
| ADI-R | 0.81 (0.45) | 3 | 0.3 (0.22) | 2 | 0.14 (0.22) | 2 | SCDC | 0.24 (0.1) | 4 |
| CAST | 0.7 (0.04) | 14 | 0.09 (0.06) | 4 | 0.27 (0.03) | 11 | | - | - |
| DAWBA | 0.75 (0.15) | 3 | - | - | 0.22 (0.17) | 2 | | - | - |
| DSM-4/DSM-5 | 0.69 (0.08) | 2 | - | - | 0.31 (0.09) | 2 | | - | - |
| ICD-9/ICD-10 | 0.8 (0.12) | 3 | 0.01 (0.1) | 2 | 0.19 (0.11) | 3 | | - | - |
| ADHD | | | | | | | | | |
| A-TAC | 0.78 (0.1) | 5 | 0.03 (0.07) | 2 | 0.25 (0.05) | 5 | CBRS | 0.13 (0.13) | 3 |
| ATBRS | 0.82 (0.07) | 3 | 0.23 (0.14) | 3 | 0.12 (0.08) | 3 | ICD-9/ICD-10 | 0.21 (0.21) | 7 |
| CBCL | 0.61 (0.09) | 14 | 0.05 (0.06) | 5 | 0.25 (0.04) | 11 | SDQ | 0.09 (0.09) | 4 |
| CBCL & YSR | 0.78 (0.06) | 3 | - | - | 0.25 (0.09) | 3 | TRF | 0.53 (0.53) | 2 |
| CBRS | 0.72 (0.03) | 29 | 0.18 (0.16) | 11 | 0.24 (0.03) | 28 | | - | - |
| DBD | 0.69 (0.25) | 3 | 0.16 (0.13) | 3 | 0.19 (0.07) | 3 | | - | - |
| DBRS | 0.76 (0.11) | 4 | 0.03 (0.1) | 3 | 0.25 (0.08) | 3 | | - | - |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| DCB | 0.67 (0.07) | 2 | - | - | - | - | | - | - |
| DICA | 0.69 (0.21) | 3 | - | - | - | - | | - | - |
| DISC | 0.51 (0.1) | 5 | 0.03 (0.16) | 2 | 0.54 (0.11) | 4 | | - | - |
| DSM-4/DSM-5 | 0.77 (0.29) | 9 | 0.11 (0.11) | 4 | 0.35 (0.08) | 7 | | - | - |
| DuPaul ADHD Rating Scale | 0.75 (0.05) | 4 | 0.29 (0.12) | 2 | 0.25 (0.07) | 4 | | - | - |
| ECRS | 0.77 (0.23) | 2 | - | - | 0.28 (0.1) | 2 | | - | - |
| ICD-9/ICD-10 | 0.87 (0.11) | 3 | - | - | 0.12 (0.05) | 3 | | - | - |
| Rutter Scales | 0.75 (0.15) | 4 | - | - | 0.26 (0.13) | 2 | | - | - |
| SBQ | 0.61 (0.26) | 2 | - | - | 0.38 (0.19) | 2 | | - | - |
| SDQ | 0.65 (0.1) | 15 | 0.07 (0.12) | 4 | 0.43 (0.07) | 14 | | - | - |
| SWAN | 0.73 (0.16) | 8 | 0.35 (0.09) | 5 | 0.14 (0.05) | 7 | | - | - |
| TRF | 0.6 (0.12) | 4 | - | - | 0.46 (0.08) | 3 | | - | - |
| Specific learning disorders | | | | | | | | | |
| Comprehensive Test of Phonological Processing | 0.55 (0.17) | 3 | 0.22 (0.16) | 3 | 0.27 (0.1) | 3 | GCSE | 0.34 (0.2) | 2 |
| FCAT | 0.46 (0.13) | 4 | 0.31 (0.14) | 4 | 0.23 (0.07) | 4 | NFER | 0.31 (0.16) | 3 |
| GCSE | 0.61 (0.07) | 5 | 0.22 (0.07) | 5 | 0.18 (0.04) | 5 | PIAT | 0.24 (0.22) | 2 |
| National Curriculum | 0.64 (0.08) | 7 | 0.15 (0.05) | 7 | 0.23 (0.03) | 7 | TOWRE | 0.36 (0.2) | 2 |
| NFER | 0.49 (0.06) | 9 | 0.17 (0.07) | 7 | 0.33 (0.05) | 7 | National Curriculum | 0.33 (0.18) | 2 |
| PIAT | 0.56 (0.07) | 21 | 0.22 (0.06) | 14 | 0.25 (0.07) | 13 | | - | - |
| PIAT & GOAL | 0.59 (0.09) | 5 | 0.21 (0.07) | 4 | 0.35 (0.1) | 4 | | - | - |
| PIAT & TOWRE | 0.66 (0.15) | 2 | - | - | - | - | | - | - |
| PIAT & WISC | 0.59 (0.15) | 5 | 0.23 (0.19) | 3 | 0.11 (0.18) | 2 | | - | - |
| PIAT & WRAT | 0.51 (0.2) | 3 | - | - | - | - | | - | - |
| TOWRE | 0.7 (0.07) | 8 | 0.13 (0.06) | 8 | 0.17 (0.04) | 8 | | - | - |
| WISC | 0.41 (0.27) | 2 | - | - | - | - | | - | - |
| The Woodcock–Johnson Tests of Cognitive Abilities | 0.57 (0.11) | 8 | 0.19 (0.1) | 7 | 0.24 (0.06) | 7 | | - | - |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| TOWRE & The Woodcock–Johnson Tests of Cognitive Abilities | 0.77 (0.16) | 2 | - | - | - | - | | - | - |
| WRAT | 0.48 (0.19) | 2 | 0.33 (0.18) | 2 | 0.2 (0.12) | 2 | | - | - |
| Motor disorders | | | | | | | | | |
| A-TAC | 0.58 (0.12) | 2 | - | - | 0.42 (0.12) | 2 | - | - | - |

Note. $H^2$= heritability; $c^2$= shared environmental influences; $e^2$= nonshared environmental influences; N= number of studies identified; SE= standard error; TOAL= Test of Adolescent and Adult Language; MCDI= MacArthur-Bates Communicative Development Inventories; TEGI= Test of Early Grammatical Impairment; A-TAC= Autism-Tics, AD/HD, and other Comorbidities Inventory; ADI-R= The Autism Diagnostic Interview-Revised; ADOS= Autism Diagnostic Observation Schedule; AQ= Autism Spectrum Quotient; CAST= Childhood Autism Spectrum Test; SCDC= Social and Communication Disorders Checklist; DAWBA= Developmental and Well-Being Assessment; DSM= Diagnostic Statistical Manual; ICD= International Classification of Diseases; ATBRS= Australian Twin Behaviour Rating Scale; CBRS= Conners Comprehensive Behaviour Rating Scale; CBCL= Child Behavior Checklist; YSR= Youth Self-Report; DBD= Disruptive Behavior Disorder Rating Scale; DBRS= The Disruptive Behavior Rating Scale; DCB= Devereux Child Behavior Rating Scale; DICA= Diagnostic Interview for Children and Adolescents; DISC= Diagnostic Interview Schedule for Children; ECRS= Emory Combined Rating Scale; SBQ= Social
Behavior Questionnaire; SDQ= Strengths and Difficulties Questionnaire; SWAN= Strengths and Weaknesses of Attention-Deficit/Hyperactivity-symptoms and Normal-behaviors; TRF= Teacher Report Form; FCAT= The Florida Comprehensive Assessment Test; GCSE= General Certificate of Secondary Education; NFER= National Foundation for Educational Research; PIAT= The Peabody Individual Achievement Test; GOAL= Greater Opportunities for Adult Learning Success; TOWRE= Test of Word Reading Efficiency; WISC= Wechsler Intelligence Scale for Children; WRAT= Wide Range Achievement Test.

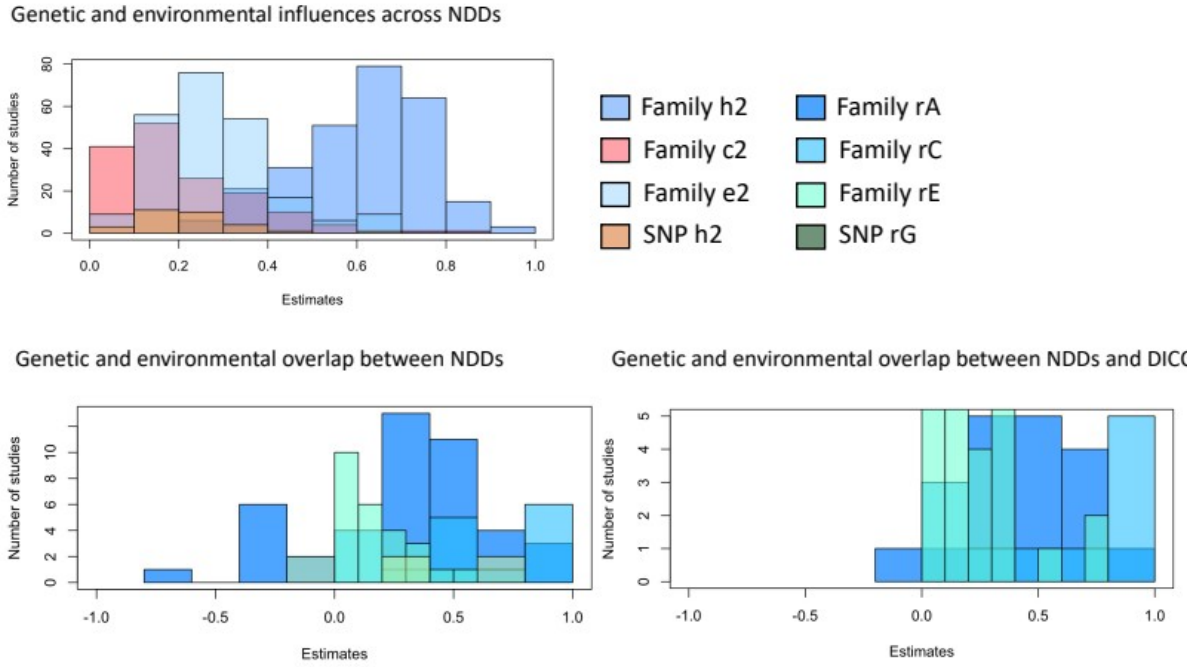
Supplementary Table 50. Genetic, shared and nonshared environmental correlations between NDDs, stratified by measurement instruments.

| NDDs | Family rA (SE) | N | Family rC (SE) | N | Family rE (SE) | N |
|---|---|---|---|---|---|---|
| ASD & ADHD | | | | | | |
| A-TAC | 0.8 (0.25) | 3 | - | - | 0.36 (0.12) | 2 |
| CAST & CBRS | 0.26 (0.1) | 2 | - | - | 0.1 (0.08) | 2 |
| ADHD & specific learning disorders | | | | | | |
| CBRS & PIAT | -0.29 (0.1) | 2 | 0.23 (0.13) | 2 | 0.1 (0.08) | 2 |
| CBRS & RDQ | 0.48 (0.13) | 2 | - | - | 0.26 (0.15) | 2 |
| DBRS & PIAT | 0.33 (0.25) | 3 | - | - | - | - |
| DICA & PIAT | 0.35 (0.18) | 2 | - | - | - | - |

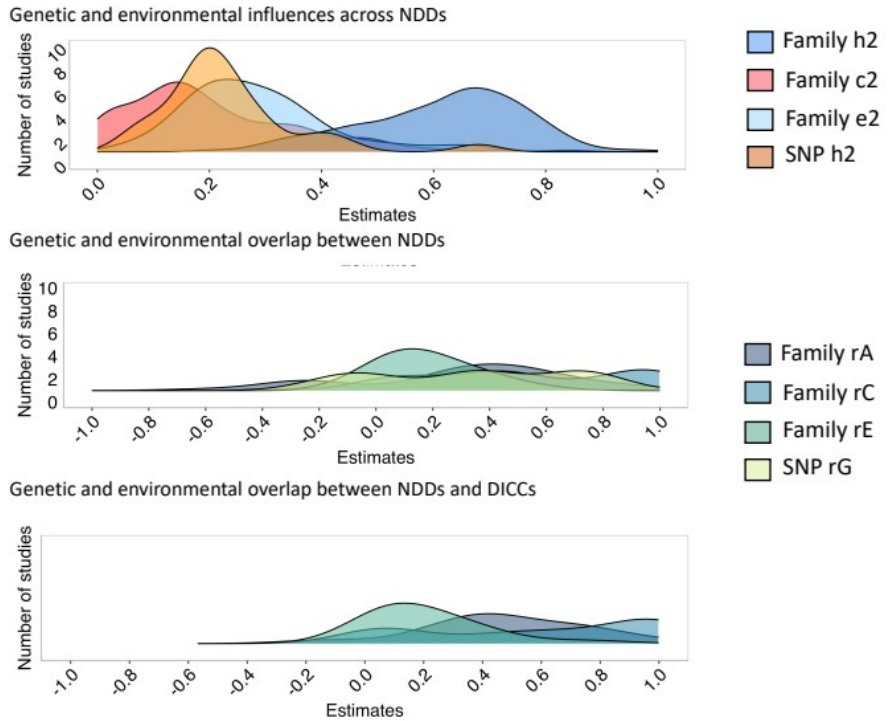
Note. rA/rG= genetic correlation; rC= shared environmental correlation; rE= nonshared environmental correlation; N= number of studies identified; SE= standard error; A-TAC= Autism-Tics, AD/HD, and other Comorbidities Inventory; CAST= Childhood Autism Spectrum Test; CBRS= Conners Comprehensive Behaviour Rating Scale; PIAT= The Peabody Individual Achievement Test; DBRS= The Disruptive Behavior Rating Scale; DICA= Diagnostic Interview for Children and Adolescents; RDQ= Reading Difficulties Questionnaire.

# Supplementary Figures

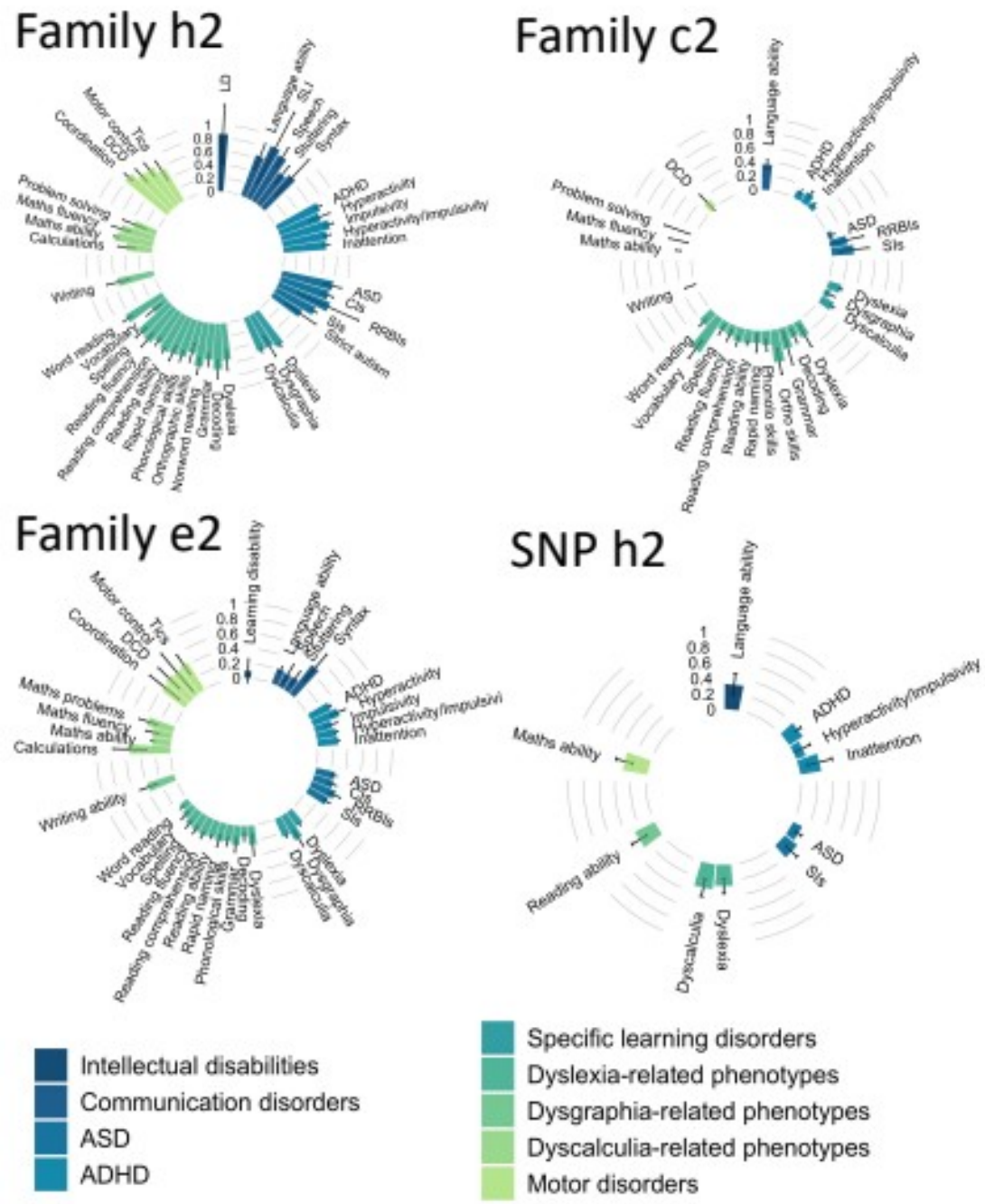
A



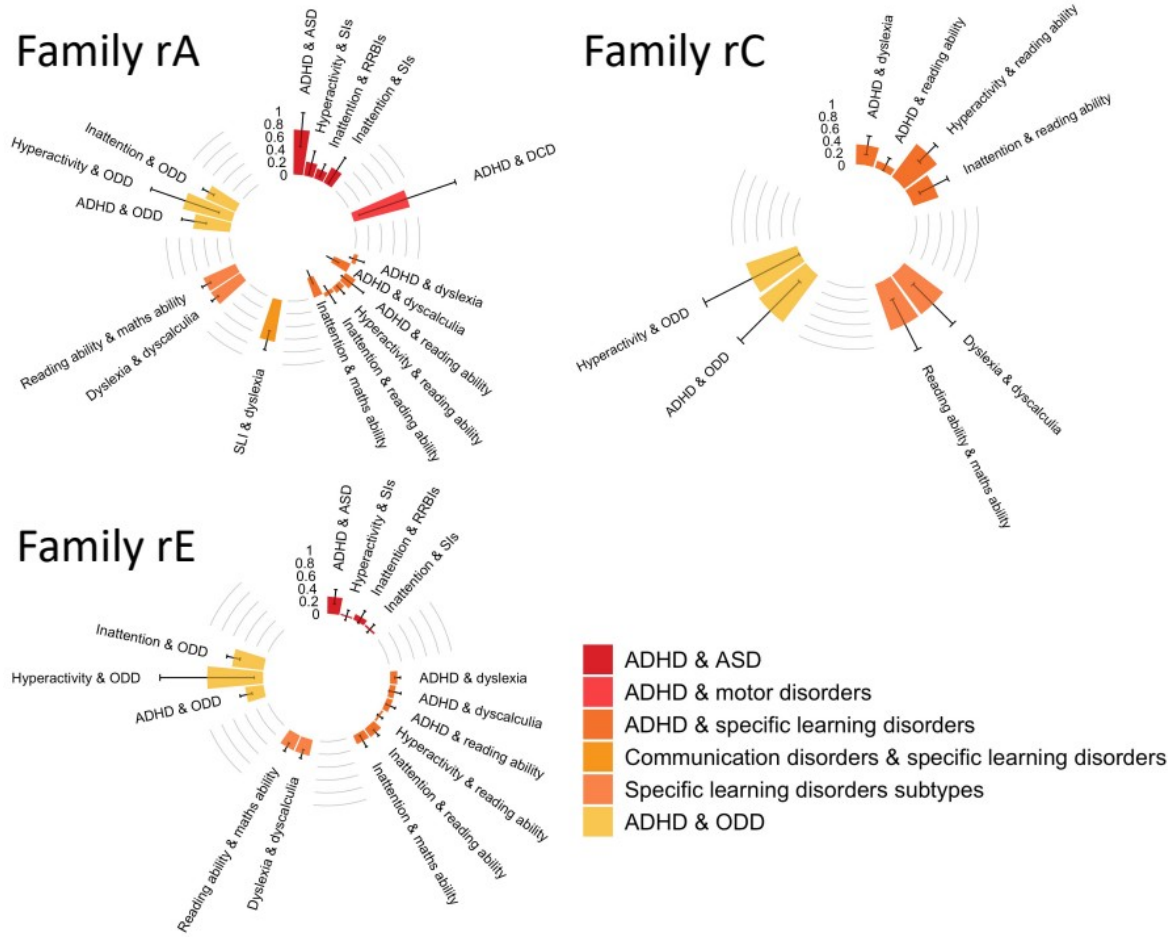

B



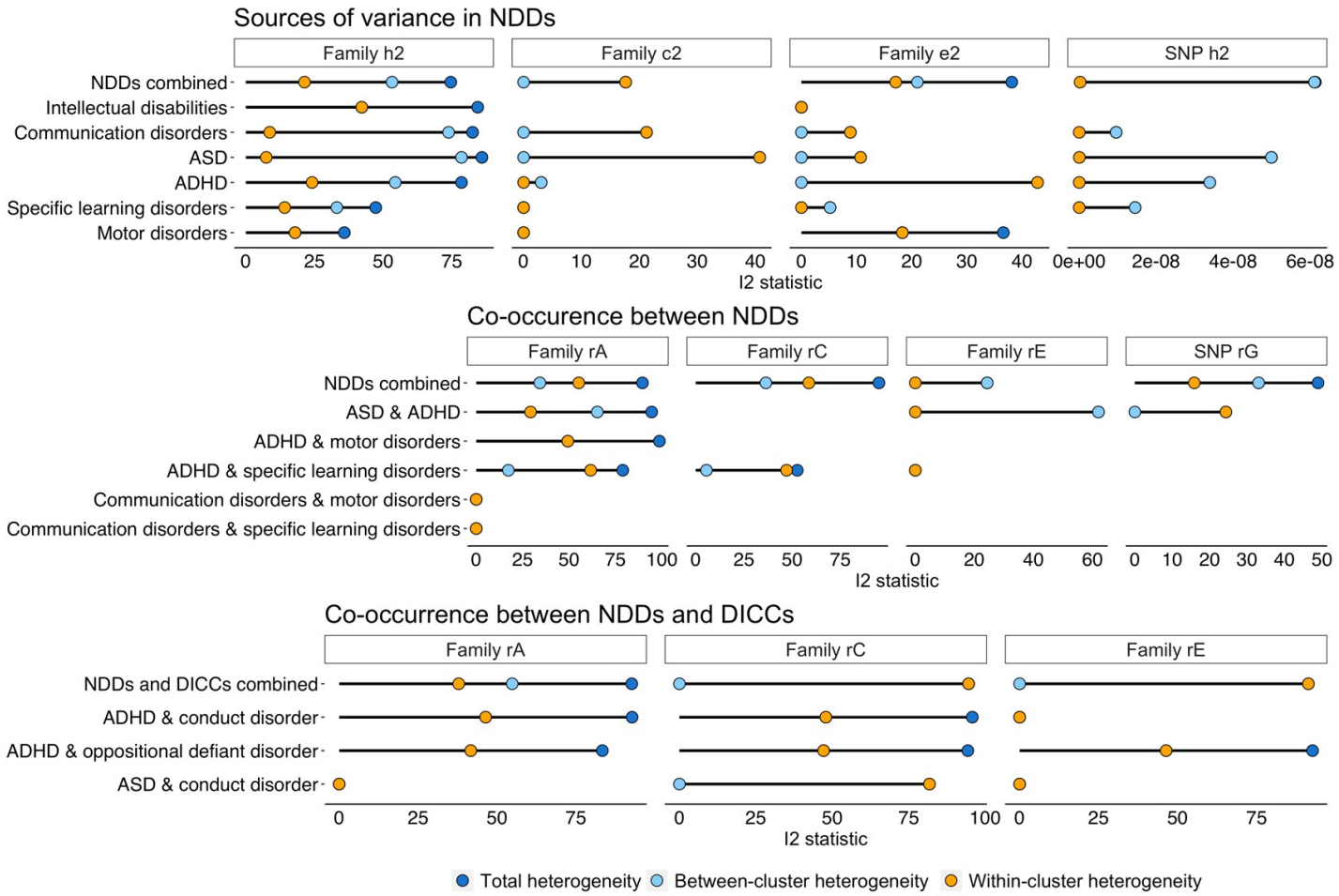

Supplementary Figure 1. Distribution of estimates. Panel A presents distribution of heritability (h2), shared (c2) and nonshared (e2) environmental influences on neurodevelopmental disorders (NDDs (top panel), as well as genetic (rA/rG), shared (rC) and nonshared (rE) environmental correlations between NDDs (right bottom panel) and between NDDs and disruptive, impulse control and conduct disorders (DICCs) (left bottom panel). Panel B presents density plot of heritability and environmental influences on NDDs (top panel), as well as genetic and environmental correlations between NDDs (middle panel) and between NDDs and DICCs (bottom panel).



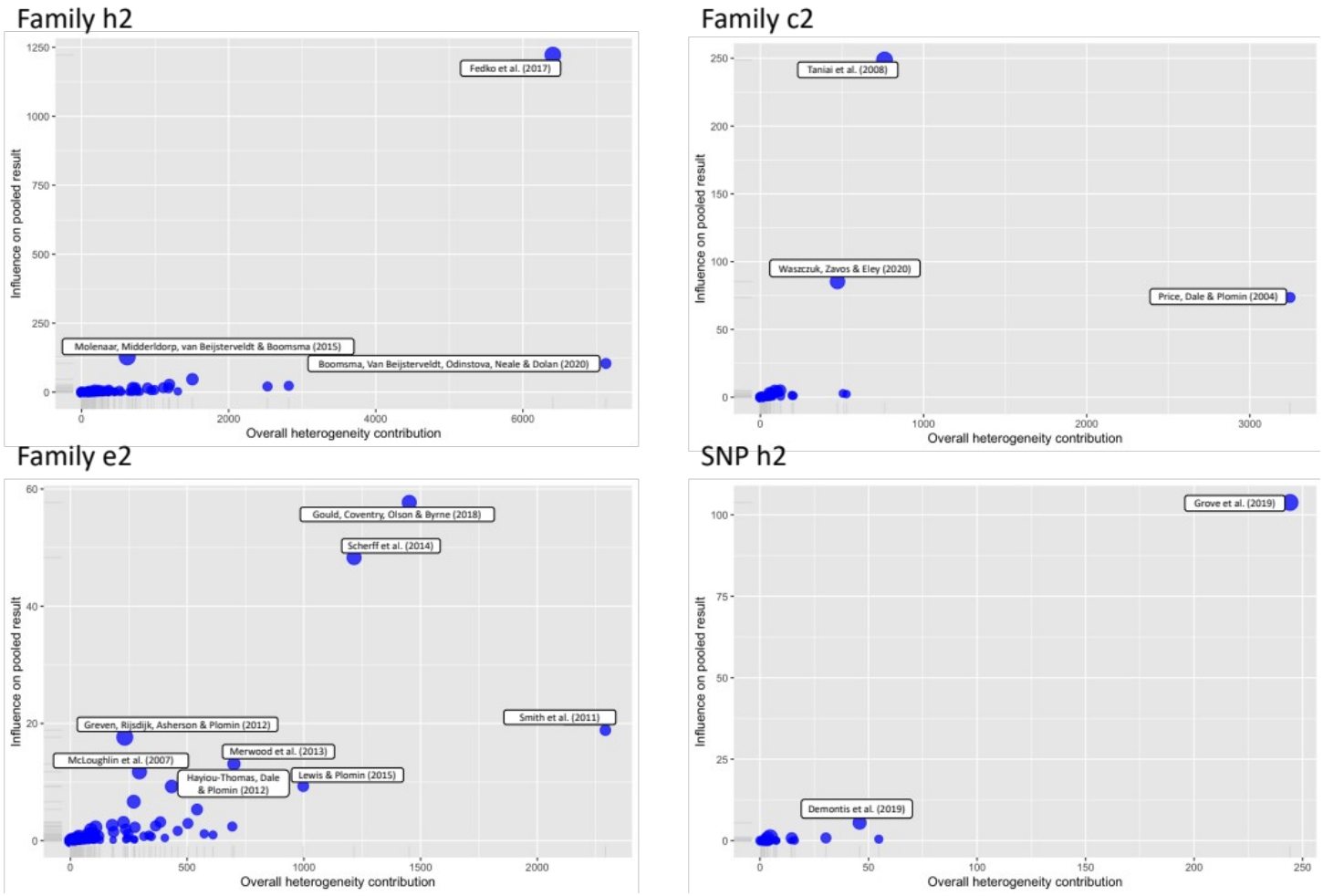

Supplementary Figure 2. Heritability (h2), shared (c2) and nonshared (e2) environmental influences on specific phenotypes within neurodevelopmental disorders (NDDs) categories.



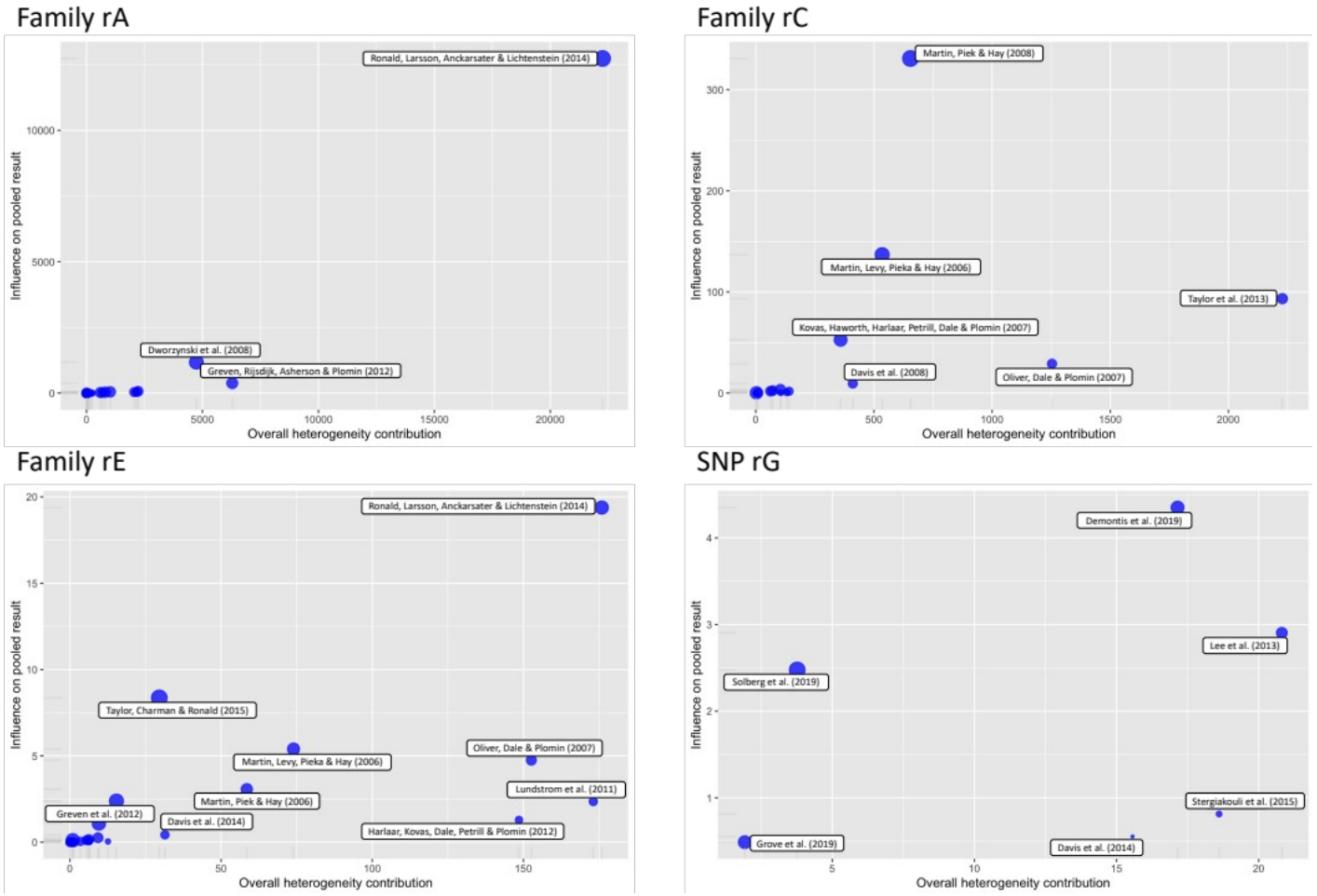

Supplementary Figure 3. Genetic (rA), shared (rC) and nonshared (rE) environmental overlap between specific phenotypes within the neurodevelopmental disorders (NDDs) category and between specific phenotypes within the NDDs and disruptive, impulse control and conduct disorders (DICCs) category.



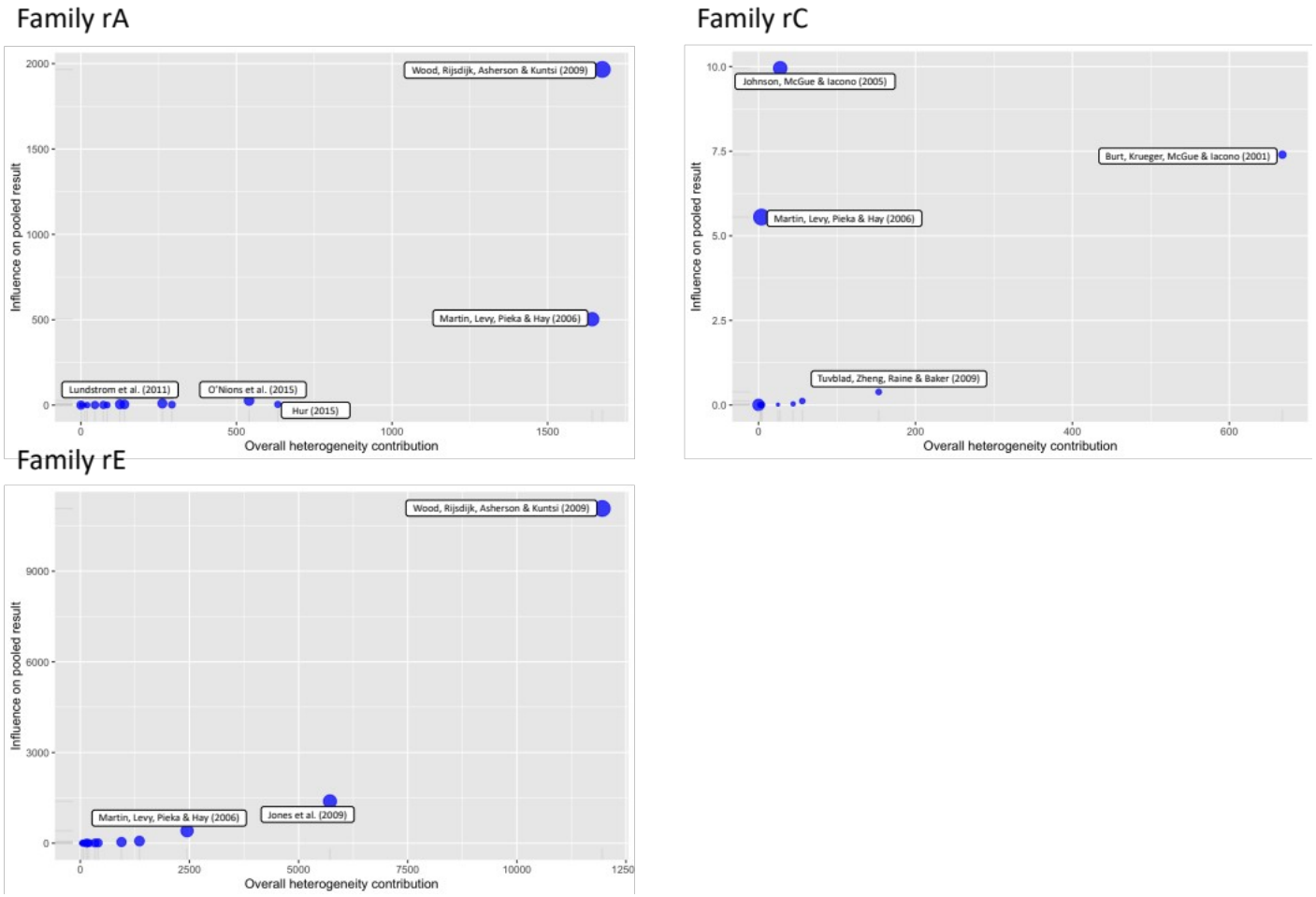

Supplementary Figure 4. Variance in heritability (h2), shared (c2) and nonshared (e2) environmental influences on neurodevelopmental disorders (NDDs) (top panel), variance in genetic (rA/rG), shared (rC) and nonshared (rE) environmental correlations between NDDs (middle panel) and variance in genetic and environmental correlations between NDDs and disruptive, impulse control and conduct disorders (DICCs) that can be attributed to heterogeneity (the I2 statistic).




Supplementary Figure 5. Results of the influential cases identification analysis. The baujat plots present studies determined to have a significant impact on the grand estimates of heritability (h2), shared (c2) and nonshared (e2) environmental influences on neurodevelopmental disorders (NDDs) and/or heterogeneity of estimates.

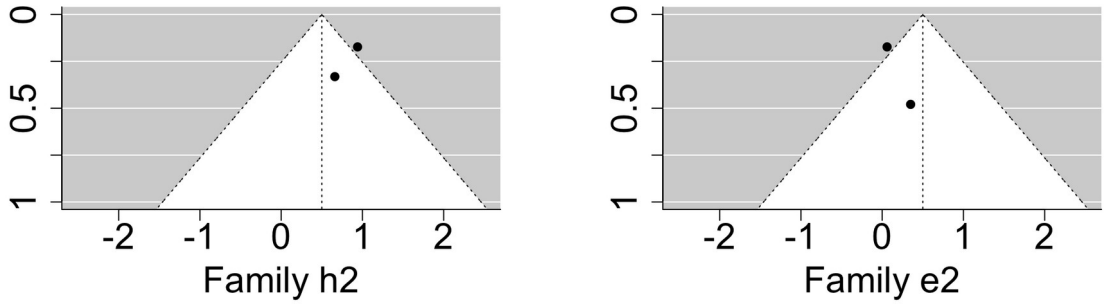



Supplementary Figure 6. Results of the influential cases identification analysis. The baujat plots present studies determined to have a significant impact on the grand estimates of genetic (rA), shared (rC) and nonshared (rE) environmental overlap between neurodevelopmental disorders (NDDs) and/or heterogeneity of estimates.

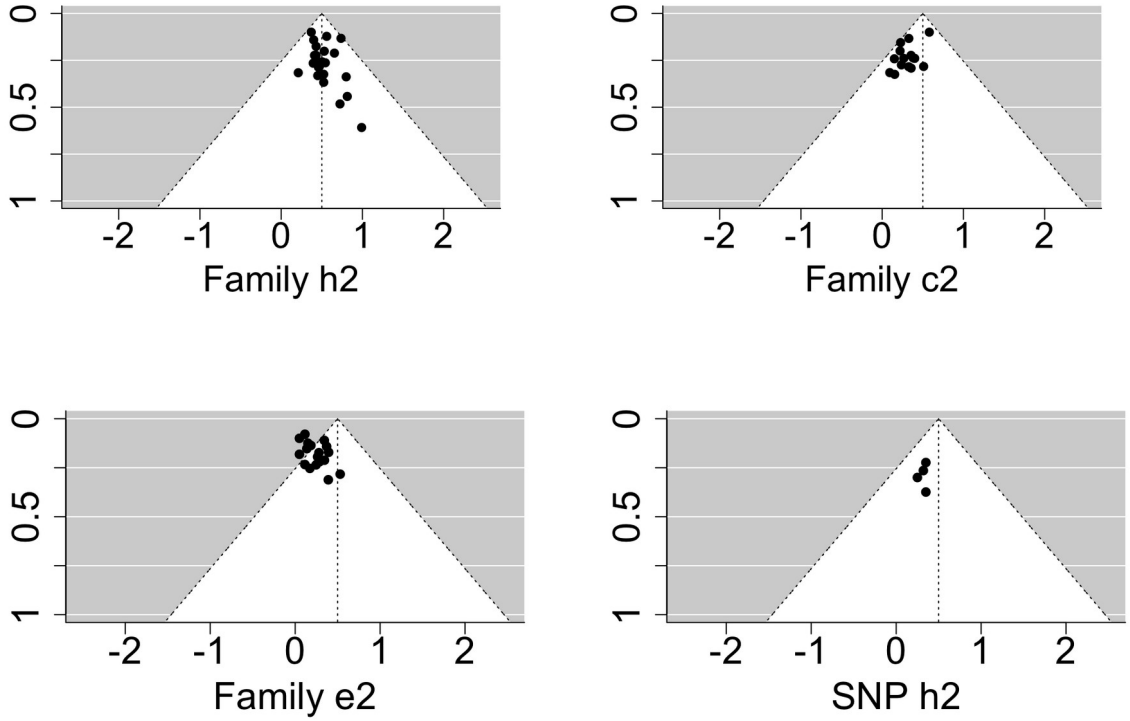



Supplementary Figure 7. Results of the influential cases identification analysis. The baujat plots present studies determined to have a significant impact on the grand estimates of genetic (rA), shared (rC) and nonshared (rE) environmental overlap between neurodevelopmental disorders (NDDs) and disruptive, impulse control and conduct disorders (DICCs) and/or heterogeneity of estimates.

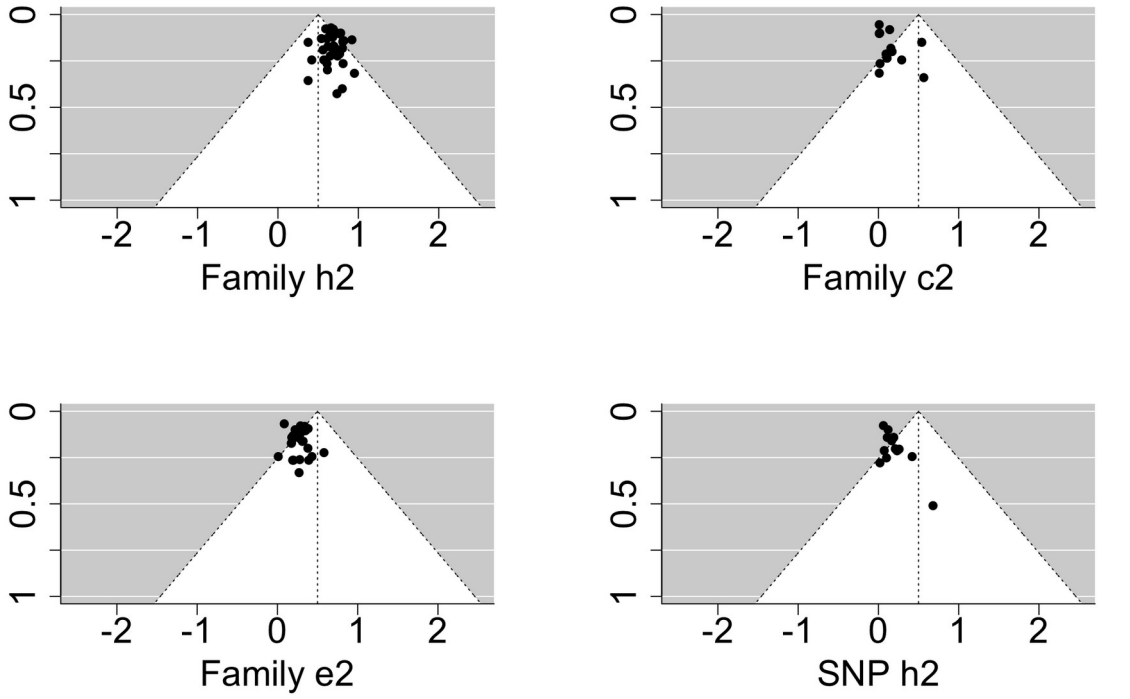

Supplementary Figure 8. Funnel plots involving all studies addressing heritability (h2), shared (c2) and nonshared (e2) environmental influences on neurodevelopmental disorders (NDDs).



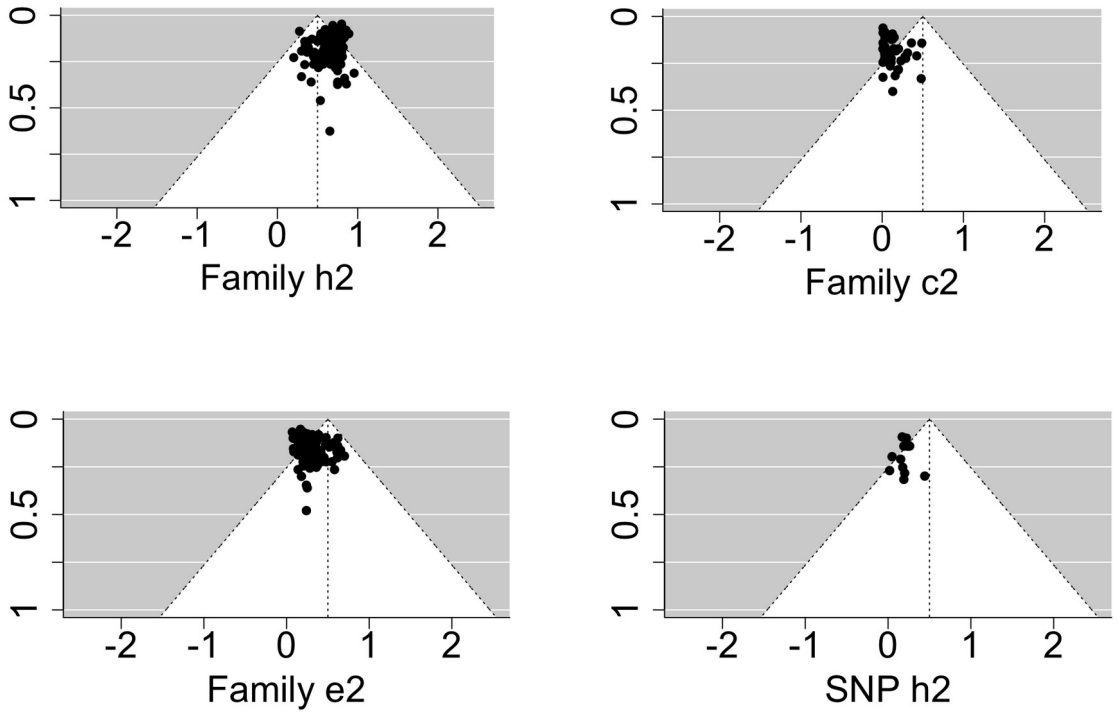

Supplementary Figure 9. Funnel plots involving all studies addressing heritability (h2) and nonshared (e2) environmental influences on intellectual disabilities.



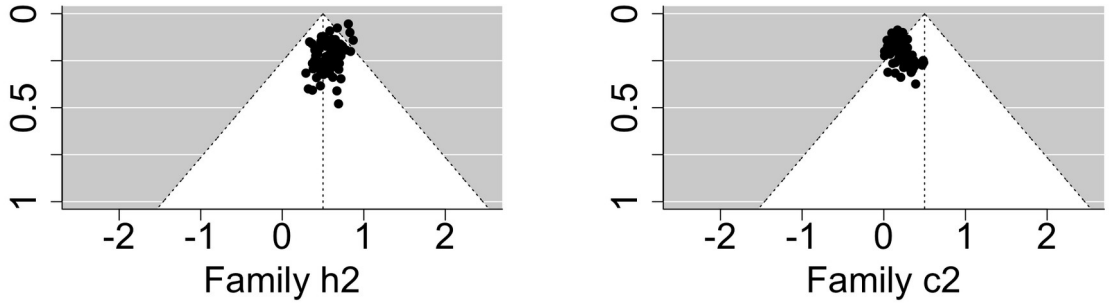

Supplementary Figure 10. Funnel plots involving all studies addressing heritability (h2), shared (c2) and nonshared (e2) environmental influences on communication disorders

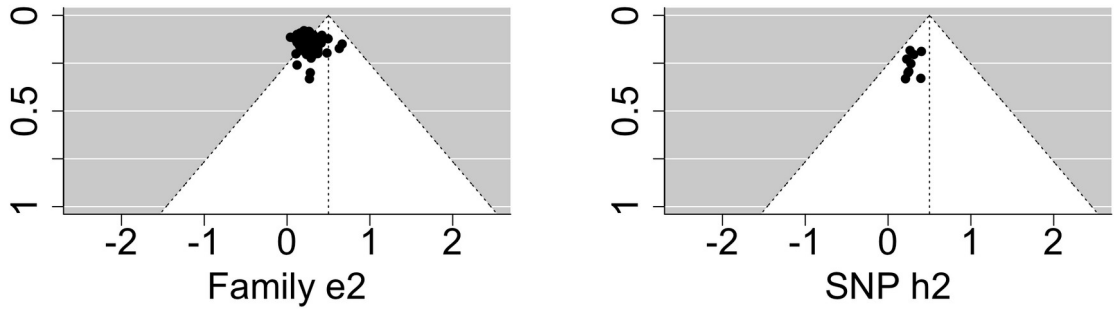


Supplementary Figure 11. Funnel plots involving all studies addressing heritability (h2), shared (c2) and nonshared (e2) environmental influences on ASD.

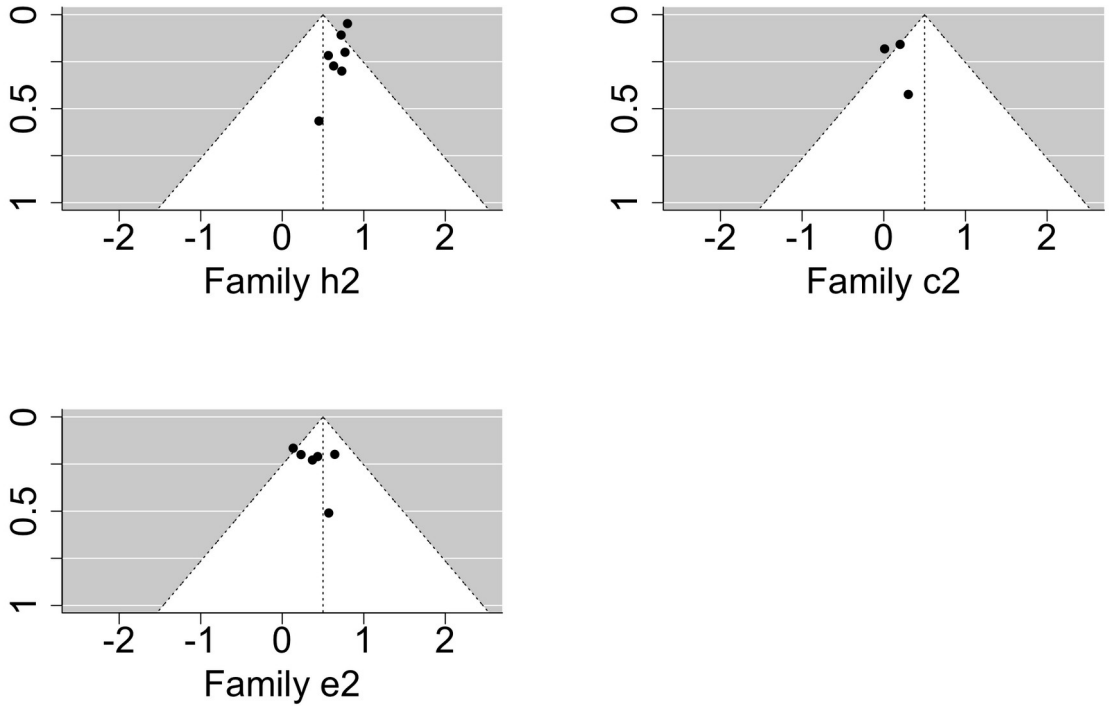



Supplementary Figure 12. Funnel plots involving all studies addressing heritability (h2), shared (c2) and nonshared (e2) environmental influences on ADHD.

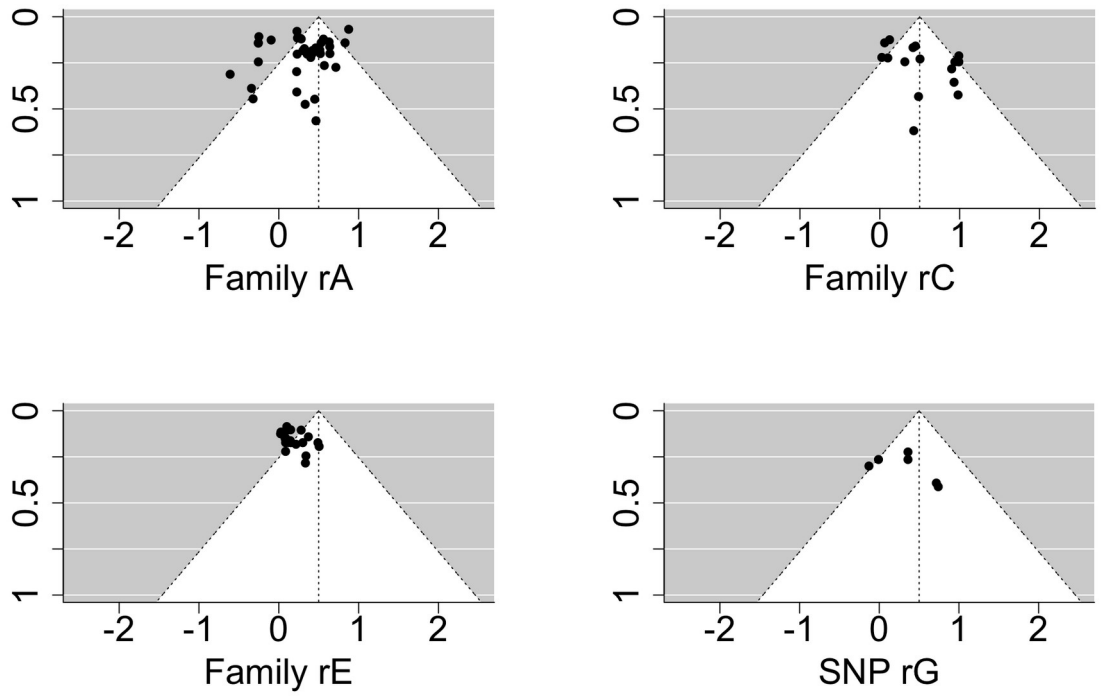




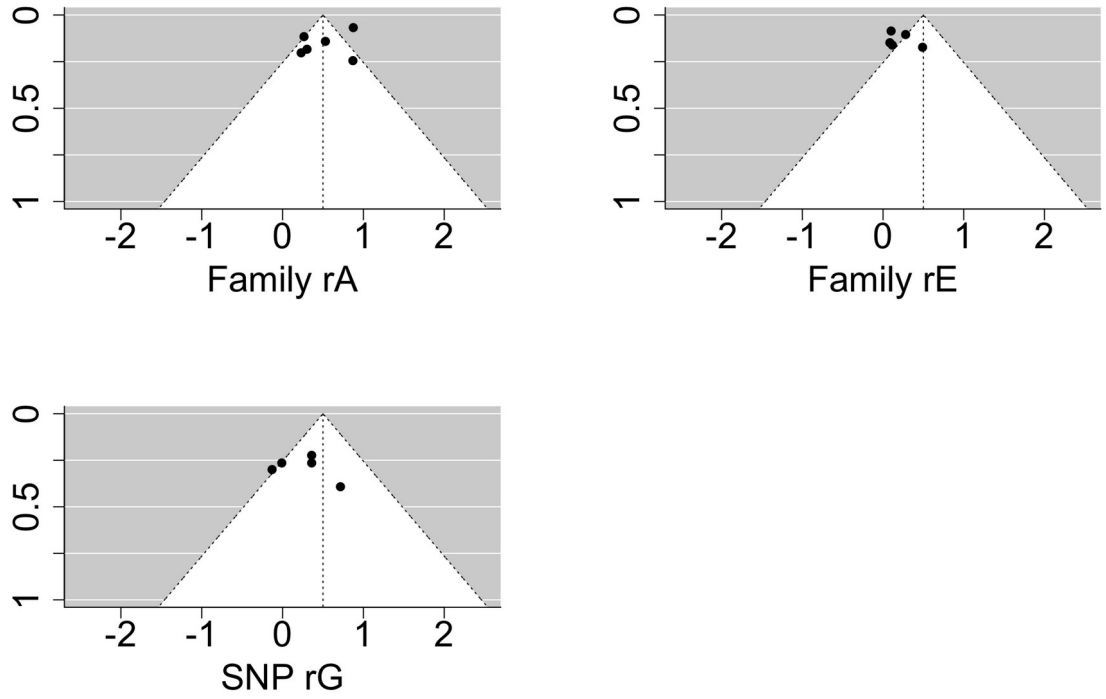

Supplementary Figure 13. Funnel plots involving all studies addressing heritability (h2), shared (c2) and nonshared (e2) environmental influences on specific learning disorders.



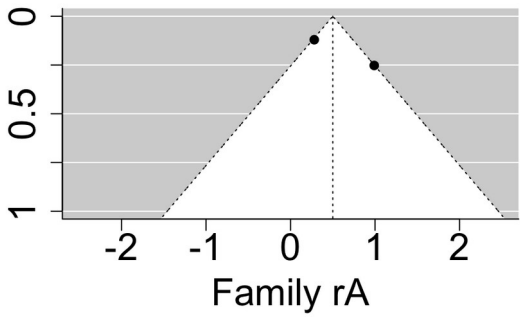

Supplementary Figure 14. Funnel plots involving all studies addressing heritability (h2), shared (c2) and nonshared (e2) environmental influences on motor disorders.



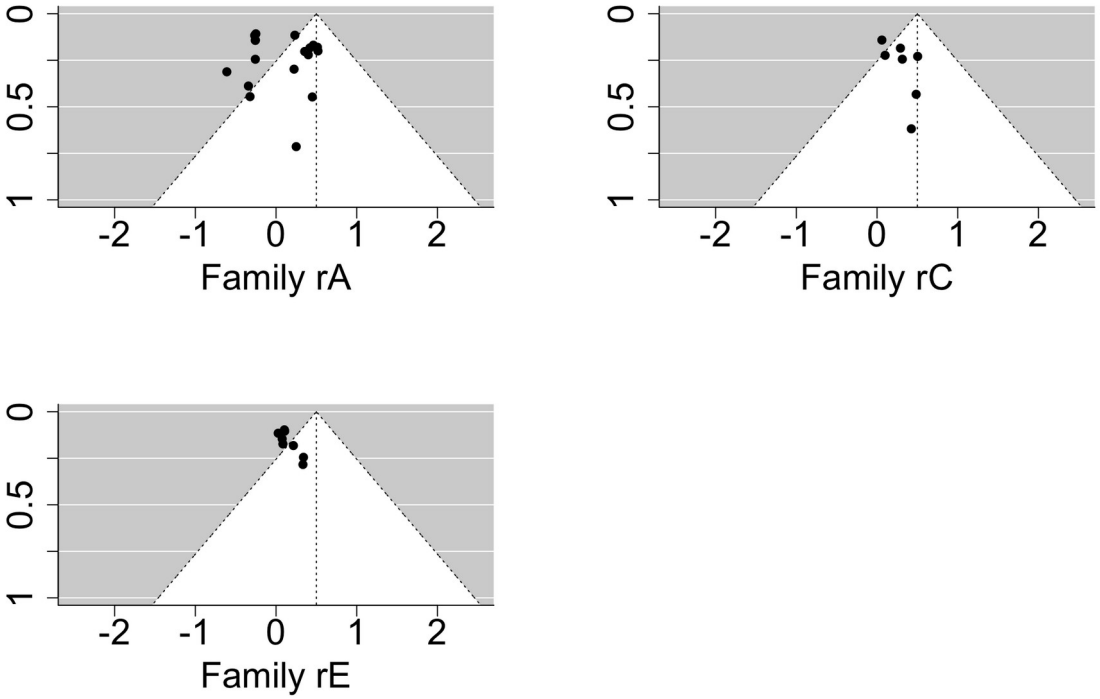

Supplementary Figure 15. Funnel plots involving all studies addressing genetic (rA), shared (rC) and nonshared (rE) environmental overlap between neurodevelopmental disorders (NDDs).



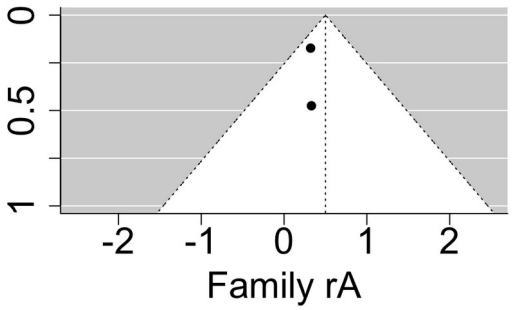

Supplementary Figure 16. Funnel plots involving all studies addressing genetic (rA), and nonshared (rE) environmental overlap between ASD & ADHD.



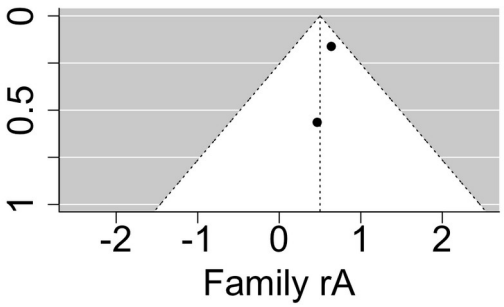

Supplementary Figure 17. Funnel plots involving all studies addressing genetic overlap (rA) between ADHD & motor disorders.



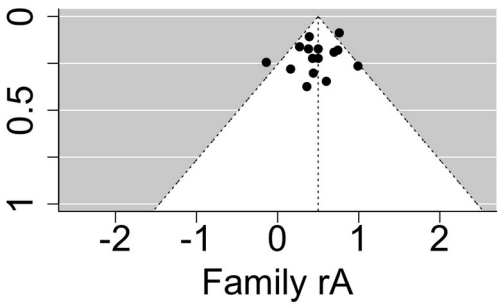

Supplementary Figure 18. Funnel plots involving all studies addressing genetic (rA), shared (rC) and nonshared (rE) environmental overlap between ADHD & specific learning disorders.

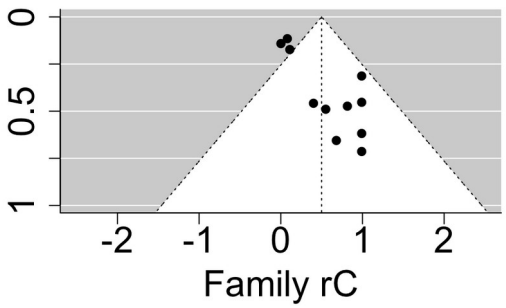


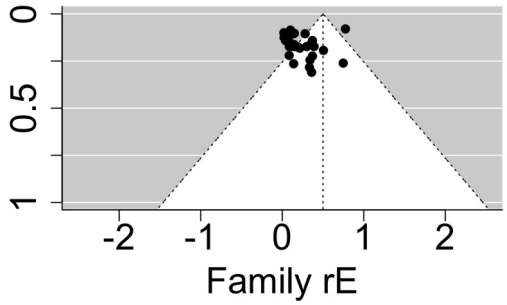

Supplementary Figure 19. Funnel plots involving all studies addressing genetic overlap (rA) between communication disorders & motor disorders.



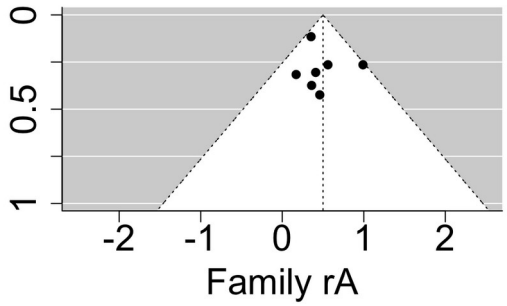

Supplementary Figure 20. Funnel plots involving all studies addressing genetic overlap (rA) between communication disorders & specific learning disorders.

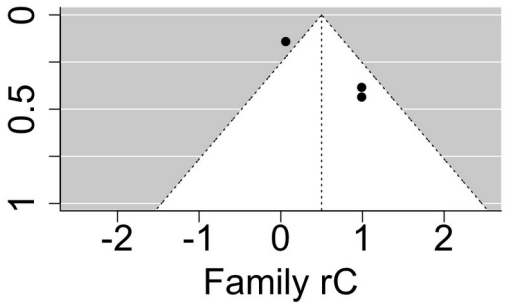


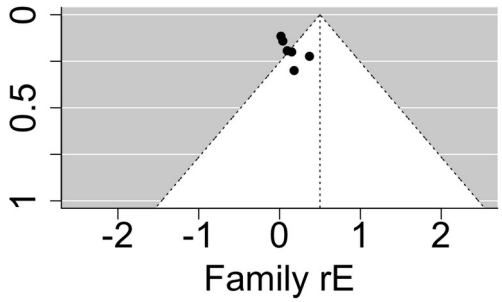





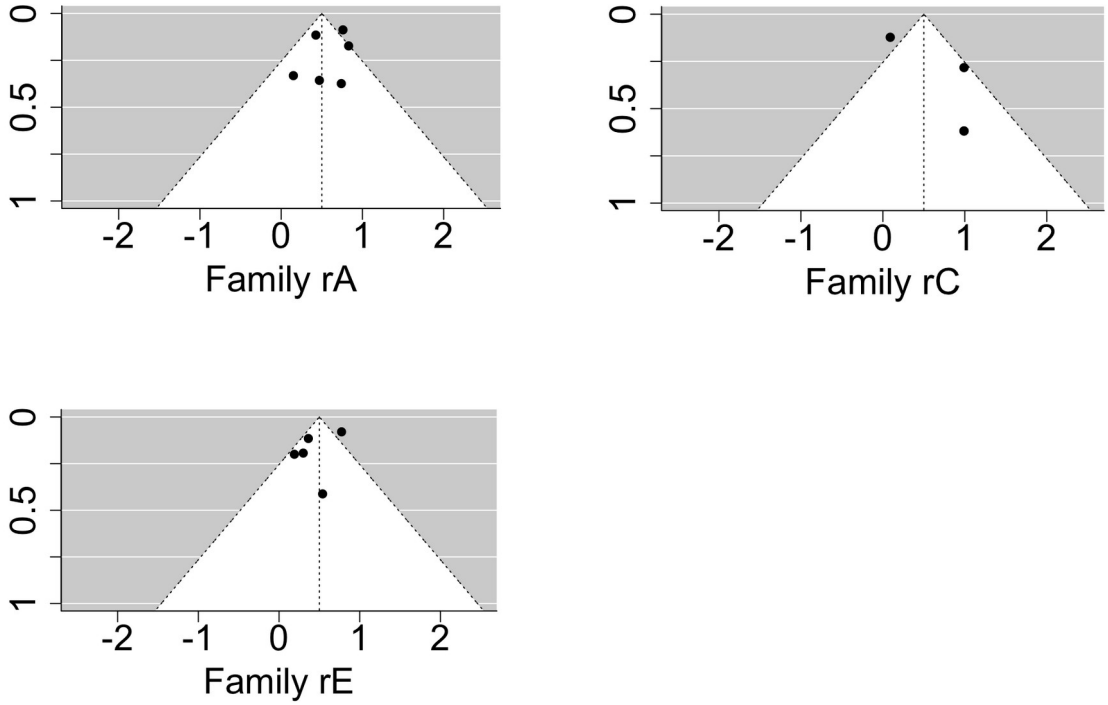

Supplementary Figure 21. Funnel plots involving all studies addressing genetic (rA), shared (rC) and nonshared (rE) environmental overlap between neurodevelopmental disorders (NDDs) and disruptive, impulse control and conduct disorders (DICCs).



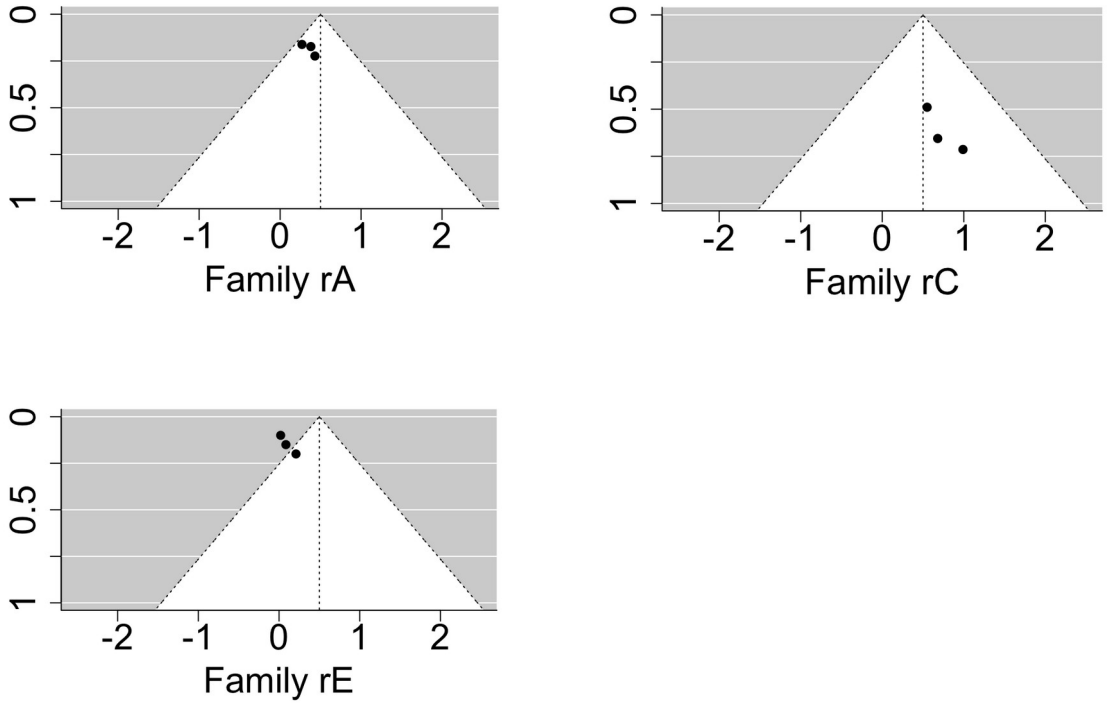



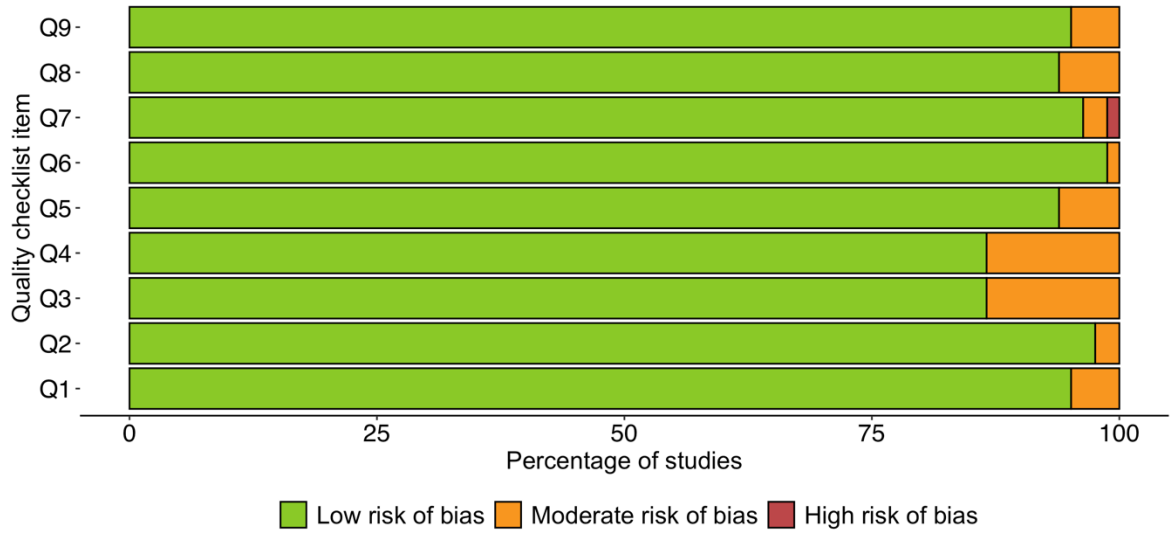

Supplementary Figure 22. Funnel plots involving all studies addressing genetic (rA), shared (rC) and nonshared (rE) environmental overlap between ADHD & conduct disorder.



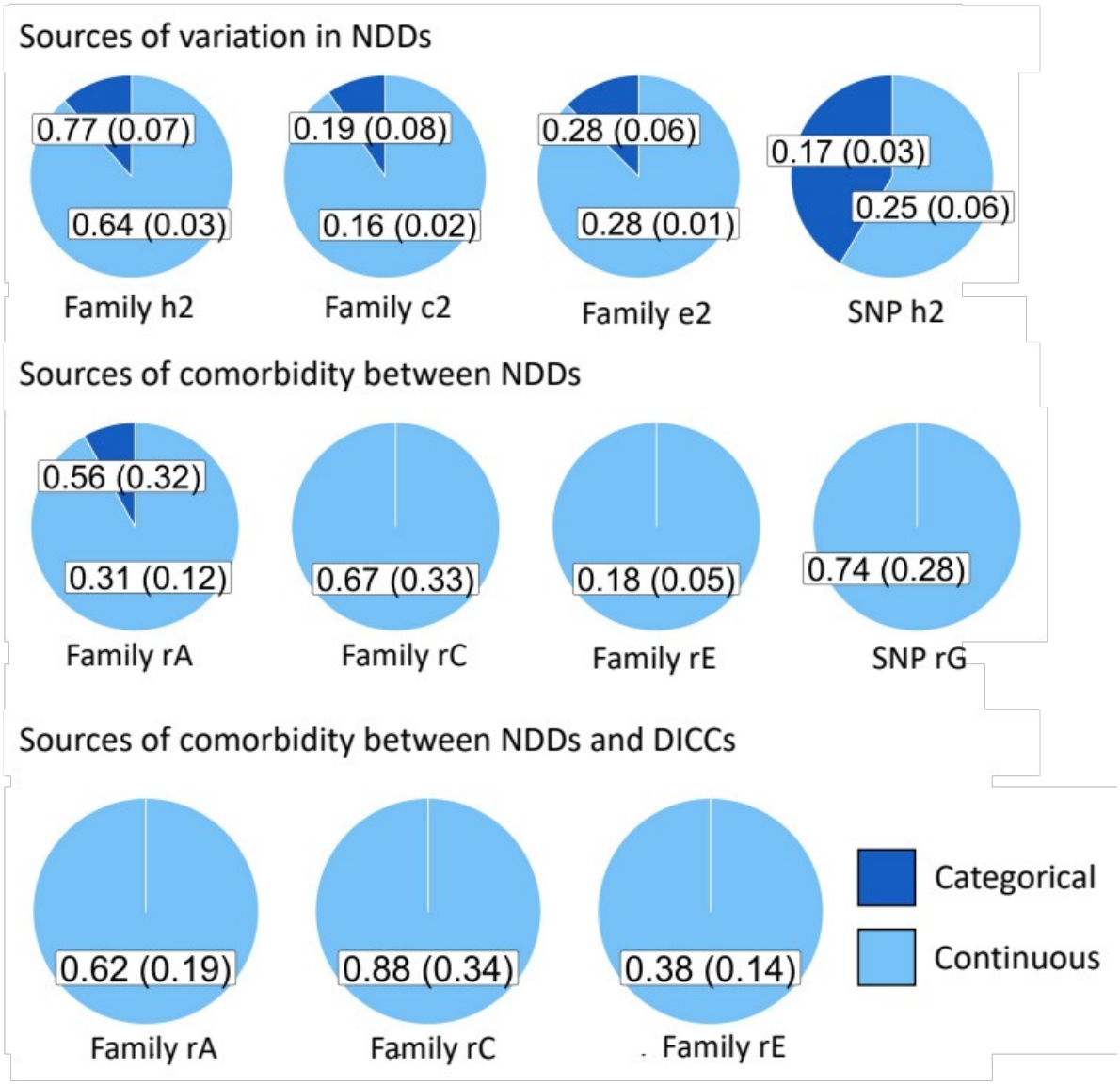

Supplementary Figure 23. Funnel plots involving all studies addressing genetic (rA), shared (rC) and nonshared (rE) environmental overlap between ADHD & oppositional defiant disorder.



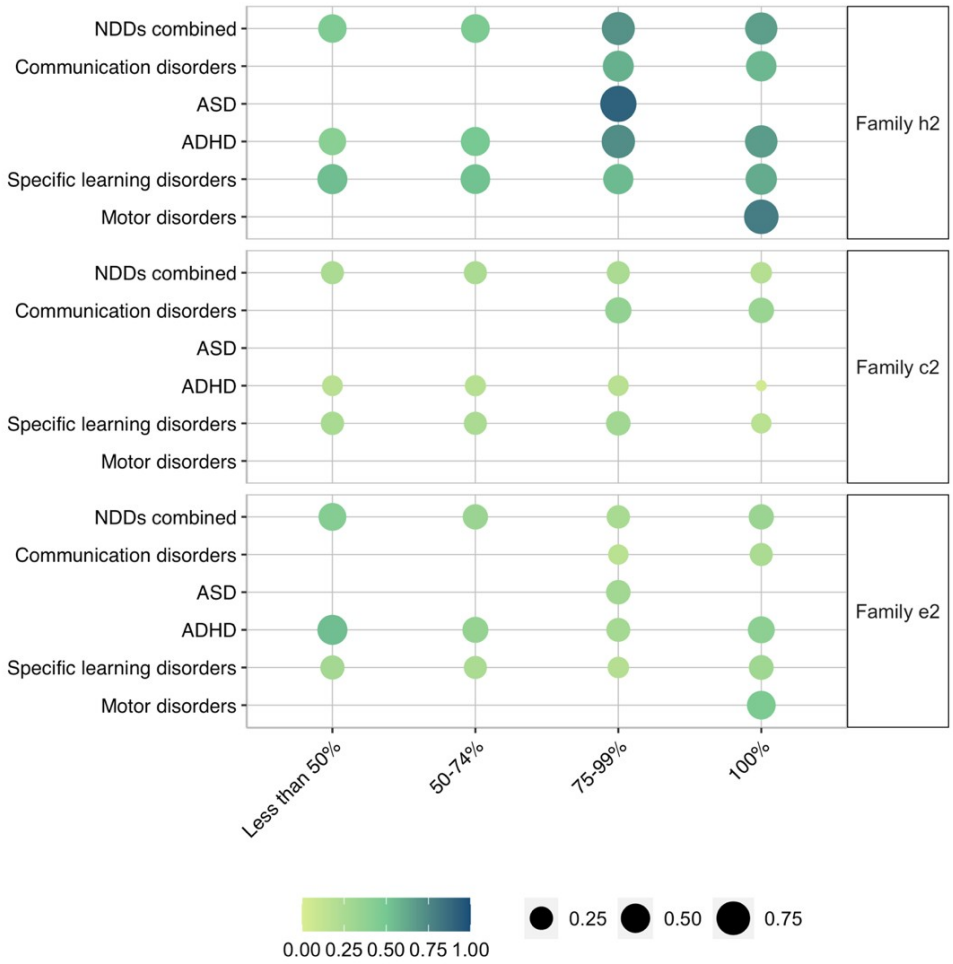

Supplementary Figure 24. Funnel plots involving all studies addressing genetic (rA), shared (rC) and nonshared (rE) environmental overlap between ASD & conduct disorder.



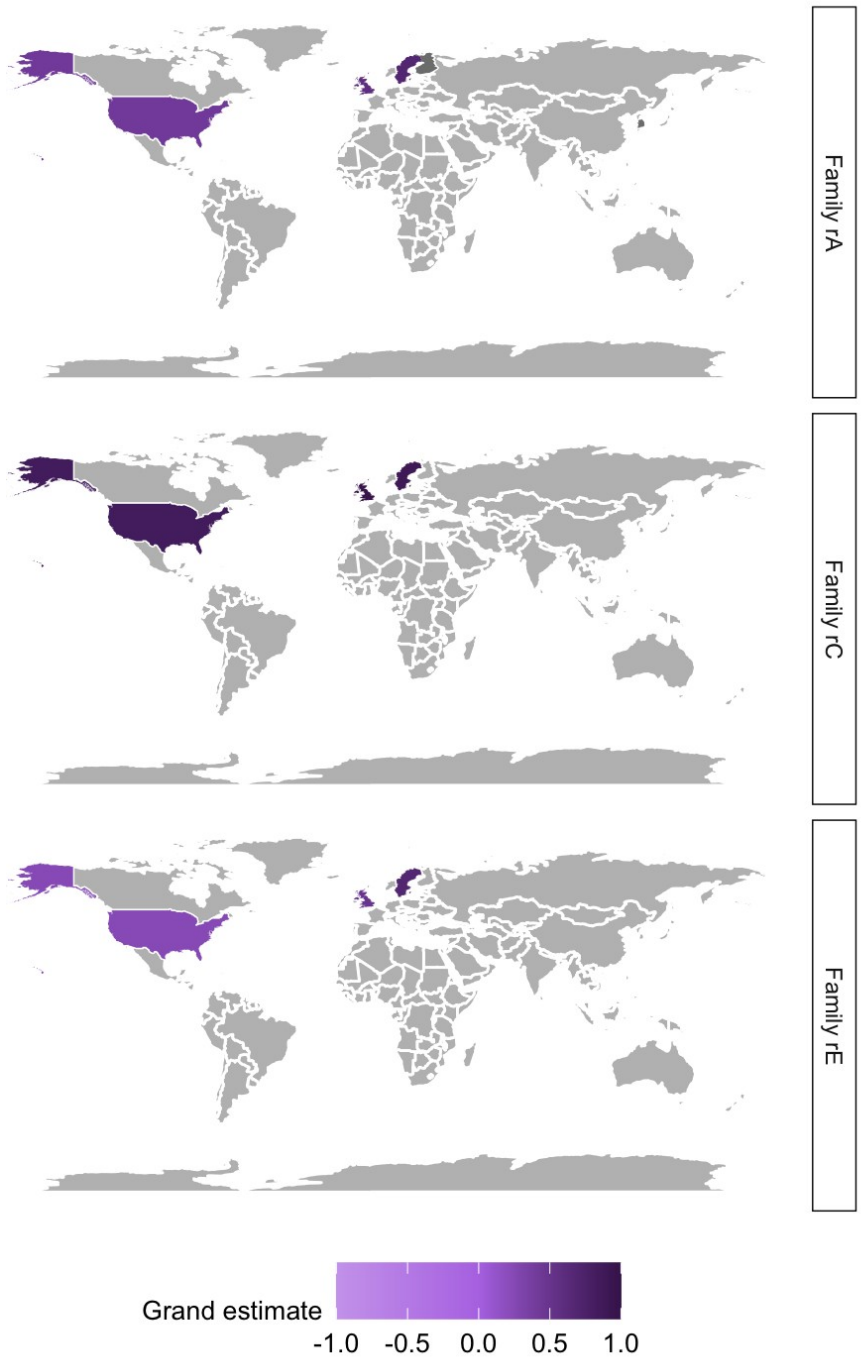

Supplementary Figure 25. Results of the study quality assessment, illustrated as the percentage of studies showing low, moderate and high risk of bias.



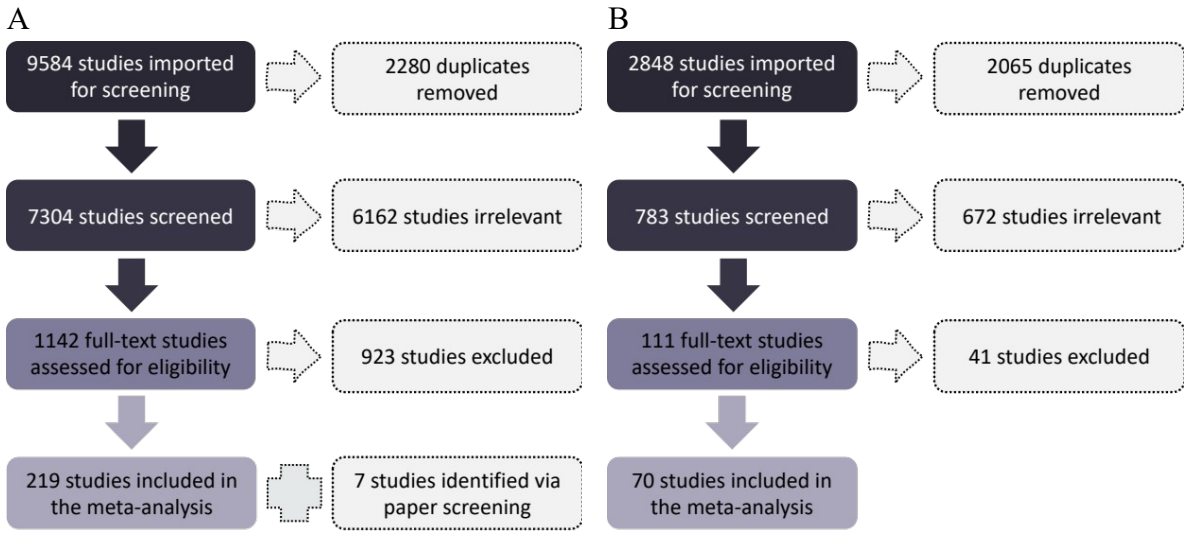

Supplementary Figure 26. Heritability (h2), shared (c2) and nonshared (e2) environmental influences on neurodevelopmental disorders (NDDs) (top panel), genetic (rA/rG), shared (rC) and nonshared (rE) environmental overlap between NDDs (middle panel) and genetic and environmental overlap between NDDs and disruptive, impulse control and conduct disorders (DICCs) (bottom panel), stratified by measurement scales, i.e., categorical versus continuous measurement.



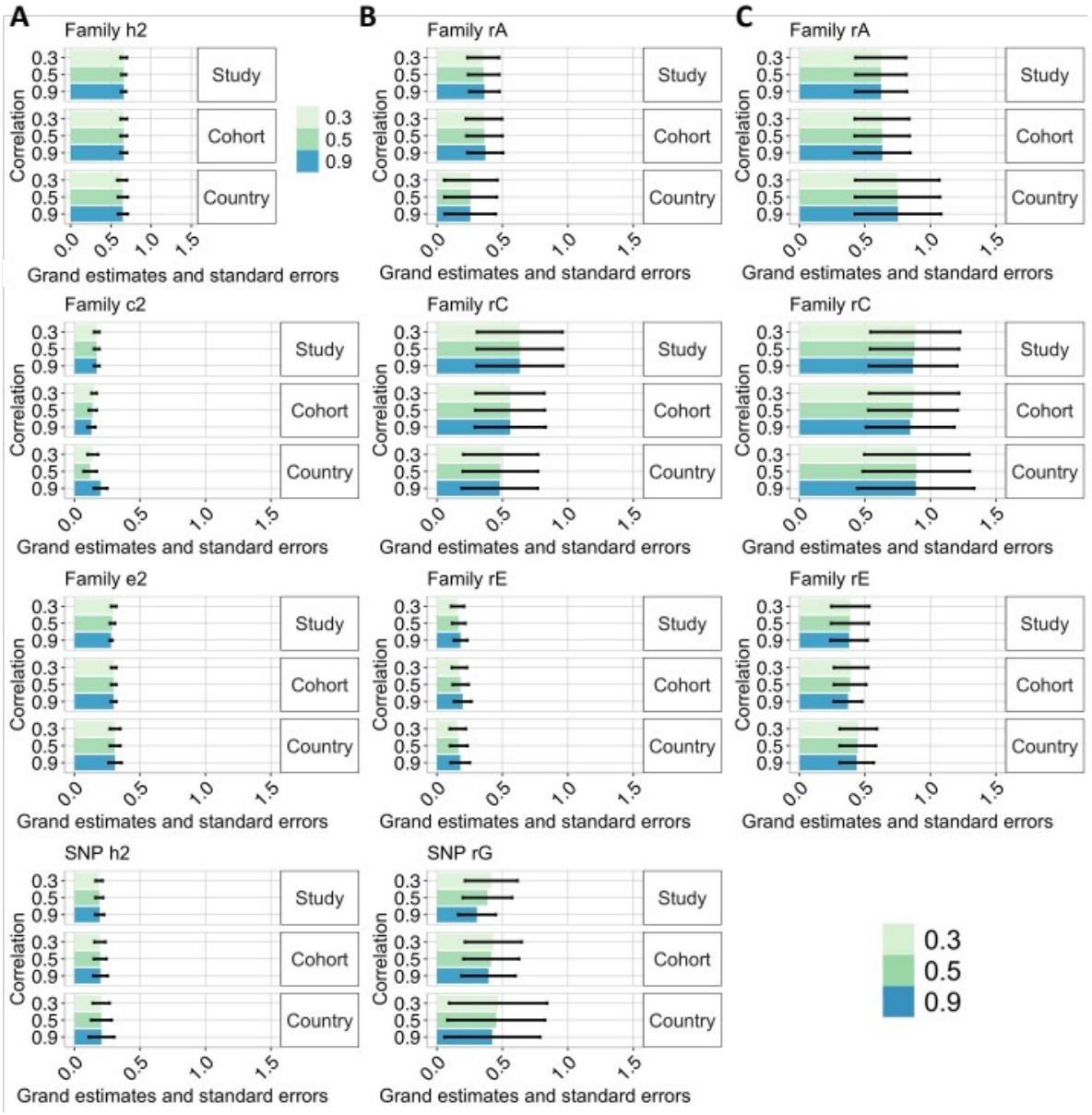

Supplementary Figure 27. Changes in family-based heritability (h2), shared (c2) and nonshared (e2) environmental influences on neurodevelopmental disorders (NDDs), as a function of sample ancestral composition. Given the general lack of diversity, ancestral composition could only be quantified, and consequently meta-analysed, as percentage of the sample being of European ancestry, different categories based on these percentages are depicted on the x-axis. Grand estimates of h2, c2 and e2 are reflected in the size and colour intensity of each circle, the larger and darker the circle, the higher the grand estimate.




Supplementary Figure 28. Geographical differences in rA, rC and rE between NDDs and disruptive, impulse control and conduct disorders (DICCs). The areas shaded in grey are regions for which not enough relevant studies were identified (<2 studies). The results for $c^2$ and $e^2$ as well as rC and rE are discussed in Supplementary Note 1.




Supplementary Figure 29. Diagram of searches and screening. Panel A shows study selection workflow of the primary search and Panel B shows workflow of the confirmatory search.




Supplementary Figure 30. Grand heritability (h2), shared (c2) and nonshared (e2) environmental influences across all neurodevelopmental disorders (NDDs) (panel A), grand genetic (rA), shared (rC) and nonshared (rE) environmental correlations across all NDDs (panel B) and grand genetic and environmental correlations across NDDs and disruptive, impulse control and conduct disorders (DICCs) (panel C) obtained using different aggregation techniques, i.e., aggregating by study, cohort, and country, using correlation thresholds of r= 0.3, r= 0.5 and r= 0.9.

# Appendix 2

## Supplementary Notes

Supplementary Note 1: Hypotheses from our OSF (Open Science Framework) statement (https://osf.io/27tpj/).

Although there are as yet no multi-PGS analyses of behaviour problems from childhood to early adulthood, we base the following OSF-registered hypotheses on varying degrees of evidence from the results of previous genetic and genomic analyses (for example, Allegrini, Karhunen, et al., 2020; Cheesman et al., 2017).

Hypothesis I

Variance in behaviour problems explained by multivariate PGS analysis (PGS heritability)

a) will be modest, less than 5%.
b) will be greater than PGS heritability for individual PGSs.
c) will increase during development as children grow closer to the target age of the mostly adult participants in the genome-wide association (GWA) studies from which the PGSs are derived.
d) will be greater for externalizing problems composites than for internalizing problems composites.
e) will be greater for parent and teacher ratings than for self-reports.
f) will be greater for longitudinal and cross-rater composites than for rater-specific measures at each age.
g) will be greater for cross-rater composites than for single-rater composites.
h) will be greater for a general factor of behaviour problems (BPp) than for individual measures of behaviour problems.
i) will be substantially lower than for cognitive and anthropometric traits.
j) will be similar for girls and boys.

Hypothesis II

SNP heritability for behaviour problems

a) will be substantially higher than PGS heritability.

b) will be substantially lower than heritability estimated from twin model-fitting analyses.
c) will be substantially lower than for cognitive and anthropometric traits.

Hypothesis III
Twin model-fitting heritability for behaviour problems
a) will be similar for parent and teacher ratings and lower for self-reports.
b) will be similar to cognitive traits but lower than anthropometric traits.
c) will reveal nonadditive genetic effects for behaviour problems but not for cognitive and anthropometric traits.

We addressed all these hypotheses in the current paper, apart from hypotheses regarding SNP heritability (IIa, b, c) and cognitive/anthropometric traits (Ia, IIIb, IIIc).

Our hypotheses were pre-registered prior to obtaining the dataset; hence we were not able to estimate the precise sample sizes for composites at that stage. Once we examined sample sizes of the obtained dataset, we did not have sufficient power to detect reliable SNP heritability estimates, according to the genome-wide complex trait analysis (GCTA) power calculator (Hermani & Yang, 2017). The power analysis revealed that with the sample of 3065 individuals we only had 16% of power to detect the SNP heritability of 10% (alpha= 0.05) (Hermani et al., 2017; for computation details refer to Vissher et al., 2014). Having acknowledged our SNP heritability estimates are unreliable due to low power, we have decided not to present them in this paper.

The other theme not covered in the paper but mentioned in the OSF pre-registration is to compare behaviour problems and cognitive and anthropometric traits. Increasing PGS heritability of cognitive/anthropometric traits could only be addressed from the longitudinal and not trans-situational perspective due to cognitive/anthropometric data only being collected on the level of a single-rater. Also, while having 15 PGSs available for behaviour problems, only 3 were available for cognitive traits (educational achievement, intelligence and income) and only 2 for anthropometric traits (height and body mass index). In order to overcome these discrepancies and enable comparability, as well as address the nonadditive

hypothesis (IIIc), major extensions to the study would be needed, which are currently beyond the scope of already complex and lengthy paper.

Supplementary Note 2: Sample description.

Our sample consists of twins born in England and Wales between 1994 and 1996 enrolled in the Twins Early Development Study (TEDS) (Rimfeld, Malanchini, Spargo, et al., 2019). Parents of twins were invited to participate in TEDS when the twins were about one year old. The invitations were sent to families by the UK Office for National Statistics after screening for infant mortality, and 16,810 families expressed interest in taking part.

The TEDS twins have been assessed a dozen times from infancy through early adulthood on a wide range of behavioural, psychological, cognitive, and physical measures, including genome-wide genotyping for a sub-sample (Rimfeld, Malanchini, Spargo, et al., 2019). Data collection procedures included questionnaires and tests administered by post, by telephone and online, as described in detail in a recent overview of TEDS (Rimfeld et al. (2019); details can be found in the TEDS data dictionary: https://www.teds.ac.uk/datadictionary/home.htm).

The sample of TEDS twins represents a broad swathe of the UK population in terms of ethnicity and socioeconomic status (SES) (Rimfeld, Malanchini, Spargo, et al., 2019), so is our selected sample of 3,065 unrelated twins (Supplementary Table 1). Individuals with severe medical conditions that affected participation were excluded from analyses. Zygosity was assessed using a parent questionnaire of the twins' physical similarity, which yielded 95% accuracy when compared to DNA tests (Price et al., 2000). For twin pairs with uncertain zygosity based on physical resemblance, DNA was used to establish reliable zygosity estimates (Price et al., 2000).

Supplementary Note 3: Polygenic scores.

The 15 polygenic scores used in the current study and the sample sizes are presented in Supplementary Table 3.

Supplementary Note 4: Additional information about the behaviour problems measures: SDQ and PBQ.

The SDQ (Strengths and difficulties questionnaire) and PBQ (Preschool behaviour questionnaire) were generally administered by post, in a form of paper questionnaires.
A small proportion of parent-report questionnaires were collected over the phone at age 7 and a larger proportion of parent and self-report questionnaires were collected online at age 21.

The PBQ questionnaire (Behar, 1977) was only administered to parents at ages 2 and 3 and included 18 items (4 items measuring hyperactivity, 8 items measuring conduct problems and 6 items measuring emotional problems). The SDQ questionnaire (Goodman, 1997) was administered to parents (ages 4- 21), teachers (ages 7- 12) and children (ages 9- 21) and included 20 items (5 items per domain, with peer problems being the fourth domain).

Both PBQ and SDQ questionnaires were rated on a three-point Likert scale (Certainly true; Sometimes true; Not true). All items were scored in the direction of problems (for example Restless, overactive, cannot stay still for long) or reversed where necessary, so that higher scores suggested more severe behaviour problems. The total hyperactivity, conduct problems, emotional problems, and peer problems scores were computed as the mean of the non-missing items (provided at least half of those items to be complete) multiplied by the number of items within the scale. The four SDQ domains from age 2 to age 21 are presented in Supplementary Figure 1.

Supplementary Note 5: Exploratory factor analysis (EFA).

Exploratory factor analyses analyses were conducted in psych for R (R Core Team, 2022; Revelle & Revelle, 2015), after residualizing all variables on age and sex for twin 1 and twin 2 separately (McGue & Bouchard, 1984). To explore the factor structure of behaviour problems in childhood, we performed the EFA of the four SDQ scales (hyperactivity, conduct problems, emotional and peer problems) at age 9, which was selected due to availability of complete data for all scales and for all three raters: parents, teachers and children themselves. The exploratory factor analysis was performed separately for parent (Supplementary Figure 2A), teacher (Supplementary Figure 2B) and child ratings (Supplementary Figure 2C).

EFA suggested a two-factor structure for all three raters. Hyperactivity and conduct problems loaded strongly on factor 1 (henceforth externalizing), and emotional problems and peer problems loaded strongly on factor 2 (henceforth internalizing). The externalizing and internalizing factors were moderately correlated (0.27, 0.56 and 0.63 for parent, teacher and child-rated data respectively), suggesting a general factor of behaviour problems (henceforth BPp).

Supplementary Note 6: Confirmatory factor analysis (CFA).

To determine the best latent model for the data structure based on the two-factor structure yielded by the EFA, we created the BPp, externalizing and internalizing composites on the cross-age level, using the bifactor and hierarchical factor modelling. Latent composites were created using the CFA data reduction technique that constructs the latent composites based on a pre-specified structure that underlies the data. CFA was conducted using lavaan for R (R Core Team, 2022; Rosseel, 2012). Full Information Maximum Likelihood (FIML) was used to account for data missingness.

The hierarchical latent factor model includes two first-order factors (here, externalizing and internalizing) loading onto a second-order factor (here, general behaviour problems, which we refer to as BPp). In contrast, the bifactor model allows all constituent variables to index a general factor (here BPp) and specific factors that account for the residual variance (here, externalizing and internalizing). Supplementary Figure 3 presents the structure of the hierarchical (Supplementary Figure 3A) and bifactor (Supplementary Figure 3B) models of BPp. Supplementary Figure 4 shows that externalizing and internalizing factors yielded moderate-to-high correlations across models and raters (0.81-0.92 in externalizing and 0.53-0.94 in internalizing). The bifactor and hierarchical BPp were highly correlated for parent ratings (0.74; Supplementary Figure 4A), but not teacher ratings or children's self-ratings (0.20 and -0.16, respectively; Figures S4B and S4C, respectively).

Finally, based on model fit indices, the hierarchical model provided significantly better fit than the bifactor model, hence the hierarchical solution was selected for downstream analyses.

Supplementary Note 7: Phenotypic and genetic correlations between cross-age and cross-rater composites.

Genetic correlations were estimated using the twin method, extended to the exploration of the covariance between pairs of traits, using OpenMx 2.0 for R (Neale et al., 2016; R Core Team, 2022). Bivariate genetic analysis allows for the decomposition of the covariance between multiple traits into genetic and environmental sources of variance, by modelling the cross-twin cross-trait covariances. Cross-twin cross-trait covariances describe the association between two variables, with twin 1's score on variable 1 correlated with twin 2's score on variable 2, which are calculated separately for monozygotic and dizygotic twins.

As presented in Supplementary Figure 5, cross-age and cross-rater effects were strongly correlated both phenotypically (range of r= 0.28- 0.93 for BPp, r= 0.26- 0.94 for externalizing and 0.27- 0.91 for internalizing) and genetically (range of r= 0.41- 0.94 for BPp, r= 0.40- 0.96 for externalizing and 0.39- 0.90 for internalizing). 95% confidence intervals for genetic correlations are presented in Supplementary Table 12.

Supplementary Note 8: Construction and results for the single-trait composites.

*Construction of the single-trait composites*

As a comparison to cross-age composites, we created separate measures of the four behaviour problems across ages but separately for parent, teacher and child ratings. As a comparison to cross-rater composites, we created separate measures of the four behaviour problems across raters but separately in childhood, adolescence and adulthood. We constructed the single-trait composites using one-factor confirmatory factor analysis, where the latent constructs of cross-age (Supplementary Figure 6A) and cross-rater (Supplementary Figure 6B) hyperactivity, conduct problems, emotional problems, and peer problems were estimated in separate models.

*Multi-PGS heritability: single-trait composites of behaviour problems*

Supplementary Figure 7 focuses on the effects of cross-age and cross-rater compositing on the four individual SDQ scales rather than BPp, externalizing and internalizing. In general, we found similar but weaker results, suggesting the usefulness of compositing across traits as well as across ages and across raters.

For cross-age comparisons (Supplementary Figure 7A), we found that multi-PGS heritability increased for teacher-rated hyperactivity (3% vs 0.3%), parent and teacher-rated conduct (2.5% vs 0.9% and 2.5% vs 0.5%, respectively) and teacher and child-rated emotional problems (1.8% vs 0.1% and 2.2% vs 1.2%, respectively). While single-trait cross-age composites yielded a mean multi-PGS heritability of only 1.3%, compositing across ages and traits (BPp, externalizing, internalizing) yielded a mean multi-PGS heritability that was almost three times as high (3.6%). In addition, due to lack of the cross-age effect for parent-rated hyperactivity and peer problems, the highest cross-age effect observed for parent-rated BPp may be driven entirely by conduct and emotional problems.

Compositing across raters also generally increased multi-PGS heritability of single-trait composites (Supplementary Figure 7B). The multi-PGS heritability showed a notable drop from childhood to adulthood for conduct (4.8% in childhood to 3.7% in adolescence to 1.1% in adulthood), which was consistent with the pattern of PGS results for cross-rater externalizing. An opposite trend was found for emotional problems, with the multi-PGS heritability increasing from childhood to adolescence and adulthood (1.3% in childhood to

3.3% in adolescence to 2% in adulthood), which also mirrored the direction of cross-rater internalizing. multi-PGS heritability for cross-rater composites of hyperactivity and peer problems remained relatively stable across development (the mean of 1.5% and 0.9%, respectively). Compared to the improvement of PGS prediction for the single-trait cross-rater composites (mean of 1.6% vs 0.9% for individual traits), the cross-rater effect was more than quadrupled for the cross-rater composites of BPp, externalizing and internalizing (mean of 3.6% vs 0.8% for individual traits).

*Twin heritability: single-trait composites of behaviour problems*

The twin results for the single-trait composites showed both cross-age (Supplementary Figure 7C) and cross-rater (Supplementary Figure 7D) effects, mirroring the twin results for BPp, externalizing and internalizing. However, the magnitudes of these effects were lower for single-trait composites, with the mean of 57% for cross-age composites vs 51% for observed traits and 61% for cross-rater composites vs 51% for observed traits.

Supplementary Note 9: Elastic net regularization.

We estimated the joint prediction of the 15 PGSs in a penalised regression elastic net model with hold-out tests of prediction accuracy, using the R package glmnet (Hastie et al., 2023; R Core Team, 2022) implemented in caret (Kuhn, 2008). We used a shrinkage model referred to as elastic net regularization to overcome problems of multicollinearity and overfitting (Zou & Hastie, 2005). Elastic net produces regression models that are penalised with both the L1-norm (Lasso) and L2-norm (Ridge) penalties to omit highly correlated predictors and reduce the risk of multicollinearity and overfitting (Pavlou et al., 2016).
Elastic net regularization tries to minimise the following loss function:

$$||y - X\beta||2 + \lambda(\alpha*|\beta|1 + (1-\alpha)*|\beta|2)$$

where ||y–X'β||2 is the residual sum of squares, |β|2 is the sum of the squared betas (the L2 penalty), |β|1 is the sum of the absolute betas (the L1 penalty) and X is an N*P ('N' observations and 'P' predictors) matrix of polygenic scores (for details, see (Allegrini, Karhunen, et al., 2020)).

For every model tested, we randomly split the sample into an independent training set (80%) and a hold-out set (20%) and used the same split for all prediction models. In the training set, we performed the 10-fold cross-validation repeated 100 times to select the model that minimises the Root Mean Square Error (RMSE), which indicates the smallest cross-validation error (Fushiki, 2011). To account for patterns of missingness in the phenotypic data and to use all available data we employed the FIML method. We then estimated variance explained ($R^2$) in the hold-out test set.

Supplementary Note 10: Meta-analytic approach to comparing multi-PGS heritability between composites and observed traits.

In the meta-analytic approach, we used a random effects meta-regression model to estimate the grand mean of multi-PGS and twin heritability of the observed traits. For multi-PGS analyses, we used the square root of $R^2$ (that is, the squared correlation between predictors and a composite in the hold-out set) and the 95% confidence intervals of the correlation coefficient as a measure of effect size. The square root of the correlation was computed to estimate 95% confidence intervals, which could not be estimated from the $R^2$. For twin analyses, the effect size was measured as twin heritability with 95% confidence intervals. Meta-analysis was conducted in the R package metafor (R Core Team, 2022; Viechtbauer, 2010)

Supplementary Figure 8 shows the multi-PGS heritability results for cross-age composites (Supplementary Figure 8A) and cross-rater composites (Supplementary Figure 8B), as compared to grand mean of observed traits. Twin heritability results are presented in Supplementary Figure 8C for cross-age composites and Supplementary Figure 8D for cross-rater composites, as compared to grand mean of observed traits.

Supplementary Figure 9 shows the multi-PGS heritability results for single-trait cross-age composites (Supplementary Figure 9A) and single-trait cross-rater composites (Supplementary Figure 9B), as compared to grand mean of observed traits. Twin heritability results are presented in Supplementary Figure 9C for single-trait cross-age composites and Supplementary Figure 9D for single-trait cross-rater composites, as compared to grand mean of observed traits.

# Supplementary Tables

Supplementary Table 1. Representativeness of the selected sample.

| Ethnicity and SES | Selected sample | 1st Contact sample | National equivalents[a,b] |
|---|---|---|---|
| % white | 99.9% | 91.7% | 93% |
| % mother A-levels or higher | 39.0% | 35.5% | 35% |
| % father A-levels or higher | 42.3% | 44.8% | 47% |
| % mother employed | 45.3% | 43.1% | 50% |
| % father employed | 85.8% | 91.6% | 91% |
| Note. [a] including cohort of parents with children born in late 1990s and early 2000s; [b] derived from Rimfeld, Malanchini, Spargo, et al. (2019). | | | |

Supplementary Table 2. Behaviour problems composites: sample characteristics.

| Composites | N twin pairs MZ | N twin pairs DZ | N total twin pairs | N genotyped |
|---|---|---|---|---|
| Cross-age | | | | |
| BPp parent-rated | 1753 | 3025 | 4778 | 3065 |
| BPp teacher-rated | 1675 | 2892 | 4567 | 2953 |
| BPp child-rated | 1753 | 3025 | 4778 | 2986 |
| Externalizing parent-rated | 1753 | 3025 | 4778 | 3065 |
| Externalizing teacher-rated | 1675 | 2892 | 4567 | 2953 |
| Externalizing child-rated | 1753 | 3025 | 4778 | 2986 |
| Internalizing parent-rated | 1753 | 3025 | 4778 | 3065 |
| Internalizing teacher-rated | 1675 | 2892 | 4567 | 2953 |
| Internalizing child-rated | 1753 | 3025 | 4778 | 2986 |
| Cross-rater | | | | |
| BPp childhood | 1753 | 3025 | 4778 | 3065 |
| BPp adolescence | 1711 | 2920 | 4631 | 2986 |
| BPp adulthood | 1472 | 2474 | 3946 | 2648 |
| Externalizing childhood | 1753 | 3025 | 4778 | 3065 |
| Externalizing adolescence | 1711 | 2920 | 4631 | 2986 |
| Externalizing adulthood | 1472 | 2474 | 3946 | 2648 |
| Internalizing childhood | 1753 | 3025 | 4778 | 3065 |
| Internalizing adolescence | 1711 | 2920 | 4631 | 2986 |
| Internalizing adulthood | 1472 | 2474 | 3946 | 2648 |
| Cross-age-and-rater (cross-age approach) * | | | | |
| BPp | 1753 | 3025 | 4778 | 3065 |
| Externalizing | 1753 | 3025 | 4778 | 3065 |
| Internalizing | 1753 | 3025 | 4778 | 3065 |
| Cross-age-and-rater (cross-rater approach) ** | | | | |
| BPp | 1753 | 3025 | 4778 | 3065 |
| Externalizing | 1753 | 3025 | 4778 | 3065 |
| Internalizing | 1753 | 3025 | 4778 | 3065 |
| Single-trait cross-age | | | | |
| Hyperactivity parent-rated | 1753 | 3025 | 4778 | 3065 |
| Hyperactivity teacher-rated | 1547 | 2665 | 4212 | 2744 |
| Hyperactivity child-rated | 1753 | 3025 | 4778 | 2691 |
| Conduct problems parent-rated | 1753 | 3025 | 4778 | 3065 |
| Conduct problems teacher-rated | 1675 | 2892 | 4567 | 2953 |

| | | | | |
|---|---|---|---|---|
| Conduct problems child-rated | 1753 | 3025 | 4778 | 2986 |
| Emotional problems parent-rated | 1753 | 3025 | 4778 | 3065 |
| Emotional problems teacher-rated | 1674 | 2891 | 4565 | 2952 |
| Emotional problems child-rated | 1753 | 3025 | 4778 | 2986 |
| Peer problems parent-rated | 1753 | 3025 | 4778 | 3065 |
| Peer problems teacher-rated | 1674 | 2892 | 4566 | 2953 |
| Peer problems child-rated | 1753 | 3025 | 4778 | 2986 |
| Single-trait cross-rater | | | | |
| Hyperactivity childhood | 1753 | 3025 | 4778 | 3065 |
| Hyperactivity adolescence | 1370 | 2342 | 3712 | 2432 |
| Hyperactivity adulthood | 1753 | 3025 | 4778 | 2648 |
| Conduct problems childhood | 1753 | 3025 | 4778 | 3065 |
| Conduct problems adolescence | 1710 | 2916 | 4626 | 2983 |
| Conduct problems adulthood | 1753 | 3025 | 4778 | 2648 |
| Emotional problems childhood | 1753 | 3025 | 4778 | 3065 |
| Emotional problems adolescence | 1709 | 2915 | 4624 | 2984 |
| Emotional problems adulthood | 1753 | 3025 | 4778 | 2647 |
| Peer problems childhood | 1750 | 3022 | 4772 | 3060 |
| Peer problems adolescence | 1709 | 2915 | 4624 | 2984 |
| Peer problems adulthood | 1750 | 3022 | 4772 | 2648 |

Note.

N= sample size; MZ= monozygotic; DZ= dizygotic.

* cross-age approach: combined individual behaviour problems at all ages (2-21) for parent, teacher and child ratings to create the first order factors of cross-age externalizing and internalizing, which were then combined across raters to create the second-order factors of cross-age-and-rater externalizing and internalizing.

** cross-rater approach: combined individual behaviour problems in adolescence and adulthood to create the first order factors of cross-rater externalizing and internalizing, which were then combined across developmental stages to create the second-order factors of cross-age-and-rater externalizing and internalizing.

Supplementary Table 3. Polygenic scores and sample sizes.

| Polygenic score | Sample size |
|---|---|
| Attention deficit hyperactivity disorder (ADHD) (Demontis et al., 2019) | 55374 |
| Anorexia nervosa (Watson et al., 2019) | 14477 |
| Autism spectrum disorder (ASD) (Grove et al., 2019) | 46350 |
| Bipolar disorder (Stahl et al., 2019) | 51710 |
| Broad depression (Howard et al., 2019) | 331374 |
| Insomnia (Jansen et al., 2019) | 386533 |
| Irritability (Seed, 2017) | 322668 |
| Major depressive disorder (MDD) (Wray et al., 2018) | 173005 |
| Mood swings (Seed, 2017) | 329428 |
| Neuroticism (Luciano et al., 2018) | 329821 |
| Obsessive-compulsive disorder (OCD) (Arnold et al., 2018) | 9725 |
| Post-traumatic stress disorder (PTSD) (L. E. Duncan et al., 2018) | 9537 |
| Risk-taking (Karlsson Linnér et al., 2019) | 325821 |
| Schizophrenia (Pardiñas et al., 2018) | 105318 |
| Well-being (Okbay et al., 2016) | 298420 |

Supplementary Table 4. Behaviour problems composites: model fit indices and predictions from elastic net regularization.

| Composites | Elastic net regularization | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | FRCT | Mean CV RMSE (train) | SD CV RMSE (train) | Mean CV R2 (train) | SD CV R2 (train) | RMSE | R2 | Alpha | Lambda | N (train) | N (test) |
| Cross-age | | | | | | | | | | | |
| BPp parent-rated | 1 | 0.973 | 0.001 | 0.023 | 0.001 | 0.981 | 0.049 | 0.6 | 0.04 | 2453 | 612 |
| BPp teacher-rated | 1 | 0.977 | 0.002 | 0.028 | 0.002 | 0.941 | 0.037 | 1.0 | 0.02 | 2365 | 588 |
| BPp child-rated | 1 | 0.981 | 0.002 | 0.030 | 0.003 | 0.979 | 0.027 | 0.2 | 0.04 | 2390 | 596 |
| Externalizing parent-rated | 1 | 0.972 | 0.002 | 0.034 | 0.002 | 0.948 | 0.047 | 0.9 | 0.02 | 2453 | 612 |
| Externalizing teacher-rated | 1 | 0.957 | 0.002 | 0.035 | 0.002 | 0.990 | 0.047 | 0.8 | 0.02 | 2365 | 588 |
| Externalizing child-rated | 1 | 0.978 | 0.002 | 0.030 | 0.002 | 0.985 | 0.039 | 0.1 | 0.09 | 2390 | 596 |
| Internalizing parent-rated | 1 | 0.984 | 0.001 | 0.019 | 0.001 | 0.976 | 0.008 | 0.8 | 0.02 | 2453 | 612 |
| Internalizing teacher-rated | 1 | 0.978 | 0.001 | 0.014 | 0.001 | 0.996 | 0.040 | 0.5 | 0.03 | 2365 | 588 |
| Internalizing child-rated | 1 | 0.977 | 0.002 | 0.024 | 0.002 | 1.007 | 0.033 | 0.1 | 0.05 | 2390 | 596 |
| Cross-rater | | | | | | | | | | | |
| BPp childhood | 1 | 0.964 | 0.002 | 0.030 | 0.002 | 0.989 | 0.029 | 0.1 | 0.11 | 2453 | 612 |
| BPp adolescence | 1 | 0.983 | 0.002 | 0.029 | 0.003 | 0.958 | 0.030 | 1.0 | 0.02 | 2390 | 596 |
| BPp adulthood | 1 | 0.982 | 0.002 | 0.029 | 0.002 | 0.959 | 0.047 | 0.1 | 0.10 | 2120 | 528 |
| Externalizing childhood | 1 | 0.965 | 0.002 | 0.034 | 0.002 | 0.941 | 0.066 | 0.1 | 0.13 | 2453 | 612 |
| Externalizing adolescence | 1 | 0.988 | 0.003 | 0.038 | 0.003 | 0.948 | 0.036 | 0.9 | 0.03 | 2390 | 596 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Externalizing adulthood | 1 | 0.980 | 0.002 | 0.035 | 0.003 | 0.978 | 0.027 | 0.1 | 0.11 | 2120 | 528 |
| Internalizing childhood | 1 | 0.987 | 0.001 | 0.016 | 0.001 | 0.960 | 0.018 | 0.7 | 0.03 | 2453 | 612 |
| Internalizing adolescence | 1 | 0.984 | 0.001 | 0.022 | 0.001 | 1.004 | 0.013 | 0.2 | 0.05 | 2390 | 596 |
| Internalizing adulthood | 1 | 0.978 | 0.001 | 0.021 | 0.002 | 0.968 | 0.061 | 0.7 | 0.04 | 2120 | 528 |
| Cross-age-and-rater (cross-age approach) * | | | | | | | | | | | |
| BPp | 1 | 0.974 | 0.002 | 0.028 | 0.002 | 0.957 | 0.040 | 0.1 | 0.05 | 2453 | 612 |
| Externalizing | 1 | 0.974 | 0.002 | 0.035 | 0.002 | 0.926 | 0.035 | 0.7 | 0.03 | 2453 | 612 |
| Internalizing | 1 | 0.982 | 0.001 | 0.022 | 0.001 | 0.979 | 0.027 | 0.5 | 0.04 | 2453 | 612 |
| Cross-age-and-rater (cross-rater approach) ** | | | | | | | | | | | |
| BPp | 1 | 0.974 | 0.002 | 0.032 | 0.001 | 0.971 | 0.027 | 0.1 | 0.05 | 2453 | 612 |
| Externalizing | 1 | 0.968 | 0.002 | 0.033 | 0.002 | 0.986 | 0.040 | 0.8 | 0.02 | 2453 | 612 |
| Internalizing | 1 | 0.976 | 0.001 | 0.024 | 0.002 | 0.995 | 0.028 | 0.2 | 0.04 | 2453 | 612 |
| Single-trait cross-age | | | | | | | | | | | |
| Hyperactivity parent-rated | 1 | 0.985 | 0.001 | 0.019 | 0.002 | 0.968 | 0.003 | 0.6 | 0.05 | 2453 | 612 |
| Hyperactivity teacher-rated | 1 | 0.994 | 0.001 | 0.029 | 0.000 | 0.980 | 0.031 | 0.6 | 0.03 | 2196 | 548 |
| Hyperactivity child-rated | 1 | 0.992 | 0.001 | 0.016 | 0.001 | 0.986 | 0.007 | 0.8 | 0.04 | 2155 | 536 |
| Conduct problems parent-rated | 1 | 0.985 | 0.001 | 0.023 | 0.000 | 0.971 | 0.025 | 0.1 | 0.05 | 2453 | 612 |
| Conduct problems teacher-rated | 1 | 0.958 | 0.001 | 0.021 | 0.001 | 0.910 | 0.025 | 0.6 | 0.04 | 2364 | 589 |
| Conduct problems child-rated | 1 | 0.986 | 0.002 | 0.023 | 0.002 | 1.029 | 0.012 | 1.0 | 0.02 | 2390 | 596 |
| Emotional problems | 1 | 0.988 | 0.001 | 0.013 | 0.000 | 0.977 | 0.004 | 0.4 | 0.04 | 2453 | 612 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| parent-rated | | | | | | | | | | | |
| Emotional problems teacher-rated | 1 | 0.996 | 0.000 | 0.008 | 0.000 | 0.965 | 0.018 | 0.2 | 0.06 | 2364 | 588 |
| Emotional problems child-rated | 1 | 0.988 | 0.001 | 0.016 | 0.000 | 1.010 | 0.022 | 0.1 | 0.09 | 2390 | 596 |
| Peer problems parent-rated | 1 | 1.008 | 0.001 | 0.007 | 0.000 | 0.991 | 0.005 | 0.4 | 0.06 | 2453 | 612 |
| Peer problems teacher-rated | 1 | 1.008 | 0.001 | 0.003 | 0.000 | 1.012 | 0.003 | 0.6 | 0.05 | 2365 | 588 |
| Peer problems child-rated | 1 | 1.002 | 0.001 | 0.008 | 0.001 | 1.018 | 0.008 | 0.3 | 0.06 | 2390 | 596 |
| Single-trait cross-rater | | | | | | | | | | | |
| Hyperactivity childhood | 1 | 0.980 | 0.001 | 0.022 | 0.001 | 0.967 | 0.018 | 0.2 | 0.05 | 2453 | 612 |
| Hyperactivity adolescence | 1 | 0.990 | 0.001 | 0.014 | 0.001 | 1.012 | 0.012 | 0.7 | 0.03 | 1948 | 484 |
| Hyperactivity adulthood | 1 | 1.004 | 0.001 | 0.013 | 0.001 | 0.985 | 0.016 | 0.2 | 0.09 | 2120 | 528 |
| Conduct problems childhood | 1 | 0.980 | 0.001 | 0.017 | 0.001 | 0.974 | 0.048 | 0.6 | 0.04 | 2453 | 612 |
| Conduct problems adolescence | 1 | 0.990 | 0.001 | 0.021 | 0.001 | 1.006 | 0.037 | 0.1 | 0.09 | 2387 | 596 |
| Conduct problems adulthood | 1 | 0.984 | 0.001 | 0.015 | 0.001 | 1.000 | 0.011 | 0.5 | 0.04 | 2120 | 528 |
| Emotional problems childhood | 1 | 0.998 | 0.001 | 0.010 | 0.001 | 0.934 | 0.001 | 0.8 | 0.04 | 2453 | 612 |
| Emotional problems adolescence | 1 | 0.987 | 0.001 | 0.020 | 0.001 | 1.042 | 0.003 | 0.6 | 0.02 | 2388 | 596 |
| Emotional problems adulthood | 1 | 0.987 | 0.001 | 0.022 | 0.002 | 0.979 | 0.021 | 0.7 | 0.05 | 2119 | 528 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Peer problems childhood | 1 | 1.010 | 0.001 | 0.005 | 0.000 | 0.992 | 0.007 | 0.5 | 0.05 | 2448 | 612 |
| Peer problems adolescence | 1 | 1.018 | 0.000 | 0.006 | 0.000 | 0.980 | 0.013 | 0.4 | 0.05 | 2388 | 596 |
| Peer problems adulthood | 1 | 0.985 | 0.001 | 0.010 | 0.001 | 0.989 | 0.007 | 0.3 | 0.07 | 2120 | 528 |
| Cross-age | | | | | | | | | | | |
| BPp parent-rated | 0.3 | 0.977 | 0.001 | 0.015 | 0.000 | 0.989 | 0.031 | 0.7 | 0.04 | 2453 | 612 |
| BPp teacher-rated | 0.3 | 0.979 | 0.001 | 0.023 | 0.001 | 0.944 | 0.032 | 0.2 | 0.05 | 2365 | 588 |
| BPp child-rated | 0.3 | 0.984 | 0.002 | 0.025 | 0.003 | 0.983 | 0.018 | 0.1 | 0.04 | 2390 | 596 |
| Externalizing parent-rated | 0.3 | 0.979 | 0.001 | 0.019 | 0.001 | 0.952 | 0.046 | 1.0 | 0.02 | 2453 | 612 |
| Externalizing teacher-rated | 0.3 | 0.959 | 0.002 | 0.030 | 0.001 | 0.995 | 0.033 | 0.8 | 0.01 | 2365 | 588 |
| Externalizing child-rated | 0.3 | 0.980 | 0.002 | 0.027 | 0.002 | 0.994 | 0.022 | 0.2 | 0.04 | 2390 | 596 |
| Internalizing parent-rated | 0.3 | 0.986 | 0.001 | 0.014 | 0.001 | 0.978 | 0.004 | 0.4 | 0.04 | 2453 | 612 |
| Internalizing teacher-rated | 0.3 | 0.979 | 0.001 | 0.012 | 0.001 | 1.002 | 0.028 | 0.8 | 0.04 | 2365 | 588 |
| Internalizing child-rated | 0.3 | 0.978 | 0.001 | 0.021 | 0.002 | 1.015 | 0.018 | 0.1 | 0.04 | 2390 | 596 |
| Cross-rater | | | | | | | | | | | |
| BPp childhood | 0.3 | 0.969 | 0.001 | 0.019 | 0.000 | 0.992 | 0.023 | 0.1 | 0.11 | 2453 | 612 |
| BPp adolescence | 0.3 | 0.987 | 0.001 | 0.021 | 0.001 | 0.960 | 0.027 | 0.2 | 0.09 | 2390 | 596 |
| BPp adulthood | 0.3 | 0.985 | 0.001 | 0.023 | 0.002 | 0.965 | 0.036 | 0.4 | 0.04 | 2120 | 528 |
| Externalizing childhood | 0.3 | 0.969 | 0.001 | 0.025 | 0.002 | 0.952 | 0.038 | 1.0 | 0.03 | 2453 | 612 |
| Externalizing adolescence | 0.3 | 0.996 | 0.001 | 0.022 | 0.001 | 0.951 | 0.033 | 0.5 | 0.04 | 2390 | 596 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Externalizing adulthood | 0.3 | 0.984 | 0.002 | 0.026 | 0.002 | 0.981 | 0.022 | 0.1 | 0.11 | 2120 | 528 |
| Internalizing childhood | 0.3 | 0.990 | 0.001 | 0.009 | 0.000 | 0.963 | 0.013 | 0.9 | 0.03 | 2453 | 612 |
| Internalizing adolescence | 0.3 | 0.985 | 0.001 | 0.020 | 0.001 | 1.009 | 0.007 | 0.1 | 0.04 | 2390 | 596 |
| Internalizing adulthood | 0.3 | 0.981 | 0.001 | 0.016 | 0.001 | 0.971 | 0.059 | 0.6 | 0.04 | 2120 | 528 |
| Cross-age-and-rater (cross-age approach) * | | | | | | | | | | | |
| BPp | 0.3 | 0.974 | 0.002 | 0.028 | 0.001 | 0.957 | 0.039 | 0.1 | 0.05 | 2453 | 612 |
| Externalizing | 0.3 | 0.974 | 0.002 | 0.036 | 0.002 | 0.926 | 0.034 | 0.6 | 0.03 | 2453 | 612 |
| Internalizing | 0.3 | 0.982 | 0.001 | 0.021 | 0.001 | 0.979 | 0.026 | 0.5 | 0.04 | 2453 | 612 |
| Cross-age-and-rater (cross-rater approach) ** | | | | | | | | | | | |
| BPp | 0.3 | 0.974 | 0.002 | 0.031 | 0.001 | 0.971 | 0.028 | 0.1 | 0.05 | 2453 | 612 |
| Externalizing | 0.3 | 0.968 | 0.002 | 0.033 | 0.002 | 0.987 | 0.039 | 0.8 | 0.02 | 2453 | 612 |
| Internalizing | 0.3 | 0.977 | 0.001 | 0.023 | 0.001 | 0.997 | 0.024 | 0.2 | 0.04 | 2453 | 612 |
| Single-trait cross-age | | | | | | | | | | | |
| Hyperactivity parent-rated | 0.3 | 0.985 | 0.001 | 0.019 | 0.002 | 0.968 | 0.003 | 0.6 | 0.05 | 2453 | 612 |
| Hyperactivity teacher-rated | 0.3 | 0.993 | 0.002 | 0.030 | 0.000 | 0.985 | 0.022 | 0.1 | 0.06 | 2196 | 548 |
| Hyperactivity child-rated | 0.3 | 0.992 | 0.001 | 0.016 | 0.001 | 0.986 | 0.008 | 0.8 | 0.04 | 2155 | 536 |
| Conduct problems parent-rated | 0.3 | 0.985 | 0.001 | 0.023 | 0.000 | 0.971 | 0.025 | 0.1 | 0.05 | 2453 | 612 |
| Conduct problems teacher-rated | 0.3 | 0.957 | 0.001 | 0.022 | 0.001 | 0.909 | 0.024 | 0.1 | 0.04 | 2364 | 589 |
| Conduct problems child-rated | 0.3 | 0.986 | 0.001 | 0.023 | 0.002 | 1.030 | 0.010 | 1 | 0.02 | 2390 | 596 |
| Emotional problems | 0.3 | 0.989 | 0.001 | 0.012 | 0.000 | 0.976 | 0.005 | 0.3 | 0.08 | 2453 | 612 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| parent-rated | | | | | | | | | | | |
| Emotional problems teacher-rated | 0.3 | 0.996 | 0.001 | 0.009 | 0.000 | 0.964 | 0.025 | 0.2 | 0.06 | 2364 | 588 |
| Emotional problems child-rated | 0.3 | 0.989 | 0.001 | 0.013 | 0.001 | 1.014 | 0.014 | 0.3 | 0.08 | 2390 | 596 |
| Peer problems parent-rated | 0.3 | 1.009 | 0.001 | 0.006 | 0.000 | 0.992 | 0.004 | 0.4 | 0.06 | 2453 | 612 |
| Peer problems teacher-rated | 0.3 | 1.008 | 0.001 | 0.003 | 0.000 | 1.010 | 0.008 | 0.5 | 0.05 | 2365 | 588 |
| Peer problems child-rated | 0.3 | 1.003 | 0.001 | 0.007 | 0.000 | 1.021 | 0.002 | 0.4 | 0.05 | 2390 | 596 |
| Single-trait cross-rater | | | | | | | | | | | |
| Hyperactivity childhood | 0.3 | 0.980 | 0.001 | 0.023 | 0.001 | 0.968 | 0.016 | 0.1 | 0.05 | 2453 | 612 |
| Hyperactivity adolescence | 0.3 | 0.991 | 0.001 | 0.011 | 0.002 | 1.011 | 0.016 | 0.8 | 0.03 | 1948 | 484 |
| Hyperactivity adulthood | 0.3 | 1.004 | 0.001 | 0.012 | 0.001 | 0.986 | 0.014 | 0.2 | 0.09 | 2120 | 528 |
| Conduct problems childhood | 0.3 | 0.980 | 0.001 | 0.018 | 0.001 | 0.973 | 0.051 | 0.6 | 0.04 | 2453 | 612 |
| Conduct problems adolescence | 0.3 | 0.991 | 0.001 | 0.020 | 0.001 | 1.008 | 0.033 | 0.1 | 0.08 | 2387 | 596 |
| Conduct problems adulthood | 0.3 | 0.985 | 0.001 | 0.015 | 0.001 | 1.001 | 0.010 | 0.6 | 0.04 | 2120 | 528 |
| Emotional problems childhood | 0.3 | 0.999 | 0.001 | 0.008 | 0.001 | 0.934 | 0.002 | 0.9 | 0.03 | 2453 | 612 |
| Emotional problems adolescence | 0.3 | 0.986 | 0.001 | 0.022 | 0.001 | 1.043 | 0.003 | 0.6 | 0.02 | 2388 | 596 |
| Emotional problems adulthood | 0.3 | 0.988 | 0.001 | 0.020 | 0.002 | 0.976 | 0.028 | 0.7 | 0.05 | 2119 | 528 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Peer problems childhood | 0.3 | 1.010 | 0.001 | 0.005 | 0.000 | 0.993 | 0.003 | 0.4 | 0.05 | 2448 | 612 |
| Peer problems adolescence | 0.3 | 1.019 | 0.001 | 0.005 | 0.000 | 0.984 | 0.000 | 0.8 | 0.05 | 2388 | 596 |
| Peer problems adulthood | 0.3 | 0.985 | 0.001 | 0.010 | 0.001 | 0.989 | 0.008 | 0.3 | 0.06 | 2120 | 528 |
| Cross-age | | | | | | | | | | | |
| BPp parent-rated | 0.01 | 0.978 | 0.001 | 0.012 | 0.001 | 0.993 | 0.015 | 0.4 | 0.04 | 2453 | 612 |
| BPp teacher-rated | 0.01 | 0.984 | 0.001 | 0.014 | 0.001 | 0.942 | 0.050 | 0.6 | 0.04 | 2365 | 588 |
| BPp child-rated | 0.01 | 0.989 | 0.001 | 0.015 | 0.001 | 0.990 | 0.005 | 0.1 | 0.08 | 2390 | 596 |
| Externalizing parent-rated | 0.01 | 0.982 | 0.001 | 0.015 | 0.001 | 0.959 | 0.026 | 0.8 | 0.02 | 2453 | 612 |
| Externalizing teacher-rated | 0.01 | 0.962 | 0.001 | 0.025 | 0.001 | 1.000 | 0.024 | 0.5 | 0.05 | 2365 | 588 |
| Externalizing child-rated | 0.01 | 0.988 | 0.000 | 0.011 | 0.001 | 0.995 | 0.021 | 0.1 | 0.06 | 2390 | 596 |
| Internalizing parent-rated | 0.01 | 0.992 | 0.001 | 0.005 | 0.000 | 0.976 | 0.009 | 0.5 | 0.05 | 2453 | 612 |
| Internalizing teacher-rated | 0.01 | 0.978 | 0.001 | 0.013 | 0.001 | 1.005 | 0.012 | 0.5 | 0.03 | 2365 | 588 |
| Internalizing child-rated | 0.01 | 0.983 | 0.001 | 0.011 | 0.001 | 1.022 | 0.005 | 0.6 | 0.03 | 2390 | 596 |
| Cross-rater | | | | | | | | | | | |
| BPp childhood | 0.01 | 0.973 | 0.001 | 0.012 | 0.001 | 0.992 | 0.027 | 0.4 | 0.04 | 2453 | 612 |
| BPp adolescence | 0.01 | 0.993 | 0.001 | 0.009 | 0.001 | 0.968 | 0.012 | 0.9 | 0.03 | 2390 | 596 |
| BPp adulthood | 0.01 | 0.990 | 0.001 | 0.014 | 0.001 | 0.976 | 0.011 | 0.8 | 0.03 | 2120 | 528 |
| Externalizing childhood | 0.01 | 0.972 | 0.001 | 0.020 | 0.002 | 0.960 | 0.019 | 1.0 | 0.02 | 2453 | 612 |
| Externalizing adolescence | 0.01 | 1.002 | 0.001 | 0.009 | 0.001 | 0.956 | 0.026 | 0.3 | 0.06 | 2390 | 596 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Externalizing adulthood | 0.01 | 0.988 | 0.001 | 0.019 | 0.001 | 0.993 | 0.003 | 0.6 | 0.02 | 2120 | 528 |
| Internalizing childhood | 0.01 | 0.993 | 0.001 | 0.006 | 0.000 | 0.966 | 0.006 | 0.4 | 0.06 | 2453 | 612 |
| Internalizing adolescence | 0.01 | 0.992 | 0.001 | 0.007 | 0.001 | 1.008 | 0.005 | 0.6 | 0.02 | 2390 | 596 |
| Internalizing adulthood | 0.01 | 0.985 | 0.000 | 0.009 | 0.001 | 0.984 | 0.026 | 0.5 | 0.06 | 2120 | 528 |
| Cross-age-and-rater (cross-age approach) * | | | | | | | | | | | |
| BPp | 0.01 | 0.979 | 0.001 | 0.019 | 0.001 | 0.9645 | 0.026 | 1.0 | 0.02 | 2453 | 612 |
| Externalizing | 0.01 | 0.979 | 0.001 | 0.024 | 0.001 | 0.9310 | 0.024 | 0.6 | 0.02 | 2453 | 612 |
| Internalizing | 0.01 | 0.987 | 0.001 | 0.011 | 0.001 | 0.9840 | 0.015 | 0.4 | 0.04 | 2453 | 612 |
| Cross-age-and-rater (cross-rater approach) ** | | | | | | | | | | | |
| BPp | 0.01 | 0.979 | 0.001 | 0.021 | 0.001 | 0.9805 | 0.008 | 1.0 | 0.02 | 2453 | 612 |
| Externalizing | 0.01 | 0.976 | 0.001 | 0.018 | 0.001 | 0.9915 | 0.038 | 0.6 | 0.04 | 2453 | 612 |
| Internalizing | 0.01 | 0.982 | 0.001 | 0.013 | 0.001 | 1.0065 | 0.004 | 0.9 | 0.04 | 2453 | 612 |
| Single-trait cross-age | | | | | | | | | | | |
| Hyperactivity parent-rated | 0.01 | 0.987 | 0.001 | 0.015 | 0.002 | 0.967 | 0.003 | 0.7 | 0.05 | 2453 | 612 |
| Hyperactivity teacher-rated | 0.01 | 0.995 | 0.002 | 0.026 | 0.001 | 0.990 | 0.012 | 1.0 | 0.02 | 2196 | 548 |
| Hyperactivity child-rated | 0.01 | 0.995 | 0.001 | 0.010 | 0.001 | 0.987 | 0.004 | 0.6 | 0.03 | 2155 | 536 |
| Conduct problems parent-rated | 0.01 | 0.989 | 0.001 | 0.015 | 0.001 | 0.968 | 0.042 | 0.6 | 0.04 | 2453 | 612 |
| Conduct problems teacher-rated | 0.01 | 0.961 | 0.001 | 0.014 | 0.001 | 0.910 | 0.035 | 0.8 | 0.04 | 2364 | 589 |
| Conduct problems child-rated | 0.01 | 0.992 | 0.000 | 0.011 | 0.001 | 1.035 | 0.002 | 0.1 | 0.06 | 2390 | 596 |
| Emotional problems | 0.01 | 0.995 | 0.001 | 0.004 | 0.000 | 0.978 | 0.002 | 1.0 | 0.03 | 2453 | 612 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| parent-rated | | | | | | | | | | | |
| Emotional problems teacher-rated | 0.01 | 1.000 | 0.001 | 0.004 | 0.000 | 0.972 | 0.002 | 0.6 | 0.05 | 2364 | 588 |
| Emotional problems child-rated | 0.01 | 0.993 | 0.001 | 0.006 | 0.000 | 1.018 | 0.008 | 0.6 | 0.06 | 2390 | 596 |
| Peer problems parent-rated | 0.01 | 1.008 | 0.000 | 0.007 | 0.001 | 0.992 | 0.004 | 0.2 | 0.05 | 2453 | 612 |
| Peer problems teacher-rated | 0.01 | 1.007 | 0.001 | 0.004 | 0.001 | 1.010 | 0.007 | 1.0 | 0.02 | 2365 | 588 |
| Peer problems child-rated | 0.01 | 1.002 | 0.001 | 0.007 | 0.000 | 1.023 | 0.000 | 0.6 | 0.03 | 2390 | 596 |
| Single-trait cross-rater | | | | | | | | | | | |
| Hyperactivity childhood | 0.01 | 0.983 | 0.001 | 0.016 | 0.001 | 0.969 | 0.013 | 0.7 | 0.05 | 2453 | 612 |
| Hyperactivity adolescence | 0.01 | 0.993 | 0.001 | 0.008 | 0.001 | 1.015 | 0.008 | 0.6 | 0.07 | 1948 | 484 |
| Hyperactivity adulthood | 0.01 | 1.007 | 0.002 | 0.008 | 0.002 | 0.991 | 0.002 | 0.6 | 0.03 | 2120 | 528 |
| Conduct problems childhood | 0.01 | 0.982 | 0.001 | 0.013 | 0.001 | 0.974 | 0.048 | 0.2 | 0.07 | 2453 | 612 |
| Conduct problems adolescence | 0.01 | 0.995 | 0.001 | 0.012 | 0.001 | 1.022 | 0.005 | 0.4 | 0.03 | 2387 | 596 |
| Conduct problems adulthood | 0.01 | 0.989 | 0.001 | 0.006 | 0.001 | 1.000 | 0.014 | 0.8 | 0.03 | 2120 | 528 |
| Emotional problems childhood | 0.01 | 1.003 | 0.001 | 0.003 | 0.000 | 0.935 | 0.001 | 1.0 | 0.03 | 2453 | 612 |
| Emotional problems adolescence | 0.01 | 0.994 | 0.001 | 0.007 | 0.001 | 1.042 | 0.001 | 0.6 | 0.03 | 2388 | 596 |
| Emotional problems adulthood | 0.01 | 0.992 | 0.001 | 0.012 | 0.001 | 0.981 | 0.018 | 0.2 | 0.09 | 2119 | 528 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Peer problems childhood | 0.01 | 1.010 | 0.001 | 0.006 | 0.001 | 0.995 | 0.001 | 0.3 | 0.05 | 2448 | 612 |
| Peer problems adolescence | 0.01 | 1.017 | 0.001 | 0.008 | 0.001 | 0.985 | 0.000 | 0.6 | 0.07 | 2388 | 596 |
| Peer problems adulthood | 0.01 | 0.986 | 0.000 | 0.008 | 0.001 | 0.990 | 0.005 | 1.0 | 0.02 | 2120 | 528 |

Note.
FRCT= fraction of SNPs; CV= cross-validated; SD= standard deviation; R2= variance explained; RMSE= root mean square error; train= training set (80%); test= hold-out set (20%); * cross-age approach: combined individual behaviour problems at all ages (2-21) for parent, teacher and child ratings to create the first order factors of cross-age externalizing and internalizing, which were then combined across raters to create the second-order factors of cross-age-and-rater externalizing and internalizing; ** cross-rater approach: combined individual behaviour problems in adolescence and adulthood to create the first order factors of cross-rater externalizing and internalizing, which were then combined across developmental stages to create the second-order factors of cross-age-and-rater externalizing and internalizing.

Supplementary Table 5. Behaviour problems composites: model fit indices and predictions from multiple regression.

| Multiple regression | | | | | | | |
|---|---|---|---|---|---|---|---|
| | FRCT | BETA | SE | T | P | Adjusted R2 | N |
| Cross-age | | | | | | | |
| BPp parent-rated | 1 | 0.089 | 0.019 | 4.673 | 0.000 | 0.019 | 3065 |
| BPp teacher-rated | 1 | 0.127 | 0.019 | 6.575 | 0.000 | 0.022 | 2953 |
| BPp child-rated | 1 | 0.073 | 0.019 | 3.779 | 0.000 | 0.027 | 2986 |
| Externalizing parent-rated | 1 | 0.125 | 0.019 | 6.612 | 0.000 | 0.024 | 3065 |
| Externalizing teacher-rated | 1 | 0.147 | 0.019 | 7.633 | 0.000 | 0.031 | 2953 |
| Externalizing child-rated | 1 | 0.086 | 0.019 | 4.420 | 0.000 | 0.028 | 2986 |
| Internalizing parent-rated | 1 | 0.038 | 0.019 | 1.993 | 0.046 | 0.013 | 3065 |
| Internalizing teacher-rated | 1 | 0.093 | 0.020 | 4.776 | 0.000 | 0.012 | 2953 |
| Internalizing child-rated | 1 | 0.053 | 0.019 | 2.732 | 0.006 | 0.025 | 2986 |
| Cross-rater | | | | | | | |
| BPp childhood | 1 | 0.111 | 0.019 | 5.866 | 0.000 | 0.020 | 3065 |
| BPp adolescence | 1 | 0.065 | 0.019 | 3.389 | 0.001 | 0.025 | 2986 |
| BPp adulthood | 1 | 0.079 | 0.020 | 3.873 | 0.000 | 0.027 | 2648 |
| Externalizing childhood | 1 | 0.146 | 0.019 | 7.799 | 0.000 | 0.028 | 3065 |
| Externalizing adolescence | 1 | 0.078 | 0.019 | 4.005 | 0.000 | 0.028 | 2986 |
| Externalizing adulthood | 1 | 0.092 | 0.020 | 4.491 | 0.000 | 0.027 | 2648 |
| Internalizing childhood | 1 | 0.056 | 0.019 | 2.937 | 0.003 | 0.011 | 3065 |
| Internalizing adolescence | 1 | 0.040 | 0.019 | 2.063 | 0.039 | 0.018 | 2986 |
| Internalizing adulthood | 1 | 0.060 | 0.020 | 2.946 | 0.003 | 0.025 | 2648 |
| Cross-age-and-rater (cross-age approach) * | | | | | | | |
| BPp | 1 | 0.114 | 0.019 | 6.051 | 0.000 | 0.033 | 3065 |
| Externalizing | 1 | 0.143 | 0.019 | 7.620 | 0.000 | 0.038 | 3065 |
| Internalizing | 1 | 0.072 | 0.019 | 3.766 | 0.000 | 0.026 | 3065 |
| Cross-age-and-rater (cross-rater approach) ** | | | | | | | |
| BPp | 1 | 0.099 | 0.019 | 5.210 | 0.000 | 0.033 | 3065 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Externalizing | 1 | 0.121 | 0.019 | 6.403 | 0.000 | 0.037 | 3065 |
| Internalizing | 1 | 0.060 | 0.019 | 3.161 | 0.002 | 0.026 | 3065 |
| Single-trait cross-age | | | | | | | |
| Hyperactivity parent-rated | 1 | 0.118 | 0.019 | 6.163 | 0.000 | 0.018 | 3065 |
| Hyperactivity teacher-rated | 1 | 0.159 | 0.020 | 7.798 | 0.000 | 0.032 | 2744 |
| Hyperactivity child-rated | 1 | 0.088 | 0.021 | 4.256 | 0.000 | 0.018 | 2691 |
| Conduct problems parent-rated | 1 | 0.113 | 0.019 | 5.925 | 0.000 | 0.024 | 3065 |
| Conduct problems teacher-rated | 1 | 0.108 | 0.019 | 5.729 | 0.000 | 0.022 | 2953 |
| Conduct problems child-rated | 1 | 0.058 | 0.020 | 2.980 | 0.003 | 0.023 | 2986 |
| Emotional problems parent-rated | 1 | 0.013 | 0.019 | 0.680 | 0.496 | 0.011 | 3065 |
| Emotional problems teacher-rated | 1 | 0.023 | 0.020 | 1.161 | 0.246 | 0.011 | 2952 |
| Emotional problems child-rated | 1 | 0.020 | 0.020 | 1.006 | 0.314 | 0.018 | 2986 |
| Peer problems parent-rated | 1 | 0.028 | 0.020 | 1.417 | 0.156 | 0.006 | 3065 |
| Peer problems teacher-rated | 1 | 0.051 | 0.020 | 2.563 | 0.010 | 0.002 | 2953 |
| Peer problems child-rated | 1 | 0.031 | 0.020 | 1.543 | 0.123 | 0.011 | 2986 |
| Single-trait cross-rater | | | | | | | |
| Hyperactivity childhood | 1 | 0.133 | 0.019 | 7.003 | 0.000 | 0.022 | 3065 |
| Hyperactivity adolescence | 1 | 0.072 | 0.022 | 3.327 | 0.001 | 0.014 | 2432 |
| Hyperactivity adulthood | 1 | 0.074 | 0.021 | 3.552 | 0.000 | 0.013 | 2648 |
| Conduct problems childhood | 1 | 0.116 | 0.019 | 6.082 | 0.000 | 0.023 | 3065 |
| Conduct problems adolescence | 1 | 0.068 | 0.020 | 3.471 | 0.001 | 0.025 | 2983 |
| Conduct problems adulthood | 1 | 0.083 | 0.021 | 4.028 | 0.000 | 0.014 | 2648 |
| Emotional problems childhood | 1 | 0.012 | 0.019 | 0.641 | 0.522 | 0.007 | 3065 |
| Emotional problems adolescence | 1 | 0.018 | 0.020 | 0.899 | 0.369 | 0.015 | 2984 |
| Emotional problems adulthood | 1 | 0.024 | 0.021 | 1.179 | 0.239 | 0.024 | 2647 |
| Peer problems childhood | 1 | 0.023 | 0.020 | 1.181 | 0.238 | 0.003 | 3060 |
| Peer problems adolescence | 1 | 0.033 | 0.020 | 1.647 | 0.100 | 0.008 | 2984 |
| Peer problems adulthood | 1 | 0.046 | 0.021 | 2.267 | 0.023 | 0.012 | 2648 |
| Cross-age | | | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| BPp parent-rated | 0.3 | 0.093 | 0.019 | 4.847 | 0.000 | 0.019 | 3065 |
| BPp teacher-rated | 0.3 | 0.135 | 0.019 | 6.957 | 0.000 | 0.026 | 2953 |
| BPp child-rated | 0.3 | 0.074 | 0.019 | 3.793 | 0.000 | 0.026 | 2986 |
| Externalizing parent-rated | 0.3 | 0.129 | 0.019 | 6.815 | 0.000 | 0.024 | 3065 |
| Externalizing teacher-rated | 0.3 | 0.154 | 0.019 | 8.015 | 0.000 | 0.033 | 2953 |
| Externalizing child-rated | 0.3 | 0.086 | 0.019 | 4.422 | 0.000 | 0.028 | 2986 |
| Internalizing parent-rated | 0.3 | 0.040 | 0.019 | 2.107 | 0.035 | 0.012 | 3065 |
| Internalizing teacher-rated | 0.3 | 0.100 | 0.020 | 5.112 | 0.000 | 0.016 | 2953 |
| Internalizing child-rated | 0.3 | 0.054 | 0.019 | 2.759 | 0.006 | 0.022 | 2986 |
| Cross-rater | | | | | | | |
| BPp childhood | 0.3 | 0.115 | 0.019 | 6.058 | 0.000 | 0.020 | 3065 |
| BPp adolescence | 0.3 | 0.069 | 0.019 | 3.583 | 0.000 | 0.024 | 2986 |
| BPp adulthood | 0.3 | 0.079 | 0.021 | 3.850 | 0.000 | 0.027 | 2648 |
| Externalizing childhood | 0.3 | 0.151 | 0.019 | 8.036 | 0.000 | 0.028 | 3065 |
| Externalizing adolescence | 0.3 | 0.080 | 0.019 | 4.121 | 0.000 | 0.026 | 2986 |
| Externalizing adulthood | 0.3 | 0.093 | 0.021 | 4.513 | 0.000 | 0.026 | 2648 |
| Internalizing childhood | 0.3 | 0.059 | 0.019 | 3.050 | 0.002 | 0.010 | 3065 |
| Internalizing adolescence | 0.3 | 0.045 | 0.020 | 2.295 | 0.022 | 0.017 | 2986 |
| Internalizing adulthood | 0.3 | 0.059 | 0.020 | 2.879 | 0.004 | 0.025 | 2648 |
| Cross-age-and-rater (cross-age approach) * | | | | | | | |
| BPp | 0.3 | 0.119 | 0.019 | 6.263 | 0.000 | 0.033 | 3065 |
| Externalizing | 0.3 | 0.147 | 0.019 | 7.846 | 0.000 | 0.038 | 3065 |
| Internalizing | 0.3 | 0.075 | 0.019 | 3.938 | 0.000 | 0.025 | 3065 |
| Cross-age-and-rater (cross-rater approach) ** | | | | | | | |
| BPp | 0.3 | 0.102 | 0.019 | 5.381 | 0.000 | 0.032 | 3065 |
| Externalizing | 0.3 | 0.125 | 0.019 | 6.571 | 0.000 | 0.036 | 3065 |
| Internalizing | 0.3 | 0.063 | 0.019 | 3.311 | 0.001 | 0.025 | 3065 |
| Single-trait cross-age | | | | | | | |
| Hyperactivity parent-rated | 0.3 | 0.122 | 0.019 | 6.359 | 0.000 | 0.018 | 3065 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Hyperactivity teacher-rated | 0.3 | 0.164 | 0.020 | 8.051 | 0.000 | 0.032 | 2744 |
| Hyperactivity child-rated | 0.3 | 0.087 | 0.021 | 4.236 | 0.000 | 0.018 | 2691 |
| Conduct problems parent-rated | 0.3 | 0.116 | 0.019 | 6.064 | 0.000 | 0.025 | 3065 |
| Conduct problems teacher-rated | 0.3 | 0.115 | 0.019 | 6.094 | 0.000 | 0.023 | 2953 |
| Conduct problems child-rated | 0.3 | 0.057 | 0.020 | 2.921 | 0.004 | 0.022 | 2986 |
| Emotional problems parent-rated | 0.3 | 0.014 | 0.019 | 0.747 | 0.455 | 0.010 | 3065 |
| Emotional problems teacher-rated | 0.3 | 0.025 | 0.020 | 1.268 | 0.205 | 0.012 | 2952 |
| Emotional problems child-rated | 0.3 | 0.017 | 0.020 | 0.885 | 0.376 | 0.013 | 2986 |
| Peer problems parent-rated | 0.3 | 0.030 | 0.020 | 1.524 | 0.128 | 0.005 | 3065 |
| Peer problems teacher-rated | 0.3 | 0.056 | 0.020 | 2.805 | 0.005 | 0.003 | 2953 |
| Peer problems child-rated | 0.3 | 0.032 | 0.020 | 1.617 | 0.106 | 0.009 | 2986 |
| Single-trait cross-rater | | | | | | | |
| Hyperactivity childhood | 0.3 | 0.137 | 0.019 | 7.206 | 0.000 | 0.022 | 3065 |
| Hyperactivity adolescence | 0.3 | 0.076 | 0.022 | 3.483 | 0.001 | 0.013 | 2432 |
| Hyperactivity adulthood | 0.3 | 0.076 | 0.021 | 3.646 | 0.000 | 0.012 | 2648 |
| Conduct problems childhood | 0.3 | 0.119 | 0.019 | 6.254 | 0.000 | 0.024 | 3065 |
| Conduct problems adolescence | 0.3 | 0.069 | 0.020 | 3.505 | 0.000 | 0.025 | 2983 |
| Conduct problems adulthood | 0.3 | 0.085 | 0.021 | 4.093 | 0.000 | 0.013 | 2648 |
| Emotional problems childhood | 0.3 | 0.013 | 0.019 | 0.666 | 0.506 | 0.006 | 3065 |
| Emotional problems adolescence | 0.3 | 0.022 | 0.020 | 1.126 | 0.260 | 0.016 | 2984 |
| Emotional problems adulthood | 0.3 | 0.022 | 0.021 | 1.047 | 0.295 | 0.023 | 2647 |
| Peer problems childhood | 0.3 | 0.026 | 0.020 | 1.309 | 0.191 | 0.003 | 3060 |
| Peer problems adolescence | 0.3 | 0.037 | 0.020 | 1.847 | 0.065 | 0.007 | 2984 |
| Peer problems adulthood | 0.3 | 0.045 | 0.021 | 2.185 | 0.029 | 0.011 | 2648 |
| Cross-age | | | | | | | |
| BPp parent-rated | 0.01 | 0.091 | 0.018 | 4.961 | 0.000 | 0.012 | 3065 |
| BPp teacher-rated | 0.01 | 0.123 | 0.019 | 6.657 | 0.000 | 0.020 | 2953 |
| BPp child-rated | 0.01 | 0.074 | 0.019 | 3.957 | 0.000 | 0.014 | 2986 |
| Externalizing parent-rated | 0.01 | 0.117 | 0.018 | 6.423 | 0.000 | 0.018 | 3065 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Externalizing teacher-rated | 0.01 | 0.137 | 0.018 | 7.429 | 0.000 | 0.024 | 2953 |
| Externalizing child-rated | 0.01 | 0.082 | 0.019 | 4.382 | 0.000 | 0.014 | 2986 |
| Internalizing parent-rated | 0.01 | 0.049 | 0.018 | 2.668 | 0.008 | 0.004 | 3065 |
| Internalizing teacher-rated | 0.01 | 0.096 | 0.019 | 5.130 | 0.000 | 0.013 | 2953 |
| Internalizing child-rated | 0.01 | 0.058 | 0.019 | 3.104 | 0.002 | 0.011 | 2986 |
| Cross-rater | | | | | | | |
| BPp childhood | 0.01 | 0.104 | 0.018 | 5.675 | 0.000 | 0.014 | 3065 |
| BPp adolescence | 0.01 | 0.079 | 0.019 | 4.219 | 0.000 | 0.010 | 2986 |
| BPp adulthood | 0.01 | 0.081 | 0.020 | 4.065 | 0.000 | 0.016 | 2648 |
| Externalizing childhood | 0.01 | 0.132 | 0.018 | 7.267 | 0.000 | 0.021 | 3065 |
| Externalizing adolescence | 0.01 | 0.082 | 0.019 | 4.348 | 0.000 | 0.012 | 2986 |
| Externalizing adulthood | 0.01 | 0.093 | 0.020 | 4.652 | 0.000 | 0.015 | 2648 |
| Internalizing childhood | 0.01 | 0.057 | 0.018 | 3.096 | 0.002 | 0.004 | 3065 |
| Internalizing adolescence | 0.01 | 0.061 | 0.019 | 3.209 | 0.001 | 0.006 | 2986 |
| Internalizing adulthood | 0.01 | 0.062 | 0.020 | 3.151 | 0.002 | 0.015 | 2648 |
| Cross-age-and-rater (cross-age approach) * | | | | | | | |
| BPp | 0.01 | 0.116 | 0.018 | 6.347 | 0.000 | 0.021 | 3065 |
| Externalizing | 0.01 | 0.136 | 0.018 | 7.493 | 0.000 | 0.026 | 3065 |
| Internalizing | 0.01 | 0.082 | 0.018 | 4.450 | 0.000 | 0.013 | 3065 |
| Cross-age-and-rater (cross-rater approach) ** | | | | | | | |
| BPp | 0.01 | 0.106 | 0.018 | 5.800 | 0.000 | 0.019 | 3065 |
| Externalizing | 0.01 | 0.122 | 0.018 | 6.662 | 0.000 | 0.022 | 3065 |
| Internalizing | 0.01 | 0.074 | 0.018 | 4.029 | 0.000 | 0.012 | 3065 |
| Single-trait cross-age | | | | | | | |
| Hyperactivity parent-rated | 0.01 | 0.111 | 0.018 | 6.039 | 0.000 | 0.012 | 3065 |
| Hyperactivity teacher-rated | 0.01 | 0.140 | 0.020 | 7.153 | 0.000 | 0.021 | 2744 |
| Hyperactivity child-rated | 0.01 | 0.086 | 0.020 | 4.306 | 0.000 | 0.007 | 2691 |
| Conduct problems parent-rated | 0.01 | 0.098 | 0.018 | 5.316 | 0.000 | 0.019 | 3065 |
| Conduct problems teacher-rated | 0.01 | 0.106 | 0.018 | 5.856 | 0.000 | 0.018 | 2953 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Conduct problems child-rated | 0.01 | 0.042 | 0.019 | 2.194 | 0.028 | 0.011 | 2986 |
| Emotional problems parent-rated | 0.01 | 0.021 | 0.019 | 1.132 | 0.258 | 0.000 | 3065 |
| Emotional problems teacher-rated | 0.01 | 0.041 | 0.019 | 2.189 | 0.029 | 0.002 | 2952 |
| Emotional problems child-rated | 0.01 | 0.017 | 0.019 | 0.890 | 0.374 | 0.004 | 2986 |
| Peer problems parent-rated | 0.01 | 0.044 | 0.019 | 2.317 | 0.021 | 0.006 | 3065 |
| Peer problems teacher-rated | 0.01 | 0.051 | 0.019 | 2.656 | 0.008 | 0.004 | 2953 |
| Peer problems child-rated | 0.01 | 0.046 | 0.019 | 2.423 | 0.015 | 0.007 | 2986 |
| Single-trait cross-rater | | | | | | | |
| Hyperactivity childhood | 0.01 | 0.122 | 0.018 | 6.626 | 0.000 | 0.015 | 3065 |
| Hyperactivity adolescence | 0.01 | 0.086 | 0.021 | 4.065 | 0.000 | 0.006 | 2432 |
| Hyperactivity adulthood | 0.01 | 0.079 | 0.020 | 3.921 | 0.000 | 0.005 | 2648 |
| Conduct problems childhood | 0.01 | 0.100 | 0.018 | 5.448 | 0.000 | 0.019 | 3065 |
| Conduct problems adolescence | 0.01 | 0.060 | 0.019 | 3.167 | 0.002 | 0.012 | 2983 |
| Conduct problems adulthood | 0.01 | 0.071 | 0.020 | 3.572 | 0.000 | 0.007 | 2648 |
| Emotional problems childhood | 0.01 | 0.012 | 0.019 | 0.671 | 0.502 | <.001 | 3065 |
| Emotional problems adolescence | 0.01 | 0.034 | 0.019 | 1.791 | 0.073 | 0.004 | 2984 |
| Emotional problems adulthood | 0.01 | 0.030 | 0.020 | 1.520 | 0.129 | 0.015 | 2647 |
| Peer problems childhood | 0.01 | 0.038 | 0.019 | 2.011 | 0.044 | 0.004 | 3060 |
| Peer problems adolescence | 0.01 | 0.052 | 0.019 | 2.698 | 0.007 | 0.006 | 2984 |
| Peer problems adulthood | 0.01 | 0.048 | 0.020 | 2.400 | 0.016 | 0.008 | 2648 |

Note.
FRCT= fraction of SNPs; SE= standard error; P= p-value; R2= variance explained; * cross-age approach: combined individual behaviour problems at all ages (2-21) for parent, teacher and child ratings to create the first order factors of cross-age externalizing and internalizing, which were then combined across raters to create the second-order factors of cross-age-and-rater externalizing and internalizing; ** cross-rater approach: combined individual behaviour problems in adolescence and adulthood to create the first order factors of cross-rater externalizing and internalizing, which were then combined across developmental stages to create the second-order factors of cross-age-and-rater externalizing and internalizing.

Supplementary Table 6. Behaviour problems composites: model fit indices and predictions from multiple regression, for males and females separately.

| Composites | Multiple regression: males only | | | | | | |
|---|---|---|---|---|---|---|---|
| | FRCT | BETA | SE | T | P | Adjusted R2 | N |
| Cross-age | | | | | | | |
| BPp parent-rated | 1 | 0.091 | 0.029 | 3.107 | 0.002 | 0.014 | 1376 |
| BPp teacher-rated | 1 | 0.179 | 0.032 | 5.595 | 0.000 | 0.035 | 1322 |
| BPp child-rated | 1 | 0.053 | 0.028 | 1.914 | 0.056 | 0.012 | 1332 |
| Externalizing parent-rated | 1 | 0.118 | 0.030 | 3.974 | 0.000 | 0.015 | 1376 |
| Externalizing teacher-rated | 1 | 0.200 | 0.033 | 6.069 | 0.000 | 0.043 | 1322 |
| Externalizing child-rated | 1 | 0.066 | 0.028 | 2.340 | 0.019 | 0.017 | 1332 |
| Internalizing parent-rated | 1 | 0.049 | 0.029 | 1.676 | 0.094 | 0.013 | 1376 |
| Internalizing teacher-rated | 1 | 0.139 | 0.031 | 4.444 | 0.000 | 0.021 | 1322 |
| Internalizing child-rated | 1 | 0.035 | 0.028 | 1.275 | 0.203 | 0.008 | 1332 |
| Cross-rater | | | | | | | |
| BPp childhood | 1 | 0.129 | 0.030 | 4.309 | 0.000 | 0.020 | 1376 |
| BPp adolescence | 1 | 0.053 | 0.029 | 1.845 | 0.065 | 0.011 | 1336 |
| BPp adulthood | 1 | 0.056 | 0.030 | 1.865 | 0.062 | 0.015 | 1126 |
| Externalizing childhood | 1 | 0.157 | 0.030 | 5.206 | 0.000 | 0.025 | 1376 |
| Externalizing adolescence | 1 | 0.063 | 0.029 | 2.172 | 0.030 | 0.015 | 1336 |
| Externalizing adulthood | 1 | 0.062 | 0.030 | 2.049 | 0.041 | 0.017 | 1126 |
| Internalizing childhood | 1 | 0.077 | 0.030 | 2.606 | 0.009 | 0.013 | 1376 |
| Internalizing adolescence | 1 | 0.033 | 0.029 | 1.125 | 0.261 | 0.009 | 1336 |
| Internalizing adulthood | 1 | 0.044 | 0.029 | 1.512 | 0.131 | 0.012 | 1126 |
| Composites | Multiple regression: females only | | | | | | |
| | Fraction of SNPs | BETA | SE | T | P | Adjusted R2 | N |
| Cross-age | | | | | | | |
| BPp parent-rated | | 0.087 | 0.025 | 3.473 | 0.001 | 0.023 | 1689 |
| BPp teacher-rated | 1 | 0.087 | 0.023 | 3.707 | 0.000 | 0.021 | 1631 |
| BPp child-rated | 1 | 0.088 | 0.027 | 3.259 | 0.001 | 0.039 | 1654 |
| Externalizing parent-rated | 1 | 0.131 | 0.024 | 5.354 | 0.000 | 0.031 | 1689 |
| Externalizing teacher-rated | 1 | 0.107 | 0.022 | 4.804 | 0.000 | 0.029 | 1631 |
| Externalizing child-rated | 1 | 0.100 | 0.027 | 3.725 | 0.000 | 0.036 | 1654 |
| Internalizing parent-rated | 1 | 0.029 | 0.025 | 1.139 | 0.255 | 0.013 | 1689 |
| Internalizing teacher-rated | 1 | 0.057 | 0.025 | 2.295 | 0.022 | 0.013 | 1631 |
| Internalizing child-rated | 1 | 0.067 | 0.027 | 2.452 | 0.014 | 0.038 | 1654 |
| Cross-rater | | | | | | | |
| BPp childhood | 1 | 0.096 | 0.024 | 3.956 | 0.000 | 0.020 | 1689 |
| BPp adolescence | 1 | 0.072 | 0.026 | 2.785 | 0.005 | 0.037 | 1650 |
| BPp adulthood | 1 | 0.100 | 0.028 | 3.571 | 0.000 | 0.035 | 1522 |
| Externalizing childhood | 1 | 0.138 | 0.024 | 5.843 | 0.000 | 0.033 | 1689 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Externalizing adolescence | 1 | 0.087 | 0.026 | 3.323 | 0.001 | 0.036 | 1650 |
| Externalizing adulthood | 1 | 0.118 | 0.028 | 4.235 | 0.000 | 0.032 | 1522 |
| Internalizing childhood | 1 | 0.038 | 0.025 | 1.511 | 0.131 | 0.008 | 1689 |
| Internalizing adolescence | 1 | 0.044 | 0.026 | 1.672 | 0.095 | 0.028 | 1650 |
| Internalizing adulthood | 1 | 0.075 | 0.028 | 2.650 | 0.008 | 0.036 | 1522 |
| Note. FRCT= fraction of SNPs; SE= standard error; P= p-value; R2= variance explained. | | | | | | | |

Supplementary Table 7. SDQ scales (observed traits): model fit indices and predictions from elastic net regularization.

| Trait | Rater | Elastic net regularization | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | FRCT | Mean CV RMSE (train) | SD CV RMSE (train) | Mean CV R2 (train) | SD CV R2 (train) | RMSE | R2 | Alpha | Lambda | N (train) | N (test) |
| Year 2 | | | | | | | | | | | | |
| Hyperactivity | Parent | 1 | 1.005 | 0.001 | 0.005 | 0.000 | 1.009 | 0.007 | 1 | 0.040 | 2182 | 544 |
| Conduct problems | Parent | 1 | 0.989 | 0.001 | 0.005 | 0.001 | 0.955 | 0.001 | 0.5 | 0.061 | 2178 | 543 |
| Emotional problems | Parent | 1 | 0.987 | 0.002 | 0.005 | 0.001 | 0.984 | 0.000 | 0.5 | 0.064 | 2186 | 544 |
| Year 3 | | | | | | | | | | | | |
| Hyperactivity | Parent | 1 | 1.006 | 0.001 | 0.007 | 0.001 | 1.004 | 0.001 | 0.4 | 0.065 | 2237 | 557 |
| Conduct problems | Parent | 1 | 0.985 | 0.001 | 0.016 | 0.000 | 0.988 | 0.003 | 0.1 | 0.089 | 2234 | 556 |
| Emotional problems | Parent | 1 | 0.990 | 0.001 | 0.005 | 0.001 | 1.005 | 0.014 | 0.5 | 0.063 | 2236 | 557 |
| Year 4 | | | | | | | | | | | | |
| Hyperactivity | Parent | 1 | 0.986 | 0.000 | 0.010 | 0.000 | 0.998 | 0.008 | 0.2 | 0.070 | 3176 | 792 |
| Conduct problems | Parent | 1 | 0.969 | 0.000 | 0.009 | 0.000 | 0.968 | 0.011 | 0.6 | 0.029 | 3176 | 791 |
| Emotional problems | Parent | 1 | 1.005 | 0.001 | 0.004 | 0.001 | 0.990 | 0.001 | 0.9 | 0.024 | 3176 | 791 |
| Peer problems | Parent | 1 | 1.002 | 0.001 | 0.003 | 0.000 | 0.996 | 0.000 | 1 | 0.032 | 3171 | 791 |
| Year 7 | | | | | | | | | | | | |
| Hyperactivity | Parent | 1 | 0.983 | 0.001 | 0.017 | 0.000 | 0.952 | 0.017 | 0.1 | 0.046 | 3251 | 812 |
| Hyperactivity | Teacher | 1 | 0.973 | 0.002 | 0.026 | 0.001 | 1.004 | 0.013 | 0.6 | 0.023 | 2695 | 672 |
| Conduct problems | Parent | 1 | 0.982 | 0.001 | 0.021 | 0.001 | 0.992 | 0.006 | 1 | 0.020 | 3253 | 812 |
| Conduct problems | Teacher | 1 | 1.276 | 0.001 | 0.018 | 0.001 | 1.277 | 0.004 | 0.5 | 0.049 | 2699 | 673 |
| Emotional problems | Parent | 1 | 0.976 | 0.000 | 0.009 | 0.001 | 1.017 | 0.003 | 0.1 | 0.054 | 3252 | 812 |
| Emotional problems | Teacher | 1 | 0.994 | 0.001 | 0.005 | 0.000 | 0.995 | 0.009 | 0.5 | 0.056 | 2684 | 669 |
| Peer problems | Parent | 1 | 1.002 | 0.001 | 0.003 | 0.001 | 0.995 | 0.000 | 0.6 | 0.047 | 3253 | 811 |
| Peer problems | Teacher | 1 | 0.991 | 0.001 | 0.006 | 0.001 | 1.015 | 0.000 | 0.2 | 0.056 | 2690 | 672 |
| Year 9 | | | | | | | | | | | | |
| Hyperactivity | Parent | 1 | 0.991 | 0.001 | 0.027 | 0.001 | 0.988 | 0.000 | 0.2 | 0.054 | 1551 | 384 |
| Hyperactivity | Teacher | 1 | 0.994 | 0.002 | 0.029 | 0.004 | 0.987 | 0.023 | 0.6 | 0.065 | 1283 | 320 |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hyperactivity | Child | 1 | 1.007 | 0.001 | 0.009 | 0.001 | 0.980 | 0.002 | 1 | 0.033 | 1532 | 380 |
| Conduct problems | Parent | 1 | 1.004 | 0.001 | 0.018 | 0.001 | 1.004 | 0.008 | 0.3 | 0.103 | 1551 | 385 |
| Conduct problems | Teacher | 1 | 0.936 | 0.002 | 0.032 | 0.003 | 0.909 | 0.000 | 1 | 0.026 | 1284 | 320 |
| Conduct problems | Child | 1 | 1.000 | 0.001 | 0.012 | 0.001 | 0.948 | 0.006 | 0.9 | 0.038 | 1529 | 380 |
| Peer problems | Parent | 1 | 1.013 | 0.002 | 0.008 | 0.001 | 0.997 | 0.002 | 0.3 | 0.063 | 1552 | 384 |
| Peer problems | Teacher | 1 | 0.997 | 0.002 | 0.006 | 0.000 | 0.995 | 0.002 | 1 | 0.045 | 1288 | 319 |
| Peer problems | Child | 1 | 0.998 | 0.002 | 0.008 | 0.001 | 0.960 | 0.004 | 0.3 | 0.080 | 1525 | 380 |
| Emotional problems | Parent | 1 | 1.004 | 0.002 | 0.006 | 0.000 | 0.986 | 0.010 | 1 | 0.053 | 1552 | 385 |
| Emotional problems | Teacher | 1 | 0.983 | 0.001 | 0.013 | 0.001 | 1.021 | 0.002 | 0.3 | 0.081 | 1282 | 320 |
| Emotional problems | Child | 1 | 1.002 | 0.001 | 0.008 | 0.000 | 0.989 | 0.033 | 0.6 | 0.065 | 1529 | 380 |
| Year 12 | | | | | | | | | | | | |
| Conduct problems | Teacher | 1 | 0.981 | 0.001 | 0.013 | 0.001 | 0.997 | 0.012 | 0.9 | 0.034 | 2272 | 565 |
| Conduct problems | Child | 1 | 0.990 | 0.001 | 0.012 | 0.001 | 0.974 | 0.018 | 0.3 | 0.032 | 2752 | 688 |
| Emotional problems | Parent | 1 | 0.997 | 0.001 | 0.007 | 0.000 | 1.029 | 0.000 | 0.4 | 0.071 | 2760 | 687 |
| Emotional problems | Teacher | 1 | 0.985 | 0.001 | 0.012 | 0.002 | 0.978 | 0.004 | 0.1 | 0.062 | 2265 | 565 |
| Emotional problems | Child | 1 | 0.998 | 0.001 | 0.016 | 0.001 | 0.982 | 0.005 | 1 | 0.020 | 2752 | 686 |
| Peer problems | Parent | 1 | 0.997 | 0.001 | 0.004 | 0.000 | 0.972 | 0.007 | 0.5 | 0.040 | 2759 | 688 |
| Peer problems | Teacher | 1 | 0.995 | 0.001 | 0.005 | 0.000 | 1.019 | 0.001 | 0.5 | 0.050 | 2271 | 566 |
| Peer problems | Child | 1 | 1.007 | 0.001 | 0.004 | 0.000 | 1.020 | 0.003 | 0.3 | 0.047 | 2753 | 687 |
| Year 16 | | | | | | | | | | | | |
| Hyperactivity | Child | 1 | 0.996 | 0.001 | 0.011 | 0.000 | 0.969 | 0.009 | 0.6 | 0.031 | 2388 | 596 |
| Hyperactivity | Parent | 1 | 0.992 | 0.001 | 0.009 | 0.001 | 0.990 | 0.007 | 0.2 | 0.067 | 2395 | 597 |
| Conduct problems | Child | 1 | 0.995 | 0.001 | 0.023 | 0.001 | 0.987 | 0.013 | 0.5 | 0.045 | 2389 | 595 |
| Conduct problems | Parent | 1 | 0.984 | 0.001 | 0.015 | 0.002 | 1.004 | 0.016 | 0.1 | 0.068 | 2400 | 598 |
| Emotional problems | Child | 1 | 1.005 | 0.001 | 0.011 | 0.001 | 0.999 | 0.014 | 0.7 | 0.037 | 2388 | 596 |
| Peer problems | Child | 1 | 0.998 | 0.000 | 0.009 | 0.001 | 1.029 | 0.001 | 0.3 | 0.052 | 2388 | 596 |
| Year 21 | | | | | | | | | | | | |
| Hyperactivity | Parent | 1 | 1.009 | 0.001 | 0.014 | 0.001 | 0.977 | 0.004 | 0.6 | 0.035 | 2496 | 622 |
| Hyperactivity | Child | 1 | 0.994 | 0.001 | 0.018 | 0.001 | 0.993 | 0.016 | 0.8 | 0.016 | 2240 | 557 |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Conduct problems | Parent | 1 | 0.990 | 0.001 | 0.010 | 0.001 | 0.981 | 0.025 | 0.8 | 0.029 | 2496 | 623 |
| Conduct problems | Child | 1 | 0.977 | 0.001 | 0.017 | 0.002 | 0.998 | 0.002 | 1 | 0.015 | 2240 | 558 |
| Emotional problems | Parent | 1 | 0.989 | 0.001 | 0.016 | 0.001 | 1.005 | 0.021 | 0.2 | 0.100 | 2496 | 621 |
| Emotional problems | Child | 1 | 0.987 | 0.001 | 0.015 | 0.000 | 1.011 | 0.024 | 0.6 | 0.040 | 2240 | 557 |
| Peer problems | Parent | 1 | 0.985 | 0.001 | 0.010 | 0.001 | 0.972 | 0.012 | 0.2 | 0.067 | 2495 | 622 |
| Peer problems | Child | 1 | 0.985 | 0.001 | 0.023 | 0.002 | 0.965 | 0.005 | 0.1 | 0.099 | 2240 | 557 |
| Year 2 | | | | | | | | | | | | |
| Hyperactivity | Parent | 0.3 | 1.005 | 0.001 | 0.004 | 0.000 | 1.009 | 0.008 | 1.0 | 0.041 | 2182 | 544 |
| Conduct problems | Parent | 0.3 | 0.989 | 0.002 | 0.005 | 0.001 | 0.956 | 0.001 | 0.5 | 0.062 | 2178 | 543 |
| Emotional problems | Parent | 0.3 | 0.987 | 0.001 | 0.004 | 0.001 | 0.983 | 0.002 | 0.6 | 0.056 | 2186 | 544 |
| Year 3 | | | | | | | | | | | | |
| Hyperactivity | Parent | 0.3 | 1.006 | 0.001 | 0.007 | 0.000 | 1.004 | 0.002 | 0.5 | 0.066 | 2237 | 557 |
| Conduct problems | Parent | 0.3 | 0.986 | 0.001 | 0.015 | 0.000 | 0.988 | 0.003 | 0.1 | 0.089 | 2234 | 556 |
| Emotional problems | Parent | 0.3 | 0.991 | 0.001 | 0.004 | 0.000 | 1.007 | 0.010 | 0.6 | 0.054 | 2236 | 557 |
| Year 4 | | | | | | | | | | | | |
| Hyperactivity | Parent | 0.3 | 0.986 | 0.000 | 0.010 | 0.000 | 0.998 | 0.008 | 0.2 | 0.071 | 3176 | 792 |
| Conduct problems | Parent | 0.3 | 0.969 | 0.001 | 0.008 | 0.000 | 0.968 | 0.011 | 0.6 | 0.029 | 3176 | 791 |
| Emotional problems | Parent | 0.3 | 1.005 | 0.001 | 0.004 | 0.001 | 0.991 | 0.000 | 0.3 | 0.056 | 3176 | 791 |
| Peer problems | Parent | 0.3 | 1.002 | 0.001 | 0.003 | 0.000 | 0.996 | 0.000 | 1.0 | 0.032 | 3171 | 791 |
| Year 7 | | | | | | | | | | | | |
| Hyperactivity | Parent | 0.3 | 0.983 | 0.001 | 0.016 | 0.001 | 0.954 | 0.016 | 0.8 | 0.046 | 3251 | 812 |
| Hyperactivity | Teacher | 0.3 | 0.973 | 0.002 | 0.026 | 0.001 | 1.004 | 0.014 | 0.6 | 0.023 | 2695 | 672 |
| Conduct problems | Parent | 0.3 | 0.982 | 0.001 | 0.020 | 0.001 | 0.992 | 0.006 | 1.0 | 0.020 | 3253 | 812 |
| Conduct problems | Teacher | 0.3 | 1.276 | 0.001 | 0.017 | 0.001 | 1.275 | 0.005 | 0.5 | 0.050 | 2699 | 673 |
| Emotional problems | Parent | 0.3 | 0.976 | 0.000 | 0.009 | 0.001 | 1.017 | 0.002 | 0.1 | 0.053 | 3252 | 812 |
| Emotional problems | Teacher | 0.3 | 0.994 | 0.001 | 0.005 | 0.000 | 0.995 | 0.006 | 0.5 | 0.053 | 2684 | 669 |
| Peer problems | Parent | 0.3 | 1.002 | 0.001 | 0.003 | 0.001 | 0.995 | 0.000 | 0.5 | 0.047 | 3253 | 811 |
| Peer problems | Teacher | 0.3 | 0.991 | 0.001 | 0.006 | 0.000 | 1.015 | 0.000 | 0.6 | 0.024 | 2690 | 672 |
| Year 9 | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hyperactivity | Parent | 0.3 | 0.991 | 0.001 | 0.028 | 0.000 | 0.989 | 0.000 | 0.2 | 0.055 | 1551 | 384 |
| Hyperactivity | Teacher | 0.3 | 0.994 | 0.002 | 0.029 | 0.004 | 0.986 | 0.023 | 0.6 | 0.065 | 1283 | 320 |
| Hyperactivity | Child | 0.3 | 1.007 | 0.002 | 0.009 | 0.001 | 0.980 | 0.002 | 0.8 | 0.034 | 1532 | 380 |
| Conduct problems | Parent | 0.3 | 1.002 | 0.001 | 0.020 | 0.001 | 1.004 | 0.008 | 0.6 | 0.045 | 1551 | 385 |
| Conduct problems | Teacher | 0.3 | 0.935 | 0.002 | 0.034 | 0.002 | 0.908 | 0.000 | 0.9 | 0.027 | 1284 | 320 |
| Conduct problems | Child | 0.3 | 1.000 | 0.001 | 0.012 | 0.001 | 0.948 | 0.006 | 0.8 | 0.038 | 1529 | 380 |
| Emotional problems | Parent | 0.3 | 1.004 | 0.002 | 0.006 | 0.000 | 0.986 | 0.011 | 1.0 | 0.046 | 1552 | 385 |
| Emotional problems | Teacher | 0.3 | 0.982 | 0.001 | 0.014 | 0.001 | 1.022 | 0.001 | 0.6 | 0.035 | 1282 | 320 |
| Emotional problems | Child | 0.3 | 1.003 | 0.001 | 0.008 | 0.000 | 0.989 | 0.032 | 0.6 | 0.063 | 1529 | 380 |
| Peer problems | Parent | 0.3 | 1.012 | 0.002 | 0.008 | 0.001 | 0.998 | 0.001 | 0.3 | 0.062 | 1552 | 384 |
| Peer problems | Teacher | 0.3 | 0.996 | 0.002 | 0.006 | 0.000 | 0.995 | 0.001 | 1.0 | 0.047 | 1288 | 319 |
| Peer problems | Child | 0.3 | 0.999 | 0.002 | 0.008 | 0.001 | 0.959 | 0.006 | 0.4 | 0.079 | 1525 | 380 |
| Year 12 | | | | | | | | | | | | |
| Conduct problems | Teacher | 0.3 | 0.982 | 0.001 | 0.011 | 0.002 | 0.997 | 0.013 | 0.9 | 0.034 | 2272 | 565 |
| Conduct problems | Child | 0.3 | 0.991 | 0.001 | 0.012 | 0.001 | 0.974 | 0.018 | 0.1 | 0.074 | 2752 | 688 |
| Emotional problems | Parent | 0.3 | 0.995 | 0.000 | 0.009 | 0.000 | 1.030 | 0.000 | 0.3 | 0.078 | 2760 | 687 |
| Emotional problems | Teacher | 0.3 | 0.983 | 0.001 | 0.015 | 0.002 | 0.977 | 0.006 | 0.1 | 0.067 | 2265 | 565 |
| Emotional problems | Child | 0.3 | 0.999 | 0.001 | 0.015 | 0.001 | 0.983 | 0.004 | 1.0 | 0.019 | 2752 | 686 |
| Peer problems | Parent | 0.3 | 0.997 | 0.001 | 0.004 | 0.000 | 0.973 | 0.007 | 0.5 | 0.040 | 2759 | 688 |
| Peer problems | Teacher | 0.3 | 0.995 | 0.001 | 0.005 | 0.000 | 1.018 | 0.001 | 0.6 | 0.051 | 2271 | 566 |
| Peer problems | Child | 0.3 | 1.007 | 0.001 | 0.004 | 0.000 | 1.019 | 0.003 | 0.3 | 0.046 | 2753 | 687 |
| Year 16 | | | | | | | | | | | | |
| Hyperactivity | Child | 0.3 | 0.997 | 0.001 | 0.010 | 0.000 | 0.968 | 0.011 | 0.8 | 0.031 | 2388 | 596 |
| Hyperactivity | Parent | 0.3 | 0.993 | 0.001 | 0.009 | 0.000 | 0.992 | 0.004 | 0.2 | 0.067 | 2395 | 597 |
| Conduct problems | Child | 0.3 | 0.996 | 0.001 | 0.022 | 0.001 | 0.987 | 0.014 | 0.1 | 0.103 | 2389 | 595 |
| Conduct problems | Parent | 0.3 | 0.985 | 0.001 | 0.015 | 0.001 | 1.004 | 0.015 | 0.1 | 0.068 | 2400 | 598 |
| Emotional problems | Child | 0.3 | 1.007 | 0.001 | 0.007 | 0.001 | 1.001 | 0.008 | 0.8 | 0.029 | 2388 | 596 |
| Peer problems | Child | 0.3 | 0.999 | 0.001 | 0.008 | 0.001 | 1.029 | 0.000 | 0.3 | 0.052 | 2388 | 596 |
| Year 21 | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hyperactivity | Parent | 0.3 | 1.010 | 0.001 | 0.012 | 0.001 | 0.977 | 0.004 | 0.6 | 0.035 | 2496 | 622 |
| Hyperactivity | Child | 0.3 | 0.994 | 0.001 | 0.019 | 0.001 | 0.994 | 0.014 | 0.8 | 0.016 | 2240 | 557 |
| Conduct problems | Parent | 0.3 | 0.990 | 0.001 | 0.010 | 0.001 | 0.981 | 0.026 | 0.8 | 0.029 | 2496 | 623 |
| Conduct problems | Child | 0.3 | 0.978 | 0.001 | 0.016 | 0.001 | 0.998 | 0.002 | 0.1 | 0.079 | 2240 | 558 |
| Emotional problems | Parent | 0.3 | 0.989 | 0.001 | 0.016 | 0.001 | 1.005 | 0.020 | 1.0 | 0.019 | 2496 | 621 |
| Emotional problems | Child | 0.3 | 0.989 | 0.001 | 0.012 | 0.001 | 1.014 | 0.016 | 0.3 | 0.075 | 2240 | 557 |
| Peer problems | Parent | 0.3 | 0.985 | 0.001 | 0.010 | 0.001 | 0.972 | 0.012 | 0.2 | 0.067 | 2495 | 622 |
| Peer problems | Child | 0.3 | 0.985 | 0.001 | 0.023 | 0.002 | 0.964 | 0.006 | 0.1 | 0.098 | 2240 | 557 |
| Year 2 | | | | | | | | | | | | |
| Hyperactivity | Parent | 0.01 | 1.003 | 0.001 | 0.006 | 0.000 | 1.010 | 0.000 | 0.5 | 0.057 | 2182 | 544 |
| Conduct problems | Parent | 0.01 | 0.987 | 0.001 | 0.007 | 0.001 | 0.955 | 0.001 | 0.3 | 0.066 | 2178 | 543 |
| Emotional problems | Parent | 0.01 | 0.987 | 0.001 | 0.005 | 0.001 | 0.982 | 0.003 | 0.5 | 0.055 | 2186 | 544 |
| Year 3 | | | | | | | | | | | | |
| Hyperactivity | Parent | 0.01 | 1.007 | 0.001 | 0.006 | 0.000 | 1.004 | 0.002 | 1.0 | 0.024 | 2237 | 557 |
| Conduct problems | Parent | 0.01 | 0.988 | 0.001 | 0.010 | 0.001 | 0.986 | 0.003 | 0.2 | 0.078 | 2234 | 556 |
| Emotional problems | Parent | 0.01 | 0.992 | 0.001 | 0.004 | 0.000 | 1.009 | 0.008 | 1.0 | 0.030 | 2236 | 557 |
| Year 4 | | | | | | | | | | | | |
| Hyperactivity | Parent | 0.01 | 0.989 | 0.001 | 0.005 | 0.001 | 0.999 | 0.007 | 1.0 | 0.027 | 3176 | 792 |
| Conduct problems | Parent | 0.01 | 0.971 | 0.001 | 0.005 | 0.001 | 0.970 | 0.007 | 0.7 | 0.023 | 3176 | 791 |
| Emotional problems | Parent | 0.01 | 1.006 | 0.001 | 0.003 | 0.000 | 0.991 | 0.001 | 0.8 | 0.037 | 3176 | 791 |
| Peer problems | Parent | 0.01 | 1.001 | 0.000 | 0.004 | 0.001 | 0.996 | 0.000 | 1.0 | 0.037 | 3171 | 791 |
| Year 7 | | | | | | | | | | | | |
| Hyperactivity | Parent | 0.01 | 0.987 | 0.001 | 0.009 | 0.002 | 0.954 | 0.014 | 0.9 | 0.016 | 3251 | 812 |
| Hyperactivity | Teacher | 0.01 | 0.977 | 0.001 | 0.019 | 0.001 | 1.005 | 0.011 | 0.8 | 0.021 | 2695 | 672 |
| Conduct problems | Parent | 0.01 | 0.986 | 0.001 | 0.013 | 0.001 | 0.993 | 0.004 | 0.8 | 0.014 | 3253 | 812 |
| Conduct problems | Teacher | 0.01 | 1.279 | 0.001 | 0.012 | 0.001 | 1.272 | 0.010 | 1.0 | 0.019 | 2699 | 673 |
| Peer problems | Parent | 0.01 | 1.003 | 0.001 | 0.003 | 0.000 | 0.995 | 0.000 | 1.0 | 0.027 | 3253 | 811 |
| Peer problems | Teacher | 0.01 | 0.990 | 0.000 | 0.007 | 0.001 | 1.016 | 0.000 | 0.2 | 0.054 | 2690 | 672 |
| Emotional problems | Parent | 0.01 | 0.980 | 0.001 | 0.003 | 0.000 | 1.017 | 0.000 | 1.0 | 0.030 | 3252 | 812 |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Emotional problems | Teacher | 0.01 | 0.995 | 0.001 | 0.004 | 0.000 | 0.995 | 0.011 | 0.6 | 0.043 | 2684 | 669 |
| Year 9 | | | | | | | | | | | | |
| Hyperactivity | Parent | 0.01 | 0.997 | 0.001 | 0.018 | 0.002 | 0.983 | 0.000 | 0.6 | 0.048 | 1551 | 384 |
| Hyperactivity | Teacher | 0.01 | 0.997 | 0.002 | 0.023 | 0.003 | 0.982 | 0.037 | 0.7 | 0.056 | 1283 | 320 |
| Hyperactivity | Child | 0.01 | 1.008 | 0.002 | 0.007 | 0.001 | 0.980 | 0.002 | 0.4 | 0.062 | 1532 | 380 |
| Conduct problems | Parent | 0.01 | 1.004 | 0.001 | 0.017 | 0.001 | 1.003 | 0.008 | 0.2 | 0.093 | 1551 | 385 |
| Conduct problems | Teacher | 0.01 | 0.938 | 0.001 | 0.029 | 0.001 | 0.899 | 0.005 | 0.6 | 0.052 | 1284 | 320 |
| Conduct problems | Child | 0.01 | 1.002 | 0.002 | 0.009 | 0.002 | 0.947 | 0.008 | 0.5 | 0.080 | 1529 | 380 |
| Peer problems | Parent | 0.01 | 1.011 | 0.001 | 0.011 | 0.001 | 1.005 | 0.000 | 0.2 | 0.061 | 1552 | 384 |
| Peer problems | Teacher | 0.01 | 0.996 | 0.002 | 0.006 | 0.000 | 0.996 | 0.003 | 1.0 | 0.045 | 1288 | 319 |
| Peer problems | Child | 0.01 | 1.002 | 0.002 | 0.006 | 0.000 | 0.961 | 0.012 | 1.0 | 0.047 | 1525 | 380 |
| Emotional problems | Parent | 0.01 | 1.005 | 0.002 | 0.007 | 0.001 | 0.987 | 0.001 | 1.0 | 0.039 | 1552 | 385 |
| Emotional problems | Teacher | 0.01 | 0.986 | 0.002 | 0.008 | 0.001 | 1.016 | 0.000 | 0.5 | 0.053 | 1282 | 320 |
| Emotional problems | Child | 0.01 | 1.007 | 0.002 | 0.007 | 0.001 | 0.995 | 0.000 | 1.0 | 0.040 | 1529 | 380 |
| Year 12 | | | | | | | | | | | | |
| Conduct problems | Teacher | 0.01 | 0.988 | 0.002 | 0.004 | 0.001 | 0.999 | 0.013 | 0.5 | 0.054 | 2272 | 565 |
| Conduct problems | Child | 0.01 | 0.994 | 0.001 | 0.005 | 0.001 | 0.978 | 0.014 | 0.9 | 0.027 | 2752 | 688 |
| Emotional problems | Parent | 0.01 | 0.998 | 0.001 | 0.006 | 0.000 | 1.030 | 0.001 | 0.5 | 0.053 | 2760 | 687 |
| Emotional problems | Teacher | 0.01 | 0.987 | 0.001 | 0.008 | 0.000 | 0.976 | 0.006 | 0.3 | 0.065 | 2265 | 565 |
| Emotional problems | Child | 0.01 | 1.004 | 0.000 | 0.006 | 0.000 | 0.984 | 0.001 | 0.4 | 0.059 | 2752 | 686 |
| Peer problems | Parent | 0.01 | 0.997 | 0.001 | 0.004 | 0.000 | 0.974 | 0.003 | 0.6 | 0.041 | 2759 | 688 |
| Peer problems | Teacher | 0.01 | 0.995 | 0.001 | 0.005 | 0.000 | 1.019 | 0.000 | 0.3 | 0.054 | 2271 | 566 |
| Peer problems | Child | 0.01 | 1.007 | 0.000 | 0.005 | 0.001 | 1.021 | 0.006 | 1.0 | 0.041 | 2753 | 687 |
| Year 16 | | | | | | | | | | | | |
| Hyperactivity | Child | 0.01 | 1.000 | 0.001 | 0.005 | 0.000 | 0.969 | 0.008 | 0.3 | 0.045 | 2388 | 596 |
| Hyperactivity | Parent | 0.01 | 0.994 | 0.001 | 0.007 | 0.000 | 0.995 | 0.001 | 0.2 | 0.055 | 2395 | 597 |
| Conduct problems | Child | 0.01 | 1.004 | 0.001 | 0.007 | 0.001 | 0.993 | 0.001 | 1.0 | 0.020 | 2389 | 595 |
| Conduct problems | Parent | 0.01 | 0.988 | 0.000 | 0.008 | 0.001 | 1.009 | 0.006 | 0.1 | 0.057 | 2400 | 598 |
| Emotional problems | Child | 0.01 | 1.008 | 0.001 | 0.005 | 0.001 | 1.001 | 0.010 | 0.4 | 0.060 | 2388 | 596 |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Peer problems | Child | 0.01 | 0.999 | 0.000 | 0.007 | 0.001 | 1.032 | 0.001 | 0.3 | 0.048 | 2388 | 596 |
| Year 21 | | | | | | | | | | | | |
| Hyperactivity | Parent | 0.01 | 1.014 | 0.001 | 0.005 | 0.002 | 0.976 | 0.006 | 1.0 | 0.030 | 2496 | 622 |
| Hyperactivity | Child | 0.01 | 0.998 | 0.001 | 0.012 | 0.002 | 0.996 | 0.011 | 0.6 | 0.033 | 2240 | 557 |
| Conduct problems | Parent | 0.01 | 0.992 | 0.001 | 0.007 | 0.000 | 0.985 | 0.017 | 1.0 | 0.025 | 2496 | 623 |
| Conduct problems | Child | 0.01 | 0.983 | 0.001 | 0.007 | 0.001 | 0.995 | 0.003 | 0.2 | 0.054 | 2240 | 558 |
| Emotional problems | Parent | 0.01 | 0.991 | 0.001 | 0.012 | 0.001 | 1.011 | 0.009 | 0.6 | 0.031 | 2496 | 621 |
| Emotional problems | Child | 0.01 | 0.991 | 0.001 | 0.007 | 0.000 | 1.017 | 0.010 | 1.0 | 0.026 | 2240 | 557 |
| Peer problems | Parent | 0.01 | 0.987 | 0.000 | 0.007 | 0.000 | 0.976 | 0.004 | 0.4 | 0.052 | 2495 | 622 |
| Peer problems | Child | 0.01 | 0.990 | 0.001 | 0.014 | 0.001 | 0.963 | 0.005 | 0.6 | 0.033 | 2240 | 557 |
| Note. CV= cross-validated; SD= standard deviation; R2= variance explained; RMSE= root mean square error; train= training set (80%); test= hold-out set (20%). | | | | | | | | | | | | |

Supplementary Table 8. SDQ scales (observed traits): univariate twin model fitting results.

| Trait | Rater | Univariate twin model fitting results | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | A | | | C | | | E | | |
| | | Est | Lower 95% CI | Upper 95% CI | Est | Lower 95% CI | Upper 95% CI | Est | Lower 95% CI | Upper 95% CI |
| Year 2 | | | | | | | | | | |
| Hyperactivity | Parent | 0.638 | 0.611 | 0.663 | 0.000 | 0.000 | 0.005 | 0.362 | 0.337 | 0.389 |
| Conduct problems | Parent | 0.510 | 0.452 | 0.568 | 0.198 | 0.147 | 0.247 | 0.292 | 0.274 | 0.312 |
| Emotional problems | Parent | 0.557 | 0.529 | 0.584 | 0.000 | 0.000 | 0.013 | 0.443 | 0.416 | 0.471 |
| Year 3 | | | | | | | | | | |
| Hyperactivity | Parent | 0.557 | 0.523 | 0.589 | 0.000 | 0.000 | 0.003 | 0.443 | 0.411 | 0.477 |
| Conduct problems | Parent | 0.505 | 0.448 | 0.562 | 0.218 | 0.168 | 0.266 | 0.278 | 0.260 | 0.297 |
| Emotional problems | Parent | 0.525 | 0.495 | 0.553 | 0.000 | 0.000 | 0.014 | 0.475 | 0.447 | 0.504 |
| Year 4 | | | | | | | | | | |
| Hyperactivity | Parent | 0.349 | 0.314 | 0.383 | 0.000 | 0.000 | 0.003 | 0.651 | 0.617 | 0.686 |
| Conduct problems | Parent | 0.622 | 0.561 | 0.662 | 0.020 | 0.000 | 0.070 | 0.358 | 0.338 | 0.379 |
| Emotional problems | Parent | 0.539 | 0.472 | 0.591 | 0.030 | 0.000 | 0.083 | 0.432 | 0.408 | 0.457 |
| Peer problems | Parent | 0.640 | 0.583 | 0.696 | 0.045 | 0.000 | 0.093 | 0.315 | 0.298 | 0.334 |
| Year 7 | | | | | | | | | | |
| Hyperactivity | Parent | 0.468 | 0.437 | 0.498 | 0.000 | 0.000 | 0.000 | 0.532 | 0.502 | 0.563 |
| Hyperactivity | Teacher | 0.527 | 0.495 | 0.553 | 0.000 | 0.000 | 0.020 | 0.473 | 0.447 | 0.500 |
| Conduct problems | Parent | 0.586 | 0.539 | 0.634 | 0.175 | 0.131 | 0.217 | 0.239 | 0.226 | 0.254 |
| Conduct problems | Teacher | 0.712 | 0.666 | 0.729 | 0.000 | 0.000 | 0.039 | 0.288 | 0.271 | 0.307 |
| Emotional problems | Parent | 0.465 | 0.404 | 0.525 | 0.149 | 0.099 | 0.199 | 0.386 | 0.365 | 0.408 |
| Emotional problems | Teacher | 0.713 | 0.693 | 0.732 | 0.000 | 0.000 | 0.008 | 0.287 | 0.268 | 0.307 |
| Peer problems | Parent | 0.660 | 0.601 | 0.689 | 0.011 | 0.000 | 0.060 | 0.330 | 0.311 | 0.349 |
| Peer problems | Teacher | 0.669 | 0.602 | 0.690 | 0.001 | 0.000 | 0.058 | 0.330 | 0.310 | 0.352 |
| Year 9 | | | | | | | | | | |
| Hyperactivity | Parent | 0.701 | 0.670 | 0.729 | 0.000 | 0.000 | 0.006 | 0.299 | 0.271 | 0.330 |
| Hyperactivity | Teacher | 0.609 | 0.569 | 0.644 | 0.000 | 0.000 | 0.023 | 0.391 | 0.356 | 0.429 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Hyperactivity | Child | 0.388 | 0.343 | 0.430 | 0.000 | 0.000 | 0.021 | 0.612 | 0.570 | 0.655 |
| Conduct problems | Parent | 0.536 | 0.472 | 0.601 | 0.257 | 0.195 | 0.315 | 0.207 | 0.190 | 0.226 |
| Conduct problems | Teacher | 0.571 | 0.504 | 0.607 | 0.000 | 0.000 | 0.049 | 0.429 | 0.393 | 0.469 |
| Conduct problems | Child | 0.442 | 0.329 | 0.517 | 0.034 | 0.000 | 0.121 | 0.523 | 0.483 | 0.567 |
| Emotional problems | Parent | 0.449 | 0.363 | 0.535 | 0.193 | 0.120 | 0.264 | 0.358 | 0.330 | 0.388 |
| Emotional problems | Teacher | 0.496 | 0.434 | 0.537 | 0.000 | 0.000 | 0.044 | 0.504 | 0.463 | 0.547 |
| Emotional problems | Child | 0.392 | 0.275 | 0.477 | 0.044 | 0.000 | 0.134 | 0.564 | 0.522 | 0.608 |
| Peer problems | Parent | 0.587 | 0.513 | 0.662 | 0.151 | 0.083 | 0.216 | 0.262 | 0.241 | 0.286 |
| Peer problems | Teacher | 0.511 | 0.397 | 0.598 | 0.049 | 0.000 | 0.139 | 0.440 | 0.402 | 0.483 |
| Peer problems | Child | 0.319 | 0.197 | 0.435 | 0.077 | 0.000 | 0.168 | 0.604 | 0.559 | 0.652 |
| Year 12 | | | | | | | | | | |
| Conduct problems | Teacher | 0.566 | 0.477 | 0.604 | 0.009 | 0.000 | 0.080 | 0.425 | 0.396 | 0.457 |
| Conduct problems | Child | 0.376 | 0.288 | 0.462 | 0.065 | 0.000 | 0.132 | 0.560 | 0.528 | 0.593 |
| Emotional problems | Parent | 0.512 | 0.443 | 0.582 | 0.109 | 0.050 | 0.167 | 0.378 | 0.355 | 0.403 |
| Emotional problems | Teacher | 0.448 | 0.405 | 0.482 | 0.000 | 0.000 | 0.027 | 0.552 | 0.518 | 0.587 |
| Emotional problems | Child | 0.350 | 0.260 | 0.439 | 0.065 | 0.000 | 0.133 | 0.585 | 0.552 | 0.620 |
| Peer problems | Parent | 0.686 | 0.629 | 0.743 | 0.076 | 0.023 | 0.127 | 0.238 | 0.223 | 0.254 |
| Peer problems | Teacher | 0.525 | 0.447 | 0.555 | 0.000 | 0.000 | 0.060 | 0.475 | 0.445 | 0.508 |
| Peer problems | Child | 0.356 | 0.263 | 0.417 | 0.026 | 0.000 | 0.097 | 0.617 | 0.583 | 0.654 |
| Year 16 | | | | | | | | | | |
| Hyperactivity | Parent | 0.763 | 0.744 | 0.780 | 0.000 | 0.000 | 0.010 | 0.237 | 0.220 | 0.256 |
| Hyperactivity | Child | 0.385 | 0.349 | 0.420 | 0.000 | 0.000 | 0.016 | 0.615 | 0.580 | 0.651 |
| Conduct problems | Parent | 0.630 | 0.569 | 0.692 | 0.118 | 0.062 | 0.172 | 0.252 | 0.235 | 0.270 |
| Conduct problems | Child | 0.350 | 0.307 | 0.385 | 0.000 | 0.000 | 0.025 | 0.650 | 0.615 | 0.685 |
| Emotional problems | Child | 0.388 | 0.341 | 0.421 | 0.000 | 0.000 | 0.000 | 0.612 | 0.579 | 0.646 |
| Peer problems | Child | 0.391 | 0.293 | 0.448 | 0.022 | 0.000 | 0.096 | 0.587 | 0.552 | 0.625 |
| Year 21 | | | | | | | | | | |
| Hyperactivity | Parent | 0.612 | 0.585 | 0.638 | 0.000 | 0.000 | 0.012 | 0.388 | 0.362 | 0.415 |
| Hyperactivity | Child | 0.342 | 0.245 | 0.381 | 0.000 | 0.000 | 0.000 | 0.658 | 0.619 | 0.699 |
| Conduct problems | Parent | 0.514 | 0.441 | 0.586 | 0.113 | 0.052 | 0.173 | 0.373 | 0.349 | 0.399 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Conduct problems | Child | 0.209 | 0.082 | 0.277 | 0.022 | 0.000 | 0.116 | 0.769 | 0.723 | 0.819 |
| Emotional problems | Parent | 0.566 | 0.523 | 0.592 | 0.000 | 0.000 | 0.000 | 0.434 | 0.408 | 0.461 |
| Emotional problems | Child | 0.309 | 0.192 | 0.381 | 0.030 | 0.000 | 0.118 | 0.661 | 0.619 | 0.706 |
| Peer problems | Parent | 0.722 | 0.659 | 0.754 | 0.015 | 0.000 | 0.072 | 0.263 | 0.246 | 0.282 |
| Peer problems | Child | 0.397 | 0.295 | 0.433 | 0.000 | 0.000 | 0.000 | 0.603 | 0.567 | 0.643 |
| Note. Est= estimate; A= genetic influences; C= shared environmental influences; E= unique environmental influences; CI= confidence interval. | | | | | | | | | | |

Supplementary Table 9. Weights for the individual polygenic scores from elastic net regularization.

| Composites | PGS weights for the multi-trait PGS | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | ADHD | AN | ASD | BPD | DS | INS | IRR | MDD | MS | NEU | OCD | PTSD | RT | SCZ | SWB |
| Cross-age | | | | | | | | | | | | | | | |
| BPp parent-rated | 0.069 | 0.000 | 0.000 | 0.000 | 0.000 | 0.002 | 0.000 | 0.015 | 0.013 | 0.023 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| BPp teacher-rated | 0.104 | -0.010 | 0.000 | 0.000 | 0.015 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.003 | 0.000 | 0.037 | 0.000 | 0.004 |
| BPp child-rated | 0.067 | -0.031 | -0.006 | -0.052 | 0.009 | 0.018 | -0.033 | 0.056 | 0.023 | 0.066 | 0.000 | 0.019 | 0.053 | 0.022 | -0.027 |
| Externalizing parent-rated | 0.104 | 0.000 | 0.000 | -0.016 | 0.000 | 0.015 | -0.015 | 0.011 | 0.049 | 0.000 | 0.000 | 0.000 | 0.014 | 0.000 | -0.018 |
| Externalizing teacher-rated | 0.128 | -0.008 | 0.000 | -0.006 | 0.021 | 0.000 | -0.005 | -0.001 | 0.000 | 0.000 | 0.021 | 0.000 | 0.050 | 0.000 | 0.028 |
| Externalizing child-rated | 0.072 | -0.028 | 0.000 | -0.027 | 0.000 | 0.022 | -0.034 | 0.018 | 0.068 | 0.015 | 0.000 | 0.003 | 0.079 | 0.014 | -0.048 |
| Internalizing parent-rated | 0.036 | 0.000 | 0.000 | -0.022 | 0.000 | 0.000 | -0.025 | 0.029 | 0.002 | 0.098 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Internalizing teacher-rated | 0.057 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.001 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Internalizing child-rated | 0.051 | -0.034 | 0.016 | -0.048 | 0.000 | 0.004 | -0.039 | 0.033 | 0.045 | 0.091 | 0.000 | 0.014 | 0.023 | 0.008 | -0.016 |
| Cross-rater | | | | | | | | | | | | | | | |
| BPp childhood | 0.094 | -0.003 | 0.017 | -0.021 | 0.000 | 0.000 | -0.031 | 0.011 | 0.020 | 0.024 | 0.019 | 0.000 | 0.000 | 0.000 | -0.010 |
| BPp adolescence | 0.061 | -0.018 | -0.003 | -0.009 | 0.000 | 0.022 | -0.015 | 0.032 | 0.038 | 0.059 | 0.000 | 0.011 | 0.052 | 0.000 | -0.008 |
| BPp adulthood | 0.060 | 0.000 | 0.000 | -0.021 | 0.000 | 0.018 | 0.000 | 0.059 | 0.053 | 0.000 | 0.000 | 0.000 | 0.023 | 0.033 | 0.000 |
| Externalizing childhood | 0.116 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.014 | 0.005 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Externalizing | 0.040 | -0.002 | 0.000 | 0.000 | 0.000 | 0.014 | 0.000 | 0.011 | 0.070 | 0.000 | 0.000 | 0.000 | 0.083 | 0.000 | 0.000 |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| adolescence | | | | | | | | | | | | | | | |
| Externalizing adulthood | 0.082 | 0.000 | 0.000 | -0.044 | 0.000 | 0.020 | 0.000 | 0.045 | 0.043 | 0.000 | 0.000 | 0.000 | 0.048 | 0.042 | -0.001 |
| Internalizing childhood | 0.031 | 0.000 | 0.007 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.056 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Internalizing adolescence | 0.036 | -0.036 | 0.018 | -0.012 | 0.000 | 0.014 | -0.041 | 0.040 | 0.000 | 0.123 | 0.000 | 0.027 | 0.021 | 0.000 | -0.008 |
| Internalizing adulthood | 0.027 | 0.000 | 0.021 | -0.007 | 0.000 | 0.001 | 0.000 | 0.041 | 0.043 | 0.015 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Cross-age-and-rater (cross-age approach) | | | | | | | | | | | | | | | |
| BPp | 0.097 | -0.025 | 0.027 | -0.043 | 0.011 | 0.000 | -0.026 | 0.038 | 0.048 | 0.047 | 0.015 | 0.003 | 0.029 | -0.001 | -0.001 |
| Externalizing | 0.129 | 0.000 | 0.000 | -0.047 | 0.000 | 0.010 | 0.000 | 0.017 | 0.044 | 0.000 | 0.001 | 0.000 | 0.046 | 0.000 | 0.000 |
| Internalizing | 0.066 | 0.000 | 0.000 | -0.015 | 0.000 | 0.002 | 0.000 | 0.026 | 0.011 | 0.074 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Single-trait cross-age | | | | | | | | | | | | | | | |
| Hyperactivity parent-rated | 0.104 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.007 | 0.000 | 0.000 |
| Hyperactivity teacher-rated | 0.138 | 0.000 | 0.005 | -0.017 | 0.000 | 0.000 | -0.012 | -0.020 | 0.000 | 0.000 | 0.005 | 0.019 | 0.051 | 0.000 | 0.015 |
| Hyperactivity child-rated | 0.071 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.004 | 0.000 | 0.000 | 0.000 | 0.000 | 0.033 | 0.000 | 0.000 |
| Conduct problems parent-rated | 0.107 | -0.024 | 0.016 | -0.017 | 0.007 | 0.010 | 0.000 | 0.037 | 0.037 | 0.000 | 0.000 | -0.022 | 0.017 | 0.023 | -0.024 |
| Conduct problems teacher-rated | 0.081 | 0.000 | 0.000 | 0.000 | 0.009 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | -0.006 | 0.054 | 0.000 | 0.000 |
| Conduct problems child-rated | 0.039 | 0.000 | -0.002 | 0.000 | 0.000 | 0.013 | 0.000 | 0.000 | 0.038 | 0.000 | 0.000 | 0.000 | 0.095 | 0.000 | -0.045 |
| Emotional problems | 0.009 | 0.000 | 0.000 | -0.004 | 0.000 | 0.000 | -0.026 | 0.024 | 0.028 | 0.077 | 0.000 | 0.002 | -0.016 | 0.000 | 0.000 |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| parent-rated | | | | | | | | | | | | | | | |
| Emotional problems teacher-rated | 0.006 | 0.000 | 0.000 | -0.010 | 0.000 | 0.000 | -0.039 | 0.013 | 0.033 | 0.052 | 0.005 | 0.000 | -0.024 | 0.017 | 0.000 |
| Emotional problems child-rated | 0.021 | -0.016 | 0.002 | -0.008 | 0.000 | -0.001 | -0.022 | 0.051 | 0.003 | 0.083 | 0.006 | 0.000 | 0.019 | 0.024 | -0.019 |
| Peer problems parent-rated | 0.013 | 0.000 | 0.033 | -0.001 | 0.000 | 0.000 | 0.000 | 0.016 | 0.000 | 0.025 | 0.000 | 0.002 | 0.000 | 0.000 | 0.000 |
| Peer problems teacher-rated | 0.010 | 0.000 | 0.023 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Peer problems child-rated | 0.032 | -0.010 | 0.007 | 0.000 | 0.000 | 0.000 | 0.000 | 0.010 | 0.020 | 0.031 | 0.000 | 0.000 | 0.000 | -0.041 | -0.007 |
| Single-trait cross-rater | | | | | | | | | | | | | | | |
| Hyperactivity childhood | 0.112 | -0.008 | -0.003 | -0.007 | 0.000 | 0.025 | -0.031 | 0.000 | 0.030 | 0.000 | 0.034 | 0.026 | 0.029 | -0.031 | 0.001 |
| Hyperactivity adolescence | 0.043 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.057 | 0.000 | 0.000 | 0.000 | 0.039 | 0.009 | 0.000 |
| Hyperactivity adulthood | 0.064 | 0.021 | 0.000 | -0.006 | -0.001 | 0.000 | 0.000 | 0.000 | 0.022 | 0.000 | 0.000 | 0.000 | 0.037 | 0.024 | 0.000 |
| Conduct problems childhood | 0.077 | 0.000 | 0.027 | 0.000 | 0.028 | 0.000 | 0.000 | 0.012 | 0.001 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Conduct problems adolescence | 0.060 | -0.003 | -0.017 | -0.021 | 0.008 | 0.012 | 0.000 | 0.021 | 0.042 | 0.015 | 0.000 | 0.000 | 0.077 | 0.014 | -0.025 |
| Conduct problems adulthood | 0.069 | 0.000 | 0.000 | 0.000 | 0.000 | 0.008 | 0.001 | 0.036 | 0.017 | 0.000 | 0.000 | 0.000 | 0.031 | 0.000 | 0.000 |
| Emotional problems | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.066 | 0.000 | 0.000 | -0.012 | 0.000 | 0.000 |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| childhood | | | | | | | | | | | | | | | |
| Emotional problems adolescence | 0.004 | -0.015 | 0.000 | 0.000 | 0.000 | 0.014 | -0.031 | 0.029 | 0.023 | 0.115 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Emotional problems adulthood | 0.000 | 0.000 | 0.001 | 0.000 | 0.000 | 0.000 | 0.000 | 0.073 | 0.014 | 0.060 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Peer problems childhood | 0.007 | 0.000 | 0.029 | -0.008 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.013 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| Peer problems adolescence | 0.031 | -0.017 | 0.017 | -0.002 | 0.000 | 0.000 | 0.000 | 0.008 | 0.000 | 0.023 | 0.000 | 0.004 | 0.000 | 0.000 | -0.001 |
| Peer problems adulthood | 0.031 | 0.000 | 0.000 | 0.000 | 0.006 | 0.020 | 0.000 | 0.023 | 0.039 | 0.000 | 0.000 | 0.000 | -0.039 | 0.000 | 0.000 |

Note. ADHD= attention deficit hyperactivity disorder; AN= anorexia Nervosa; ASD= autism spectrum disorder; BPD= bipolar disorder; DS= depressive symptoms; INS= insomnia; IRR= irritability; MDD= major depressive disorder; MS= mood swings; NEU= neuroticism; OCD= obsessive-compulsive disorder; PTSD= post-traumatic stress disorder; RT= risk taking; SCZ= schizophrenia; SWB= subjective wellbeing.

Supplementary Table 10. Behaviour problems composites: univariate twin model fitting results.

| Composites | Univariate twin model fitting results | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | A | | | C | | | E | | |
| | Est | Lower 95% CI | Upper 95% CI | Est | Lower 95% CI | Upper 95% CI | Est | Lower 95% CI | Upper 95% CI |
| Cross-age | | | | | | | | | |
| BPp parent-rated | 0.592 | 0.545 | 0.641 | 0.265 | 0.218 | 0.310 | 0.143 | 0.133 | 0.154 |
| BPp teacher-rated | 0.721 | 0.662 | 0.740 | 0.000 | 0.000 | 0.051 | 0.279 | 0.260 | 0.300 |
| BPp child-rated | 0.483 | 0.398 | 0.567 | 0.077 | 0.007 | 0.146 | 0.440 | 0.411 | 0.471 |
| Externalizing parent-rated | 0.825 | 0.807 | 0.837 | 0.000 | 0.000 | 0.014 | 0.175 | 0.163 | 0.189 |
| Externalizing teacher-rated | 0.736 | 0.708 | 0.754 | 0.000 | 0.000 | 0.021 | 0.264 | 0.246 | 0.284 |
| Externalizing child-rated | 0.531 | 0.442 | 0.565 | 0.005 | 0.000 | 0.077 | 0.464 | 0.435 | 0.496 |
| Internalizing parent-rated | 0.480 | 0.430 | 0.530 | 0.325 | 0.278 | 0.370 | 0.195 | 0.182 | 0.210 |
| Internalizing teacher-rated | 0.653 | 0.580 | 0.701 | 0.027 | 0.000 | 0.089 | 0.320 | 0.298 | 0.345 |
| Internalizing child-rated | 0.463 | 0.378 | 0.547 | 0.093 | 0.048 | 0.161 | 0.445 | 0.416 | 0.476 |
| Cross-rater | | | | | | | | | |
| BPp childhood | 0.654 | 0.601 | 0.708 | 0.173 | 0.121 | 0.223 | 0.173 | 0.161 | 0.186 |
| BPp adolescence | 0.543 | 0.474 | 0.612 | 0.145 | 0.130 | 0.204 | 0.312 | 0.290 | 0.335 |
| BPp adulthood | 0.515 | 0.431 | 0.599 | 0.106 | 0.034 | 0.175 | 0.379 | 0.352 | 0.409 |
| Externalizing childhood | 0.790 | 0.773 | 0.805 | 0.000 | 0.000 | 0.008 | 0.210 | 0.195 | 0.227 |
| Externalizing adolescence | 0.672 | 0.599 | 0.707 | 0.013 | 0.000 | 0.076 | 0.315 | 0.293 | 0.338 |
| Externalizing adulthood | 0.565 | 0.480 | 0.643 | 0.054 | 0.000 | 0.125 | 0.381 | 0.353 | 0.411 |
| Internalizing childhood | 0.514 | 0.459 | 0.570 | 0.259 | 0.208 | 0.309 | 0.227 | 0.211 | 0.244 |
| Internalizing adolescence | 0.511 | 0.438 | 0.584 | 0.142 | 0.079 | 0.203 | 0.347 | 0.324 | 0.373 |
| Internalizing adulthood | 0.502 | 0.414 | 0.589 | 0.092 | 0.018 | 0.164 | 0.406 | 0.377 | 0.438 |
| Cross-trait-and-rater (cross-age approach) * | | | | | | | | | |
| BPp | 0.622 | 0.675 | 0.729 | 0.108 | 0.160 | 0.210 | 0.154 | 0.165 | 0.178 |
| Externalizing | 0.805 | 0.831 | 0.842 | 0.000 | 0.000 | 0.023 | 0.158 | 0.169 | 0.182 |
| Internalizing | 0.505 | 0.558 | 0.613 | 0.189 | 0.240 | 0.289 | 0.188 | 0.202 | 0.217 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Cross-trait-and-rater (cross-rater approach) ** | | | | | | | | | |
| BPp | 0.574 | 0.628 | 0.684 | 0.131 | 0.184 | 0.234 | 0.175 | 0.188 | 0.202 |
| Externalizing | 0.789 | 0.803 | 0.817 | 0.000 | 0.000 | 0.051 | 0.183 | 0.197 | 0.211 |
| Internalizing | 0.487 | 0.543 | 0.599 | 0.183 | 0.236 | 0.286 | 0.206 | 0.222 | 0.238 |
| Single-trait cross-age | | | | | | | | | |
| Hyperactivity parent-rated | 0.646 | 0.613 | 0.676 | 0.000 | 0.000 | 0.003 | 0.354 | 0.324 | 0.387 |
| Hyperactivity teacher-rated | 0.712 | 0.688 | 0.734 | 0.000 | 0.000 | 0.010 | 0.288 | 0.266 | 0.312 |
| Hyperactivity child-rated | 0.429 | 0.391 | 0.465 | 0.000 | 0.000 | 0.017 | 0.571 | 0.535 | 0.609 |
| Conduct problems parent-rated | 0.617 | 0.565 | 0.670 | 0.206 | 0.156 | 0.255 | 0.177 | 0.165 | 0.190 |
| Conduct problems teacher-rated | 0.654 | 0.609 | 0.677 | 0.000 | 0.000 | 0.036 | 0.346 | 0.323 | 0.370 |
| Conduct problems child-rated | 0.425 | 0.357 | 0.458 | 0.000 | 0.000 | 0.051 | 0.575 | 0.542 | 0.609 |
| Emotional problems parent-rated | 0.554 | 0.492 | 0.618 | 0.173 | 0.116 | 0.228 | 0.272 | 0.254 | 0.292 |
| Emotional problems teacher-rated | 0.550 | 0.520 | 0.578 | 0.000 | 0.000 | 0.022 | 0.450 | 0.422 | 0.480 |
| Emotional problems child-rated | 0.462 | 0.373 | 0.492 | 0.000 | 0.000 | 0.069 | 0.538 | 0.508 | 0.570 |
| Peer problems parent-rated | 0.694 | 0.636 | 0.754 | 0.094 | 0.039 | 0.147 | 0.212 | 0.197 | 0.228 |
| Peer problems teacher-rated | 0.592 | 0.514 | 0.656 | 0.040 | 0.000 | 0.104 | 0.368 | 0.342 | 0.395 |
| Peer problems child-rated | 0.466 | 0.376 | 0.540 | 0.043 | 0.000 | 0.114 | 0.490 | 0.459 | 0.524 |
| Single-trait cross-rater | | | | | | | | | |
| Hyperactivity childhood | 0.614 | 0.578 | 0.647 | 0.000 | 0.000 | 0.003 | 0.386 | 0.353 | 0.422 |
| Hyperactivity adolescence | 0.736 | 0.712 | 0.757 | 0.000 | 0.000 | 0.010 | 0.264 | 0.243 | 0.288 |
| Hyperactivity adulthood | 0.600 | 0.569 | 0.629 | 0.000 | 0.000 | 0.014 | 0.400 | 0.371 | 0.431 |
| Conduct problems childhood | 0.631 | 0.576 | 0.687 | 0.174 | 0.122 | 0.225 | 0.195 | 0.181 | 0.210 |
| Conduct problems adolescence | 0.578 | 0.496 | 0.625 | 0.021 | 0.000 | 0.088 | 0.401 | 0.375 | 0.430 |
| Conduct problems adulthood | 0.502 | 0.421 | 0.582 | 0.131 | 0.063 | 0.197 | 0.367 | 0.341 | 0.396 |
| Emotional problems childhood | 0.598 | 0.531 | 0.667 | 0.100 | 0.040 | 0.158 | 0.302 | 0.281 | 0.324 |
| Emotional problems adolescence | 0.495 | 0.403 | 0.538 | 0.012 | 0.000 | 0.084 | 0.493 | 0.462 | 0.527 |
| Emotional problems adulthood | 0.555 | 0.523 | 0.585 | 0.000 | 0.000 | 0.031 | 0.445 | 0.415 | 0.477 |
| Peer problems childhood | 0.704 | 0.640 | 0.759 | 0.040 | 0.000 | 0.097 | 0.256 | 0.238 | 0.275 |
| Peer problems adolescence | 0.561 | 0.487 | 0.635 | 0.093 | 0.029 | 0.154 | 0.346 | 0.323 | 0.372 |
| Peer problems adulthood | 0.702 | 0.648 | 0.724 | 0.000 | 0.000 | 0.047 | 0.298 | 0.276 | 0.320 |

Note. Est= estimate; A= genetic influences; C= shared environmental influences; E= unique environmental influences; CI= confidence interval;* cross-age approach: combined individual behaviour problems at all ages (2-21) for parent, teacher and child ratings to create the first order factors of cross-age externalizing and internalizing, which were then combined across raters to create the second-order factors of cross-age-and-rater externalizing and internalizing; ** cross-rater approach: combined individual behaviour problems in adolescence and adulthood to create the first order factors of cross-rater externalizing and internalizing, which were then combined across developmental stages to create the second-order factors of cross-age-and-rater externalizing and internalizing.

Supplementary Table 11. Behaviour problems composites: univariate twin model fitting results, for males and females separately.

| Composites | Univariate twin model fitting results: males only | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | A | | | C | | | E | | |
| | Est | Lower 95% CI | Upper 95% CI | Est | Lower 95% CI | Upper 95% CI | Est | Lower 95% CI | Upper 95% CI |
| Cross-age | | | | | | | | | |
| BPp parent-rated | 0.574 | 0.505 | 0.647 | 0.277 | 0.207 | 0.342 | 0.149 | 0.134 | 0.167 |
| BPp teacher-rated | 0.714 | 0.615 | 0.765 | 0.024 | 0.000 | 0.112 | 0.262 | 0.235 | 0.293 |
| BPp child-rated | 0.508 | 0.377 | 0.596 | 0.043 | 0.000 | 0.144 | 0.449 | 0.404 | 0.499 |
| Externalizing parent-rated | 0.828 | 0.793 | 0.846 | 0.000 | 0.000 | 0.031 | 0.172 | 0.154 | 0.193 |
| Externalizing teacher-rated | 0.748 | 0.672 | 0.774 | 0.000 | 0.000 | 0.067 | 0.252 | 0.226 | 0.281 |
| Externalizing child-rated | 0.521 | 0.404 | 0.565 | 0.000 | 0.000 | 0.088 | 0.479 | 0.435 | 0.526 |
| Internalizing parent-rated | 0.446 | 0.372 | 0.522 | 0.347 | 0.277 | 0.412 | 0.207 | 0.186 | 0.232 |
| Internalizing teacher-rated | 0.671 | 0.566 | 0.733 | 0.032 | 0.000 | 0.122 | 0.297 | 0.266 | 0.331 |
| Internalizing child-rated | 0.497 | 0.366 | 0.597 | 0.056 | 0.000 | 0.157 | 0.447 | 0.402 | 0.497 |
| Cross-rater | | | | | | | | | |
| BPp childhood | 0.591 | 0.514 | 0.671 | 0.227 | 0.151 | 0.298 | 0.182 | 0.163 | 0.204 |
| BPp adolescence | 0.559 | 0.458 | 0.661 | 0.141 | 0.054 | 0.226 | 0.300 | 0.269 | 0.335 |
| BPp adulthood | 0.529 | 0.392 | 0.642 | 0.069 | 0.000 | 0.176 | 0.401 | 0.355 | 0.455 |
| Externalizing childhood | 0.788 | 0.762 | 0.810 | 0.000 | 0.000 | 0.023 | 0.212 | 0.190 | 0.238 |
| Externalizing adolescence | 0.658 | 0.553 | 0.731 | 0.043 | 0.000 | 0.132 | 0.299 | 0.268 | 0.334 |
| Externalizing adulthood | 0.563 | 0.423 | 0.637 | 0.027 | 0.000 | 0.136 | 0.410 | 0.363 | 0.464 |
| Internalizing childhood | 0.447 | 0.365 | 0.530 | 0.313 | 0.239 | 0.383 | 0.240 | 0.215 | 0.268 |
| Internalizing adolescence | 0.525 | 0.415 | 0.634 | 0.130 | 0.037 | 0.220 | 0.345 | 0.310 | 0.385 |
| Internalizing adulthood | 0.526 | 0.386 | 0.633 | 0.061 | 0.000 | 0.169 | 0.413 | 0.366 | 0.468 |
| Composites | Univariate twin model fitting results: females only | | | | | | | | |
| | A | | | C | | | E | | |
| | Est | Lower 95% CI | Upper 95% CI | Esti | Lower 95% CI | Upper 95% CI | Est | Lower 95% CI | Upper 95% CI |
| Cross-age | | | | | | | | | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| BPp parent-rated | 0.607 | 0.544 | 0.673 | 0.255 | 0.190 | 0.316 | 0.138 | 0.126 | 0.152 |
| BPp teacher-rated | 0.693 | 0.631 | 0.721 | 0.000 | 0.000 | 0.052 | 0.307 | 0.279 | 0.338 |
| BPp child-rated | 0.464 | 0.352 | 0.577 | 0.103 | 0.008 | 0.195 | 0.433 | 0.396 | 0.472 |
| Externalizing parent-rated | 0.821 | 0.795 | 0.838 | 0.000 | 0.000 | 0.022 | 0.179 | 0.162 | 0.198 |
| Externalizing teacher-rated | 0.711 | 0.681 | 0.739 | 0.000 | 0.000 | 0.025 | 0.289 | 0.261 | 0.319 |
| Externalizing child-rated | 0.521 | 0.404 | 0.583 | 0.024 | 0.000 | 0.119 | 0.455 | 0.417 | 0.497 |
| Internalizing parent-rated | 0.506 | 0.439 | 0.575 | 0.307 | 0.242 | 0.369 | 0.187 | 0.170 | 0.206 |
| Internalizing teacher-rated | 0.628 | 0.525 | 0.684 | 0.024 | 0.000 | 0.111 | 0.348 | 0.316 | 0.383 |
| Internalizing child-rated | 0.440 | 0.327 | 0.553 | 0.119 | 0.023 | 0.211 | 0.441 | 0.405 | 0.481 |
| Cross-rater | | | | | | | | | |
| BPp childhood | 0.708 | 0.635 | 0.784 | 0.125 | 0.084 | 0.194 | 0.167 | 0.152 | 0.184 |
| BPp adolescence | 0.533 | 0.439 | 0.628 | 0.147 | 0.062 | 0.227 | 0.321 | 0.292 | 0.352 |
| BPp adulthood | 0.498 | 0.390 | 0.606 | 0.137 | 0.042 | 0.227 | 0.366 | 0.332 | 0.402 |
| Externalizing childhood | 0.789 | 0.766 | 0.810 | 0.000 | 0.000 | 0.012 | 0.211 | 0.190 | 0.234 |
| Externalizing adolescence | 0.672 | 0.589 | 0.701 | 0.000 | 0.000 | 0.072 | 0.328 | 0.299 | 0.359 |
| Externalizing adulthood | 0.556 | 0.447 | 0.661 | 0.080 | 0.000 | 0.172 | 0.364 | 0.331 | 0.401 |
| Internalizing childhood | 0.569 | 0.494 | 0.647 | 0.213 | 0.140 | 0.281 | 0.218 | 0.198 | 0.240 |
| Internalizing adolescence | 0.500 | 0.402 | 0.599 | 0.152 | 0.065 | 0.234 | 0.349 | 0.318 | 0.383 |
| Internalizing adulthood | 0.486 | 0.372 | 0.600 | 0.114 | 0.015 | 0.209 | 0.400 | 0.365 | 0.439 |

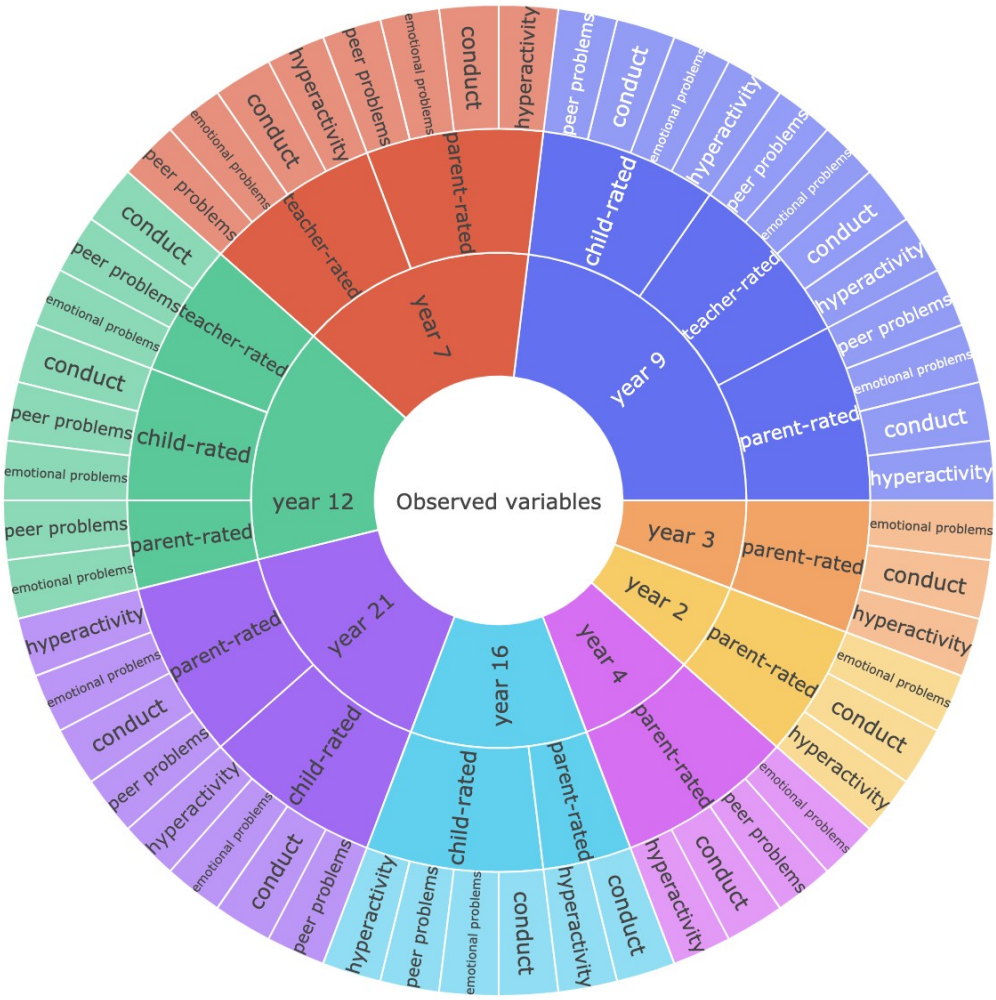
Note. Est= estimate; A= genetic influences; C= shared environmental influences; E= unique environmental influences; CI= confidence interval; * cross-age approach: combined individual behaviour problems at all ages (2-21) for parent, teacher and child ratings to create the first order factors of cross-age externalizing and internalizing, which were then combined across raters to create the second-order factors of cross-age-and-rater externalizing and internalizing; ** cross-rater approach: combined individual behaviour problems in adolescence and adulthood to create the first order factors of cross-rater externalizing and internalizing, which were then combined across developmental stages to create the second-order factors of cross-age-and-rater externalizing and internalizing.

Supplementary Table 12. Cross-age and cross-rater behaviour problems composites: bivariate twin model fitting results.

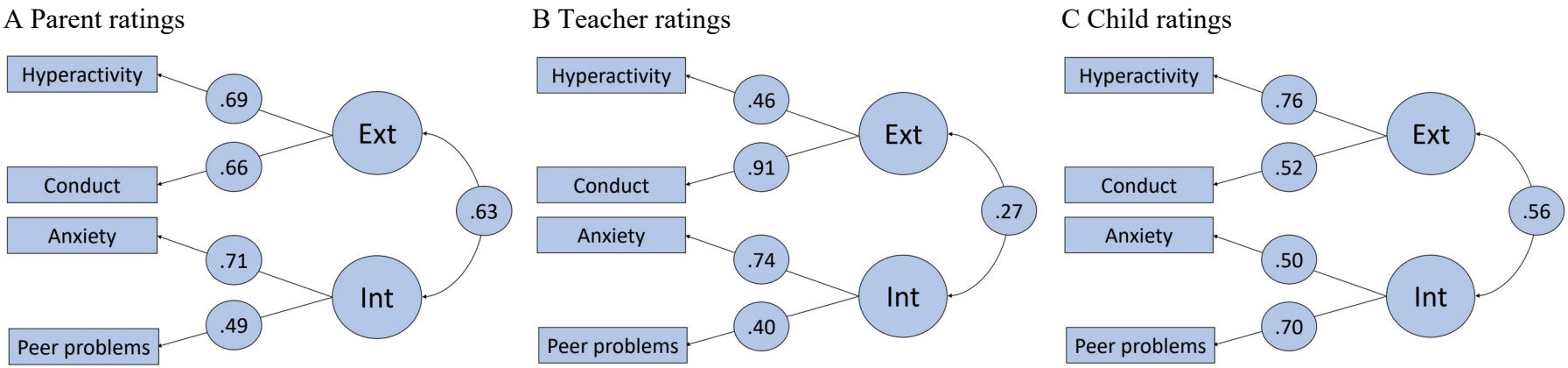
| Composite 1 | Composite 2 | Bivariate twin model fitting results | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | bivA | | | bivC | | | bivE | | |
| | | Est | Lower 95% CI | Upper 95% CI | Est | Lower 95% CI | Upper 95% CI | Est | Lower 95% CI | Upper 95% CI |
| Cross-age | Cross-rater | | | | | | | | | |
| BPp parent-rated | BPp childhood | 0.943 | 0.933 | 0.952 | 0.992 | 0.966 | 1.000 | 0.836 | 0.821 | 0.849 |
| BPp parent-rated | BPp adolescence | 0.717 | 0.669 | 0.765 | 0.840 | 0.840 | 0.996 | 0.379 | 0.338 | 0.418 |
| BPp parent-rated | BPp adulthood | 0.664 | 0.602 | 0.727 | 0.880 | 0.675 | 1.000 | 0.337 | 0.292 | 0.381 |
| BPp teacher-rated | BPp childhood | 0.662 | 0.620 | 0.702 | -1.000 | -1.000 | 1.000 | 0.448 | 0.409 | 0.485 |
| BPp teacher-rated | BPp adolescence | 0.500 | 0.438 | 0.565 | 1.000 | 0.994 | 1.000 | 0.225 | 0.179 | 0.270 |
| BPp teacher-rated | BPp adulthood | 0.408 | 0.329 | 0.498 | 0.999 | -1.000 | NA | 0.039 | -0.012 | 0.091 |
| BPp child-rated | BPp childhood | 0.504 | 0.425 | 0.584 | 0.682 | 0.341 | 1.000 | 0.110 | 0.064 | 0.156 |
| BPp child-rated | BPp adolescence | 0.860 | 0.823 | 0.896 | 0.951 | 0.784 | 1.000 | 0.744 | 0.723 | 0.764 |
| BPp child-rated | BPp adulthood | 0.715 | 0.664 | 0.760 | 1.000 | 0.777 | 1.000 | 0.644 | 0.616 | 0.671 |
| Externalizing parent-rated | Externalizing childhood | 0.960 | 0.955 | 0.965 | 1.000 | 0.943 | 1.000 | 0.900 | 0.890 | 0.908 |
| Externalizing parent-rated | Externalizing adolescence | 0.722 | 0.700 | 0.748 | 1.000 | -1.000 | 1.000 | 0.292 | 0.250 | 0.333 |
| Externalizing parent-rated | Externalizing adulthood | 0.683 | 0.651 | 0.725 | 1.000 | 0.909 | 1.000 | 0.277 | 0.232 | 0.322 |
| Externalizing teacher-rated | Externalizing childhood | 0.621 | 0.586 | 0.657 | -1.000 | -1.000 | 1.000 | 0.430 | 0.390 | 0.469 |
| Externalizing teacher-rated | Externalizing adolescence | 0.447 | 0.407 | 0.493 | 1.000 | -1.000 | 1.000 | 0.169 | 0.123 | 0.214 |
| Externalizing teacher-rated | Externalizing adulthood | 0.399 | 0.337 | 0.467 | 0.371 | -1.000 | 1.000 | 0.038 | -0.013 | 0.088 |
| Externalizing child-rated | Externalizing childhood | 0.515 | 0.480 | 0.564 | 1.000 | -1.000 | 1.000 | 0.091 | 0.046 | 0.135 |
| Externalizing child-rated | Externalizing adolescence | 0.866 | 0.835 | 0.898 | -0.994 | -1.000 | 1.000 | 0.751 | 0.731 | 0.771 |
| Externalizing child-rated | Externalizing adulthood | 0.719 | 0.667 | 0.772 | 1.000 | -1.000 | 1.000 | 0.624 | 0.594 | 0.652 |
| Internalizing parent-rated | Internalizing childhood | 0.902 | 0.886 | 0.919 | 0.996 | 0.973 | 1.000 | 0.811 | 0.795 | 0.827 |
| Internalizing parent-rated | Internalizing adolescence | 0.704 | 0.644 | 0.761 | 0.836 | 0.716 | 0.998 | 0.424 | 0.385 | 0.462 |
| Internalizing parent-rated | Internalizing adulthood | 0.624 | 0.554 | 0.700 | 0.980 | 0.754 | 1.000 | 0.339 | 0.293 | 0.383 |
| Internalizing teacher-rated | Internalizing childhood | 0.575 | 0.513 | 0.633 | 0.595 | 0.174 | 1.000 | 0.408 | 0.368 | 0.447 |
| Internalizing teacher-rated | Internalizing adolescence | 0.539 | 0.465 | 0.615 | 0.865 | 0.581 | 1.000 | 0.280 | 0.236 | 0.324 |
| Internalizing teacher-rated | Internalizing adulthood | 0.393 | 0.303 | 0.499 | 0.703 | -1.000 | 1.000 | 0.049 | -0.002 | 0.100 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Internalizing child-rated | Internalizing childhood | 0.473 | 0.380 | 0.568 | 0.685 | 0.430 | 1.000 | 0.127 | 0.081 | 0.172 |
| Internalizing child-rated | Internalizing adolescence | 0.835 | 0.794 | 0.878 | 0.964 | 0.802 | 1.000 | 0.714 | 0.690 | 0.735 |
| Internalizing child-rated | Internalizing adulthood | 0.737 | 0.685 | 0.786 | 1.000 | 0.916 | 1.000 | 0.646 | 0.619 | 0.672 |
| Note. Est= estimate; bivA= genetic correlation; bivC= shared environmental correlation; bivE= unique environmental correlation; CI= confidence interval. | | | | | | | | | | |

# Supplementary Figures



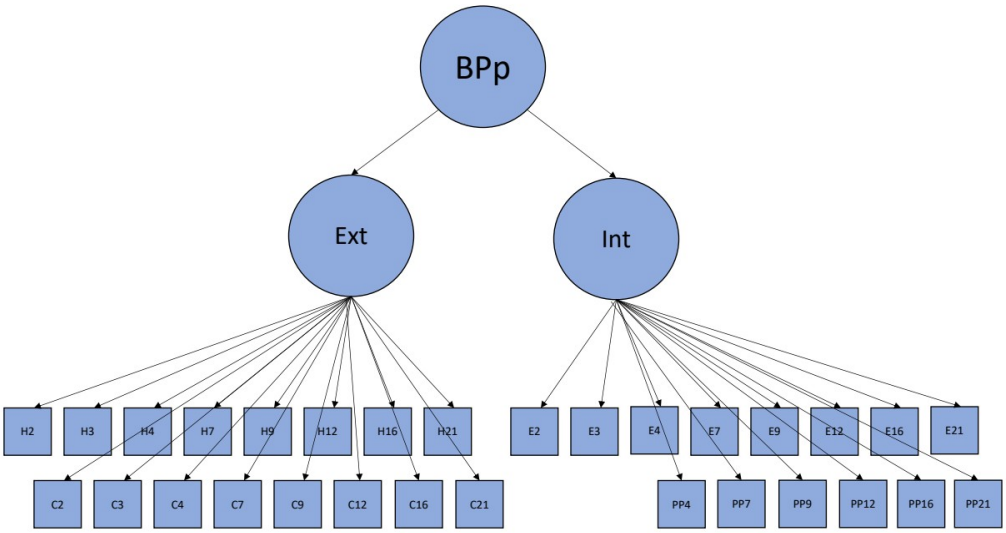

Supplementary Figure 1. The sunburst plot showing the observed variables at each age.



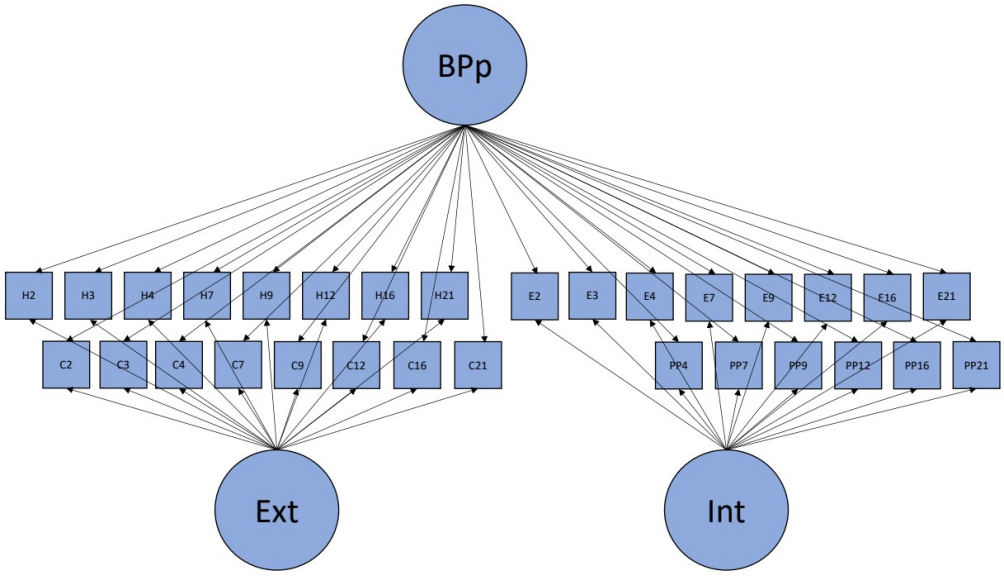

Supplementary Figure 2. Exploratory factor analyses for parent, teacher and child-rated data.

Note. Ext= Externalizing behaviour problems factor; Int= Internalizing behaviour problems factor.

A Hierarchical cross-age model

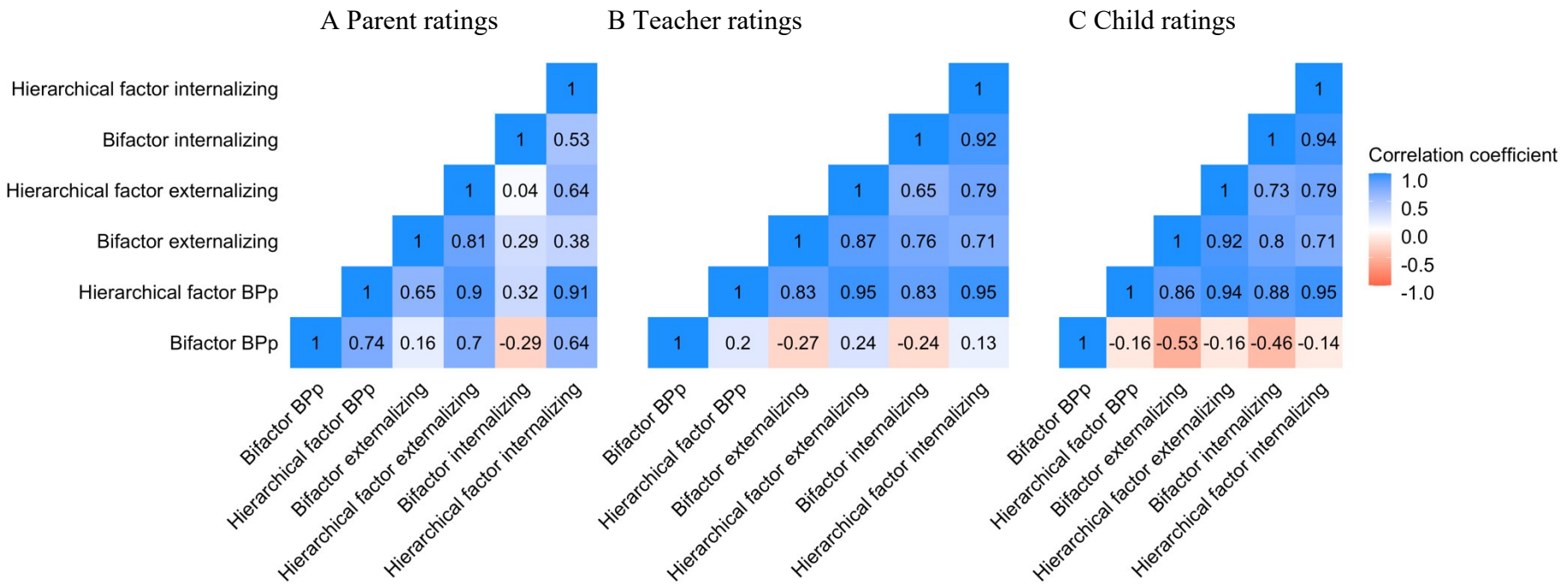



B Bifactor cross-age model

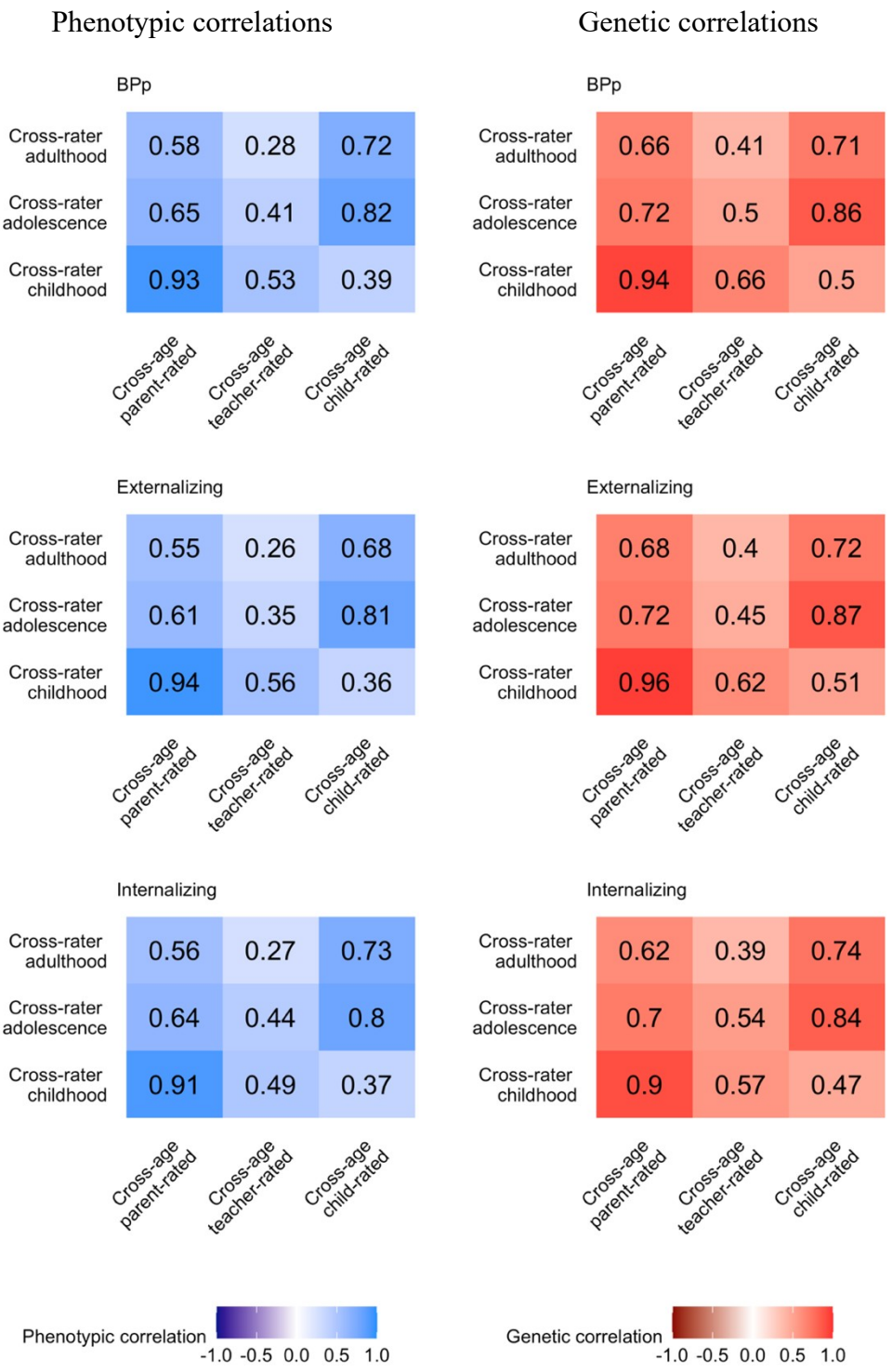



Supplementary Figure 3. Hierarchical and bifactor cross-age model of BPp, externalizing and internalizing.

Note. We ran three separate hierarchical and bifactor cross-age models: one for parent-report, one for teacher-report and one for self-report (child). H= hyperactivity; C= conduct problems; E= emotional problems; PP= peer problems; numbers indicate age of measurement.

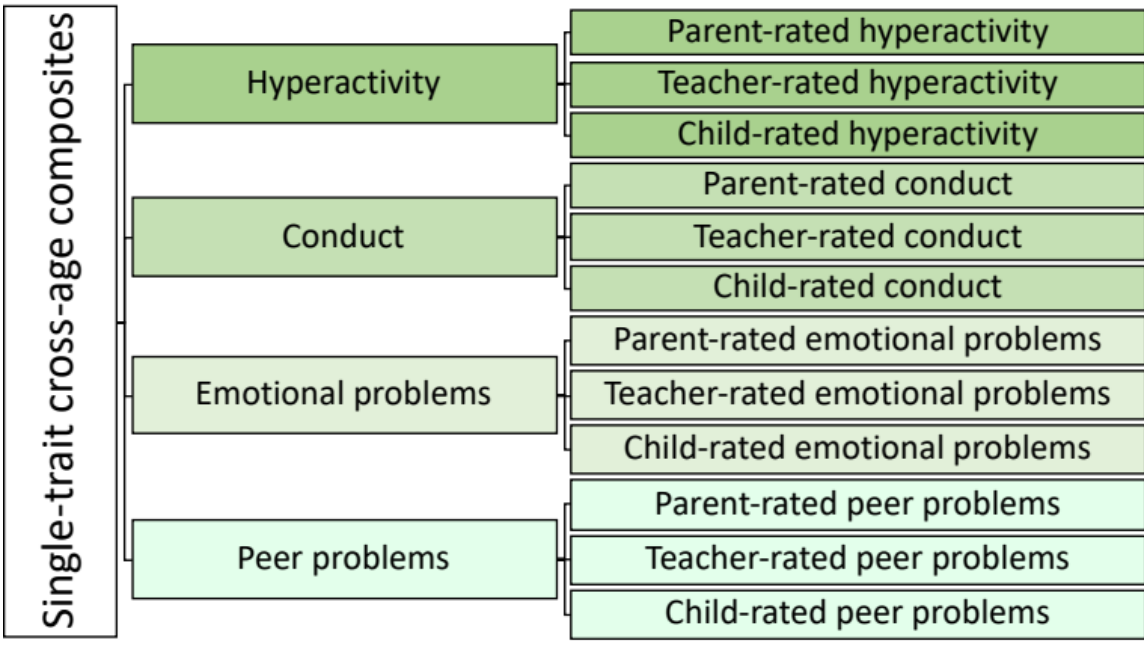



Supplementary Figure 4. Correlations between hierarchical and bifactor composites of BPp, externalizing and internalizing for parent, teacher and child ratings.

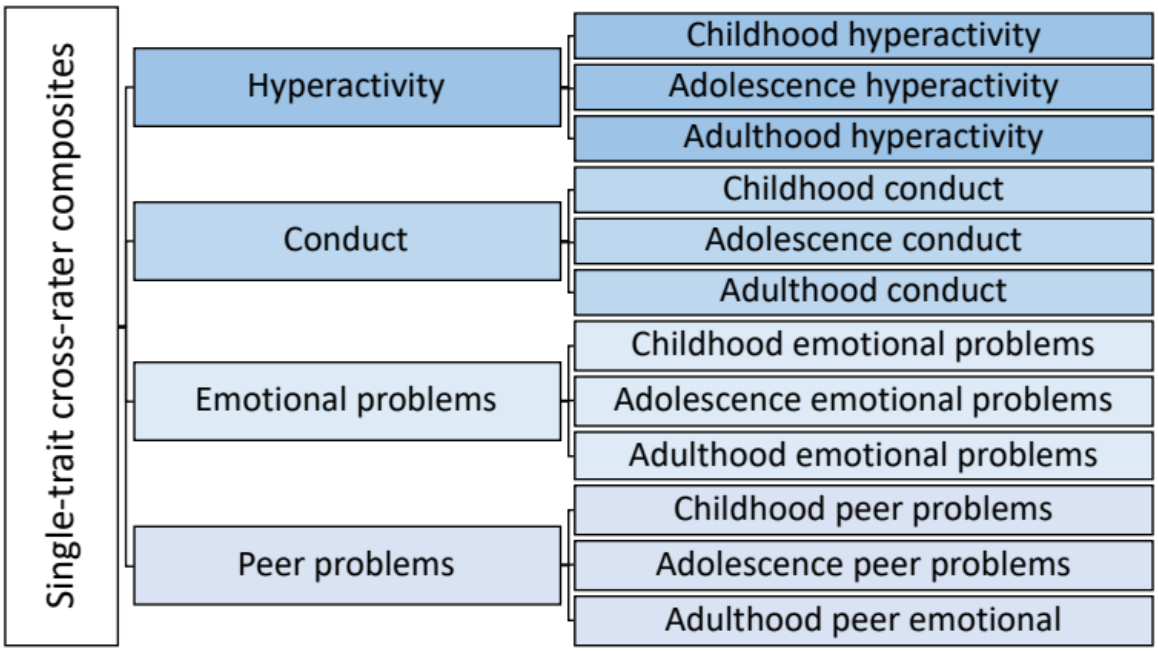



Supplementary Figure 5. Phenotypic and genetic correlations between cross-age and cross-rater composites of BPp, externalizing and internalizing.

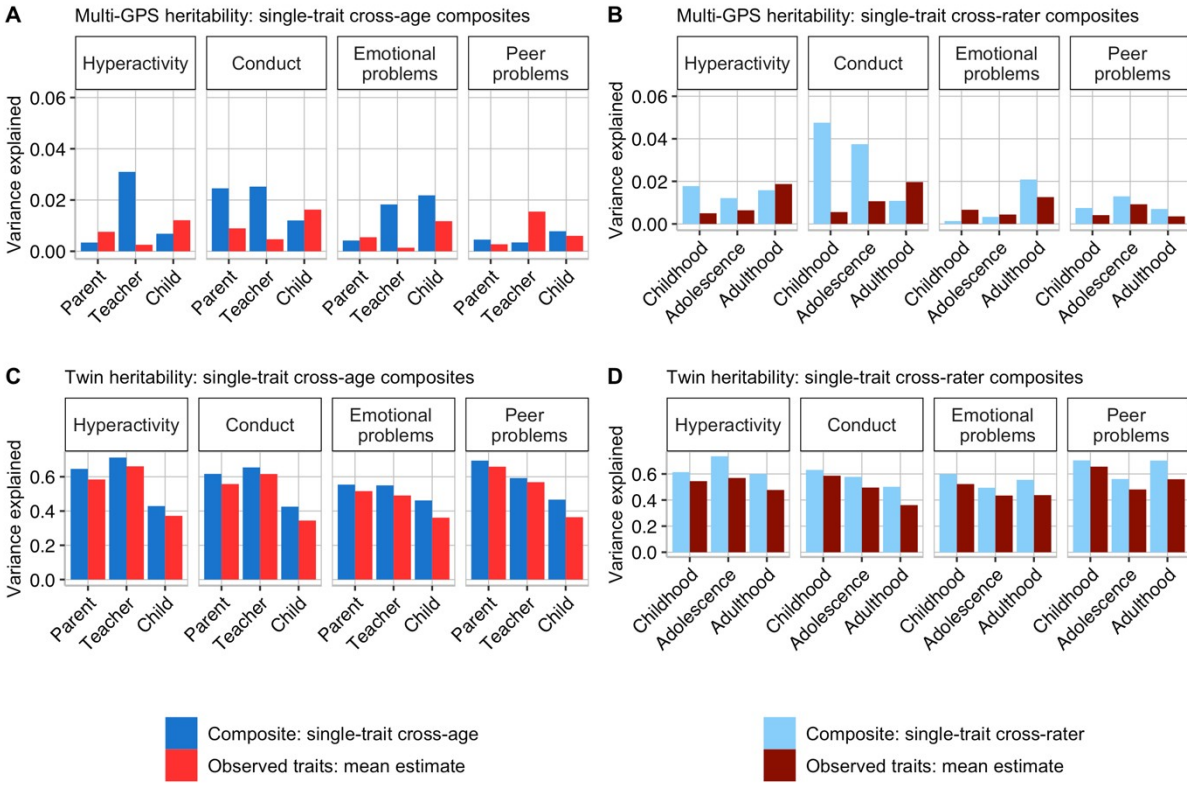
A Single-trait cross-age composites.



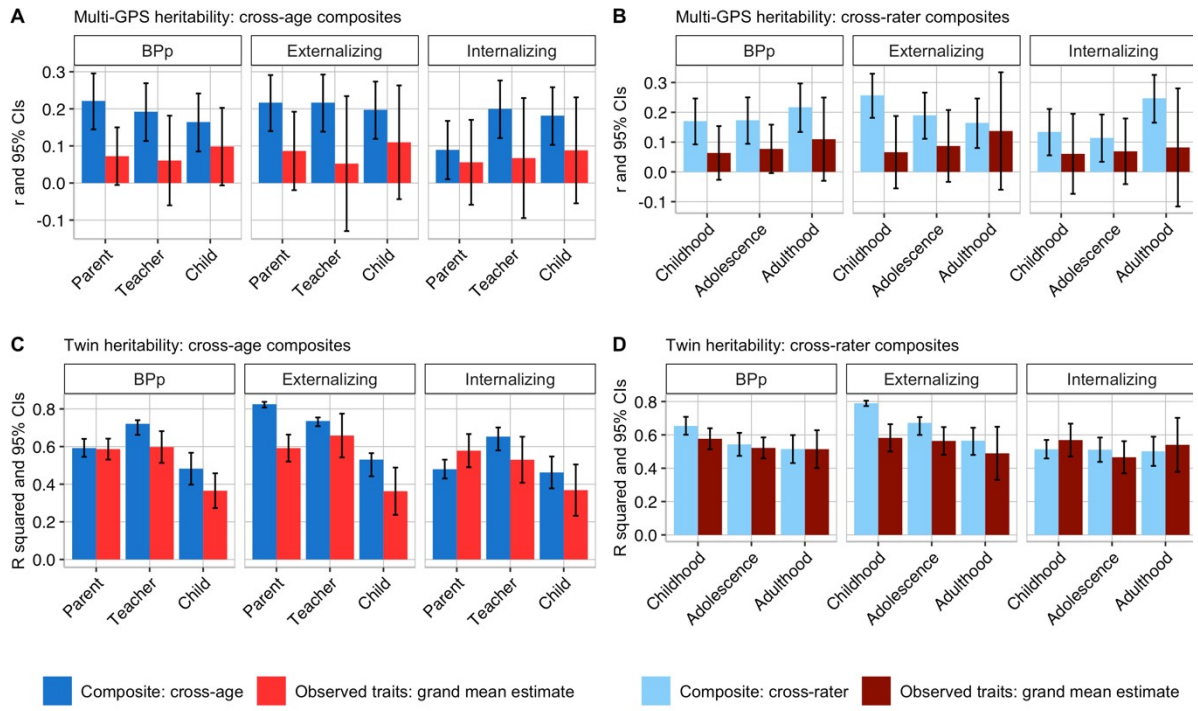

B Single-trait cross-rater composites.




Supplementary Figure 6. Summary of the construction of the single-trait cross-age and single-trait cross-rater composites.




Supplementary Figure 7. Multi-PGS and twin heritability results for single-trait cross-age composites and single-trait cross-rater composites as compared to the mean multi-PGS and twin heritability of observed traits.




Supplementary Figure 8. Multi-GPS correlation and twin heritability results for cross-age composites and cross-rater composites as compared to the grand mean multi-GPS correlation and twin heritability of observed traits.

Note. R squared= variance explained; r= correlation coefficient; 95% CIs= confidence intervals.

# Appendix 3

## Supplementary Notes

Supplementary Note 1: Statement of hypotheses pre-registered with the Open Science Framework.

The following hypotheses were pre-registered with the Open Science Framework (OSF; https://osf.io/rbv9q). Here, we address each hypothesis according to obtained results.

Hypothesis 1: In univariate twin analyses of behaviour problems, nonshared environment (NSE) accounts for more variance in behaviour problems than nurture (shared environment) and nature (genetics) combined.
Hypothesis 1 was only supported for self-ratings of behaviour problem symptoms across ages (average NSE influence of 59%), but not parent or teacher ratings (37% and 40%, respectively)

Hypothesis 2: In bivariate twin analyses between environmental measures and behaviour problems, NSE-mediated links cumulatively account for significant but modest (<5%) total variance in behaviour problems.
Hypothesis 2 was supported. On average across childhood, adolescence and adulthood, NSE-mediated links accounted for 1% of the total variance in parent-rated behaviour problem symptoms, 0.2% in teacher-rated behaviour problem symptoms and 0.5% in self-rated behaviour problem symptoms.

Hypothesis 3: In bivariate twin analyses between environmental measures and behaviour problems, links mediated by shared environment cumulatively account for significant but modest (<5%) total variance in behaviour problems.
Hypothesis 3 was supported. On average across childhood, adolescence and adulthood, links mediated by shared environment accounted for 2% of the total variance in parent-rated behaviour problem symptoms, 0.4% in teacher-rated behaviour problem symptoms and 0.9% in self-rated behaviour problem symptoms.

Hypothesis 4: Most of the association between environmental measures and behaviour problems is mediated genetically.

Hypothesis 4 was supported. On average across childhood, adolescence and adulthood, links mediated by shared environment accounted for 11.9% of the total variance in parent-rated behaviour problem symptoms, 5.1% in teacher-rated behaviour problem symptoms and 5.3% in self-rated behaviour problem symptoms.

Hypothesis 5: The MZ differences design yields comparable results about the E-mediated links between environmental measures and behavioural problems, although the MZ differences design does not assess the extent to which the total variance of behavioural problems is explained by E-related processes.
Hypothesis 5 was supported. On average, poly-E MZ difference scores predicted 3.2% of the variance in parent-rated, 0.4% in teacher-rated and 0.9% In self-rated MZ differences in symptoms of childhood behaviour problems. Our Cholesky analyses estimated that on average across childhood, adolescence and adulthood, parent-rated NSE measures accounted for 3.4% of the reliable NSE variance in parent-rated behaviour problem symptoms, 0.3% in teacher-rated behaviour problem symptoms and 0.9% in self-rated behaviour problem symptoms.

For each of these hypotheses, we predict:

a) Results are stronger when the same person (parent, teacher, child) rates the environment and behaviour problems as compared to cross-rater analyses.
b) Results are similar for males and females.

We have no hypotheses about:

a) Differential results for specific behaviour problems (emotional problems hyperactivity/attention problems, conduct problems and peer problems).
b) Developmental trends across the three ages.

Supplementary Note 2: Description of the TEDS sample.

Our sampling frame consisted of up to 4039 pairs of twins born in England and Wales between 1994 and 1996 who have been enrolled in the Twins Early Development Study (TEDS) (Rimfeld, Malanchini, Spargo, et al., 2019). The TEDS twins have been assessed a dozen times from infancy through early adulthood on a wide range of behavioural, psychological, cognitive, physical and environmental measures (Rimfeld et al., 2019). Data collection procedures included questionnaires administered by post, by telephone and online, as described in an overview of TEDS (Rimfeld, Malanchini, Spargo, et al., 2019). Details can be found in the TEDS data dictionary: https://www.teds.ac.uk/datadictionary/home.htm).

The sample of TEDS twins is representative of the UK population in terms of ethnicity and socioeconomic status (SES) (Supplementary Table 1); for details of representativeness and attrition, see Rimfeld et al. (2019). Individuals with severe medical conditions were excluded from analyses. These conditions include detrimental prenatal and postnatal conditions, as well as other conditions that could seriously impact later development. In addition, twins with uncertain and unknown zygosity were excluded from the analyses. Zygosity was recorded using a parent questionnaire of physical similarity between twins, with 95% accuracy when ascertained by DNA tests (Price et al., 2000).

Supplementary Note 3: Selection of environmental measures.

In order to create composite environmental measures in preschool, childhood and adolescence, we reduced the number of environmental items from several hundred to fewer than one hundred using two criteria. Our first criterion was a moderate phenotypic correlation between environmental measures and behaviour problem symptoms. We correlated environmental measures in preschool with symptoms of each of the four behaviour problems in childhood, environmental measures in childhood with behaviour problem symptoms in adolescence and environmental measures in adolescence with behaviour problem symptoms in adulthood for each rater (parent, teacher, and self-report) separately. We explored the distributions of correlation coefficients (Supplementary Figure 1) and used r= 0.20 as a cut-off above which environmental measures were included.

The second criterion excluded highly correlated environmental measures. We used penalized elastic net regularization with training and test iterations (Allegrini, Karhunen, et al., 2020; Gidziela et al., 2022; Zou & Hastie, 2005) to predict symptoms of each of the four behaviour problems in childhood from environmental measures in preschool, behaviour problem symptoms in adolescence from environmental measures in childhood and behaviour problem symptoms in adulthood from environmental measures in adolescence. Elastic net regularization accounts for intercorrelations between environmental predictors (multicollinearity) by deleting redundant measures.

Supplementary Table 2 describes the environmental variables selected to be included in the poly-environmental (poly-E) composite for each of the four target behaviour problem symptoms at each age. Additional information about environmental measures can be found in the TEDS data dictionary (https://www.teds.ac.uk/datadictionary/home.htm).

Supplementary Note 4: Construction of the poly-E composites.

We used a penalized elastic net regularization to predict parent-rated behaviour problem symptoms in childhood from parent-rated E measures in preschool, parent-rated behaviour problem symptoms in adolescence from parent-rated E measures in childhood and parent-rated behaviour problem symptoms in adulthood from parent-rated E measures in adolescence. Elastic net regularization accounts for intercorrelations between predictors (multicollinearity) by deleting redundant measures.
We used regression weights to create poly-E composites in preschool, childhood and adolescence:

$$poly-E_i = \sum_{j=1}^{k} E_{ij}\,\beta_j$$

where $poly-E$ is the poly-E measure for individual $i$ in the full sample, $j = ¿\ \{1, 2, \ldots\}$ and denotes the E value for the k E measures for individual $i$ and ß indicates the elastic net coefficient of the association between the $jth$ predictor E and the behaviour problem measure.

Supplementary Note 5: Description of univariate and multivariate twin analyses.

The univariate twin method to estimate 'anonymous' (unmeasured) NSE influences

The twin method allows for the decomposition of individual differences in a trait into genetic and environmental sources of variance by capitalizing on the genetic relatedness between monozygotic twins (MZ), who share 100% of their genetic makeup, and dizygotic twins (DZ), who share on average 50% of the genes that differ between individuals (Knopik et al., 2017). By comparing how similar MZ and DZ twins are for a given trait, it is possible to estimate the relative contribution of genetic factors and environments to variation in that trait. Heritability, the amount of variance in a trait that can be attributed to genetic variance (A), can be roughly estimated as double the difference between the MZ and DZ twin correlations. The variance can be further partitioned into shared environment (C), which describes the extent to which twins raised in the same family resemble each other beyond their shared genetic variance, and non-shared environment (E), which describes environmental variance that does not contribute to similarities between twin pairs (and also includes measurement error). The twin model-fitting analyses were conducted using OpenMx for R (Neale et al., 2016; R Core Team, 2022).

The multivariate twin method to estimate the NSE-related covariance between measures of environment and behaviour problem symptoms after controlling for genetics and shared environment

Multivariate (Cholesky) twin model-fitting is theoretically akin to hierarchical regression (Rijsdijk & Sham, 2002) in the sense that the degree to which NSE influences on a measure of behaviour problem symptoms can be explained by the NSE influences on a measure of the environment. The bivariate model as illustrated in Supplementary Figure 3A, called a Cholesky model, decomposes the genetic and environmental variance in behaviour problem symptoms) into two components of variance: one component that is shared with the environmental measure and a component that is independent of the environmental measure. The sum of squared paths (standardised partial regressions) $e_{12}$ and $e_{22}$ estimates the NSE variance in the measure of behaviour problems, equivalent to NSE influence estimated from the univariate twin model. Squaring the path $e_{12}$ estimates NSE-related processes in behaviour problem symptoms attributable to the environmental measure. Dividing this estimate (i.e., squared path $e_{12}$) by the NSE estimate of behaviour problem symptoms (i.e., the sum of squared paths $e_{12}$ and $e_{22}$) results in the proportion of NSE variance accounted for by the

environmental measure. Squaring the path from the residual latent variable $e_{22}$ estimates NSE-related processes in the measure of behaviour problem symptoms independent of the environmental variable, which includes error of measurement.

By simultaneously including poly-E measures in preschool, childhood and adolescence as predictors of a measure of symptoms of behaviour problems in adulthood, we can estimate cumulative NSE influence on the measure of behaviour problem symptoms (Supplementary Figure 3B).

Supplementary Note 6: Description of MZ differences analyses.

The MZ differences design correlates MZ differences on an environmental measure with MZ differences on a measure of symptoms of behaviour problems. It provides a within-family estimate of the E latent variable in Supplementary Figure 3A because MZ twins reared together differ due to NSE because they are identical in terms of inherited DNA differences and shared environmental influences are those that make members of an MZ twin pair similar, not different (Vitaro et al., 2009).

To assess the NSE influence on a trait using the MZ differences design, MZ co-twins were randomly assigned as Twin 1 or Twin 2, followed by calculation of a relative difference scored by subtracting Twin 2's score from Twin 1's score for both the environmental measure and the measure of behaviour problems. These two difference scores were then correlated to estimate NSE-mediated links between the environmental measure and the measure of behaviour problems. Although previously criticized for reliability concerns (Bereiter, 1963), the MZ differences design is thought to provide a reliable and unbiased approximation of differences (Rovine, 2013). A variant of the MZ differences design regresses Twin 1's scores on Twin 2's scores, resulting in standardized residuals as an index of within-pair discrepancy. Residuals obtained for the environmental measure and the measure of behavioural problems are then correlated to estimate NSE-mediated links. This alternative design is expected to yield results similar to the simple MZ differences design (Turkheimer & Waldron, 2000).

Supplementary Note 7: Results of MZ differences analyses.

On average, preschool poly-E MZ difference scores predicted 1.5% of the variance in parent-rated, 0.2% in teacher-rated and 0.4% in self-rated MZ differences in childhood behaviour problem symptoms. Our Cholesky analyses estimated on average that preschool poly-E scores predicted equivalent amount of variance. Similarly, for childhood poly-E and symptoms of adolescent behaviour problems, on average MZ differences in poly-E scores predicted 6.1% of the variance of MZ differences for parent-rated behaviour problems, 0.7% for teacher-rated behaviour problems and 2% in self-rated behaviour problems. Our corresponding Cholesky results were 6.8%, 0.8% and 1.8%, respectively. Finally, for adolescent poly-E and adult behaviour problem symptoms, on average, parent-rated poly-E MZ difference scores predicted 0.6% of the variance in parent-rated and 0.1% in self-rated behaviour problems MZ difference scores. These are the same as the results from our Cholesky analyses. As illustrated in Supplementary Figure 8, similar results were obtained from residualised MZ scores and MZ differences analyses.

# Supplementary Tables

Supplementary Table 1. Representativeness of the selected sample used in the present study.

| Ethnicity and socioeconomic status (SES) | Selected sample | 1st Contact sample | National equivalents[ab] |
|---|---|---|---|
| % white | 94.9% | 91.7% | 93% |
| % mother A-levels or higher | 50.4% | 35.5% | 35% |
| % father A-levels or higher | 54.8% | 44.8% | 47% |
| % mother employed | 50.2% | 43.1% | 50% |
| % father employed | 94.9% | 91.6% | 91% |

Note. [a] including cohort of parents with children born in late 1990s and early 2000s;
[b] from (Rimfeld, Malanchini, Spargo, et al., 2019). The selected sample is the sample used in the present analyses; The first contact sample is the sample who responded to the first TEDS contact when the twins were infants.

Supplementary Table 1. Environmental measures selected to create poly-E composites specific to each behaviour problem measure.

| Target behaviour problem measure in childhood | Selected parent-rated environmental measures in preschool |
|---|---|
| Hyperactivity | Year 3:<br>Parental discipline (Deater-Deckard et al., 1998): smack/shout;<br>Twin environment risk[1] (Cox et al., 1987; Matheny et al., 1995)<br>Year 4:<br>Parental discipline (Deater-Deckard et al., 1998): smack/shout;<br>Twin environment risk (Cox et al., 1987; Matheny et al., 1995) |
| Conduct problems | Year 3:<br>Parental discipline (Deater-Deckard et al., 1998): smack/slap;<br>Parental discipline overall scale (Deater-Deckard et al., 1998);<br>Parental feelings overall scale (Deater-Deckard et al., 1998);<br>Twin environment risk (Cox et al., 1987; Matheny et al., 1995)<br>Year 4:<br>Parental discipline (Deater-Deckard et al., 1998): smack/shout;<br>Parental discipline (Deater-Deckard et al., 1998): smack/slap;<br>Parental discipline (Deater-Deckard et al., 1998): shout/tell off;<br>Parental discipline overall scale (Deater-Deckard et al., 1998);<br>Parental feelings (Deater-Deckard et al., 1998): angry;<br>Parental negativity scale[2] (Deater-Deckard et al., 1998);<br>Parental feelings overall scale (Deater-Deckard et al., 1998);<br>Twin environment risk (Cox et al., 1987; Matheny et al., 1995) |
| Emotional problems | Year 3:<br>Twin environment risk (Cox et al., 1987; Matheny et al., 1995)<br>Year 4:<br>Twin environment risk (Cox et al., 1987; Matheny et al., 1995) |
| Peer problems | Year 3:<br>Twin environment risk (Cox et al., 1987; Matheny et al., 1995)<br>Year 4:<br>Twin environment risk (Cox et al., 1987; Matheny et al., 1995) |
| Target behaviour problem measure in adolescence | Selected parent-rated environmental measures in childhood |

| | |
|---|---|
| Hyperactivity | Year 7:<br>Parental harsh discipline scale[3] (Deater-Deckard et al., 1998);<br>Parental negativity scale (Deater-Deckard et al., 1998);<br>Parental feelings (Deater-Deckard et al., 1998)<br>Year 9:<br>Parental feelings (Deater–Deckard et al., 1998): feel impatient with child;<br>Parental feelings (Deater-Deckard et al., 1998): wish child would leave alone;<br>Parental feelings (Deater-Deckard et al., 1998): feel frustrated by child;<br>Parental feelings overall scale (Deater-Deckard et al., 1998);<br>Home environment: parent help with homework when needed;<br>Home environment: homework should be done alone;<br>Classroom environment (Ainley & Bourke, 1992): likes to be in a classroom;<br>Classroom environment (Ainley & Bourke, 1992): feels happy in a classroom;<br>Classroom environment (Ainley & Bourke, 1992): friends often in trouble;<br>Classroom friends/peer context[4] (Ainley & Bourke, 1992);<br>Classroom adventure context[5] (Ainley & Bourke, 1992);<br>Classroom acceptance[6] (Ainley & Bourke, 1992) |
| Conduct problems | Year 7:<br>Parental discipline (Deater-Deckard et al., 1998): smack or restrain;<br>Parental discipline (Deater-Deckard et al., 1998): send to room;<br>Parental feelings scale (Deater-Deckard et al., 1998): angry;<br>Parental harsh discipline scale (Deater-Deckard et al., 1998);<br>Parental feelings overall scale (Deater-Deckard et al., 1998)<br>Year 9:<br>Parental feelings scale (Deater-Deckard et al., 1998): wish child would leave alone;<br>Parental feelings scale (Deater-Deckard et al., 1998): child makes me angry;<br>Parental feelings scale (Deater-Deckard et al., 1998): feel frustrated by child;<br>Parental feelings overall scale (Deater-Deckard et al., 1998) |
| Emotional problems | Year 9:<br>Classroom environment (Ainley & Bourke, 1992): feels worried;<br>Classroom negative affect[7] (Ainley & Bourke, 1992) |

| | |
|---|---|
| Peer problems | Year 9:<br>Classroom environment (Ainley & Bourke, 1992): accepted by other children;<br>Classroom environment (Ainley & Bourke, 1992): gets on well with children;<br>Classroom environment (Ainley & Bourke, 1992): feels lonely;<br>Classroom environment (Ainley & Bourke, 1992): feels happy;<br>Classroom environment (Ainley & Bourke, 1992): people think a lot of;<br>Classroom environment (Ainley & Bourke, 1992): popular with other children;<br>Classroom negative affect (Ainley & Bourke, 1992);<br>Classroom acceptance (Ainley & Bourke, 1992) |
| Target behaviour problem measure in adulthood | Selected parent-rated environmental measures in adolescence |
| Hyperactivity | Year 12:<br>Parental feelings scale (Deater-Deckard, 2000): feel frustrated by child |
| Conduct problems | Year 12:<br>Parental feelings scale (Deater-Deckard, 2000): child makes me angry;<br>Parental feelings scale (Deater-Deckard, 2000): feel frustrated by child |

Note.

[1] Twin environment risk measure was computed as a standardized mean of family socio-economic status (SES), prenatal and perinatal medical risk, household chaos (the Confusion, Hubbub and Order Scale; Matheny et al. (1995)), maternal postnatal depression (the Edinburgh Postnatal Depression Scale; Cox et al. (1987)), life events (such as changes to marital status, new siblings, mother's pregnancy, job changes and serious illness/accident), Parental feelings overall scale (Deater-Deckard et al., 1998) and Parental discipline overall scale (Deater-Deckard et al., 1998).

[2] Parental negativity scale was computed as a standardized mean of the following items from the Parental feelings overall scale (Deater-Deckard et al., 1998): angry, frustrated, impatient and wish the child would go away for a few minutes.

[3] Parental harsh discipline scale was computed as a standardized mean of the following items from the Parental discipline overall scale (Deater-Deckard et al., 1998): smack or restrain, send the child to their room, shout or raise voice and ignore the child.

[4] Classroom friends/peer context scale was computed as a standardized mean of the following items from the Classroom Environment scale (Ainley & Bourke, 1992): child's friends care about work, child's friends try their best, child's friends enjoy learning, child's friends often in trouble.

[5] Classroom adventure context scale was computed as a standardized mean of the following items from the Classroom Environment scale (Ainley & Bourke, 1992): work is interesting, child gets excited about work, child likes to do extra work, child finds learning fun.

[6] Classroom acceptance scale was computed as a standardized mean of the following items from the Classroom Environment scale (Ainley & Bourke, 1992): child is accepted by other children, child gets on well with children, people think a lot of the child, child is popular with other children.

[7] Classroom negative affect scale was computed as a standardized mean of the following items from the Classroom Environment scale (Ainley & Bourke, 1992): child feels upset, child feels unhappy, child feels lonely, child feels worried.

Supplementary Table 2. Genetic, shared and nonshared environmental influences on behaviour problem symptoms and poly-E composites (i.e., environmental measures) estimated for the total sample.

| Behaviour problem symptoms | h2 (95% CIs) | c2 (95% CIs) | e2 (95% CIs) | N total | N MZ | N DZ |
|---|---|---|---|---|---|---|
| Preschool hyperactivity parent-rated | 0.45 (0.42, 0.48) | 0.00 (0.00, 0.00) | 0.55 (0.52, 0.58) | 9004 | 3061 | 5943 |
| Preschool conduct problems parent-rated | 0.61 (0.56, 0.66) | 0.10 (0.05, 0.14) | 0.30 (0.28, 0.31) | 9000 | 3061 | 5939 |
| Preschool emotional problems parent-rated | 0.59 (0.54, 0.61) | 0.00 (0.00, 0.04) | 0.41 (0.39, 0.43) | 8999 | 3059 | 5940 |
| Preschool peer problems parent-rated | 0.59 (0.54, 0.61) | 0.00 (0.00, 0.04) | 0.41 (0.39, 0.43) | 8999 | 3059 | 5940 |
| Childhood hyperactivity parent-rated | 0.53 (0.50, 0.56) | 0.00 (0.00, 0.00) | 0.47 (0.44, 0.50) | 8100 | 2872 | 5228 |
| Childhood hyperactivity teacher-rated | 0.70 (0.68, 0.72) | 0.00 (0.00, 0.01) | 0.30 (0.28, 0.32) | 6673 | 2387 | 4286 |
| Childhood hyperactivity child-rated | 0.38 (0.34, 0.43) | 0.00 (0.00, 0.02) | 0.62 (0.57, 0.66) | 3306 | 1220 | 2082 |
| Childhood conduct problems parent-rated | 0.63 (0.59, 0.68) | 0.14 (0.09, 0.18) | 0.23 (0.22, 0.24) | 8106 | 2874 | 5232 |
| Childhood conduct problems teacher-rated | 0.69 (0.68, 0.71) | 0.00 (0.00, 0.04) | 0.31 (0.29, 0.32) | 6677 | 2387 | 4290 |
| Childhood conduct problems child-rated | 0.45 (0.34, 0.52) | 0.03 (0.00, 0.11) | 0.52 (0.48, 0.57) | 3305 | 1218 | 2087 |
| Childhood emotional problems parent-rated | 0.48 (0.42, 0.53) | 0.16 (0.11, 0.21) | 0.36 (0.34, 0.38) | 8103 | 2874 | 5229 |
| Childhood emotional problems teacher-rated | 0.51 (0.49, 0.54) | 0.00 (0.00, 0.02) | 0.49 (0.46, 0.51) | 6655 | 2375 | 4280 |
| Childhood emotional problems child-rated | 0.39 (0.27, 0.47) | 0.04 (0.00, 0.13) | 0.57 (0.53, 0.61) | 3303 | 1217 | 2086 |
| Childhood peer problems parent-rated | 0.67 (0.65, 0.69) | 0.00 (0.00, 0.01) | 0.33 (0.31, 0.35) | 8103 | 2874 | 5229 |
| Childhood peer problems teacher-rated | 0.66 (0.64, 0.68) | 0.00 (0.00, 0.03) | 0.34 (0.32, 0.36) | 6661 | 2382 | 4279 |
| Childhood peer problems child-rated | 0.31 (0.20, 0.43) | 0.08 (0.00, 0.17) | 0.60 (0.56, 0.65) | 3275 | 1210 | 2065 |
| Adolescence hyperactivity parent-rated | 0.74 (0.72, 0.75) | 0.00 (0.00, 0.00) | 0.26 (0.25, 0.28) | 6924 | 2480 | 4444 |
| Adolescence hyperactivity teacher-rated | 0.63 (0.59, 0.65) | 0.00 (0.00, 0.03) | 0.37 (0.35, 0.40) | 4319 | 1565 | 2754 |
| Adolescence hyperactivity child-rated | 0.46 (0.43, 0.49) | 0.00 (0.00, 0.01) | 0.54 (0.51, 0.57) | 6872 | 2460 | 4412 |
| Adolescence conduct problems parent-rated | 0.71 (0.66, 0.76) | 0.07 (0.03, 0.12) | 0.21 (0.20, 0.23) | 6927 | 2480 | 4447 |
| Adolescence conduct problems teacher-rated | 0.62 (0.57, 0.65) | 0.00 (0.00, 0.04) | 0.38 (0.35, 0.41) | 4322 | 1566 | 2756 |
| Adolescence conduct problems child-rated | 0.47 (0.43, 0.49) | 0.00 (0.00, 0.03) | 0.53 (0.51, 0.56) | 6872 | 2460 | 4412 |
| Adolescence emotional problems parent-rated | 0.56 (0.48, 0.62) | 0.05 (0.00, 0.10) | 0.40 (0.37, 0.42) | 5826 | 2115 | 3711 |
| Adolescence emotional problems teacher-rated | 0.44 (0.39, 0.47) | 0.00 (0.00, 0.03) | 0.56 (0.53, 0.60) | 4312 | 1566 | 2746 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Adolescence emotional problems child-rated | 0.41 (0.34, 0.44) | 0.00 (0.00, 0.05) | 0.59 (0.56, 0.62) | 6873 | 2460 | 4413 |
| Adolescence peer problems parent-rated | 0.74 (0.72, 0.75) | 0.00 (0.00, 0.02) | 0.26 (0.25, 0.28) | 5826 | 2115 | 3711 |
| Adolescence peer problems teacher-rated | 0.56 (0.53, 0.59) | 0.00 (0.00, 0.02) | 0.44 (0.41, 0.47) | 4317 | 1565 | 2752 |
| Adolescence peer problems child-rated | 0.50 (0.45, 0.52) | 0.00 (0.00, 0.04) | 0.50 (0.48, 0.53) | 6872 | 2460 | 4412 |
| Adulthood hyperactivity parent-rated | 0.58 (0.55, 0.61) | 0.00 (0.00, 0.01) | 0.42 (0.39, 0.45) | 5295 | 1896 | 3399 |
| Adulthood hyperactivity child-rated | 0.34 (0.31, 0.38) | 0.00 (0.00, 0.07) | 0.66 (0.62, 0.69) | 3879 | 1501 | 2378 |
| Adulthood conduct problems parent-rated | 0.55 (0.48, 0.58) | 0.00 (0.00, 0.05) | 0.45 (0.42, 0.48) | 5303 | 1898 | 3405 |
| Adulthood conduct problems child-rated | 0.27 (0.16, 0.31) | 0.00 (0.00, 0.08) | 0.73 (0.69, 0.77) | 3881 | 1501 | 2380 |
| Adulthood emotional problems parent-rated | 0.53 (0.49, 0.55) | 0.00 (0.00, 0.02) | 0.47 (0.45, 0.50) | 5291 | 1891 | 3400 |
| Adulthood emotional problems child-rated | 0.31 (0.19, 0.38) | 0.04 (0.00, 0.12) | 0.66 (0.62, 0.70) | 3881 | 1501 | 2380 |
| Adulthood peer problems parent-rated | 0.68 (0.65, 0.70) | 0.00 (0.00, 0.02) | 0.32 (0.30, 0.35) | 5296 | 1896 | 3400 |
| Adulthood peer problems child-rated | 0.39 (0.29, 0.43) | 0.00 (0.00, 0.08) | 0.61 (0.57, 0.64) | 3881 | 1501 | 2380 |
| | | | | | | |
| Poly-E composites | h2 (95% CIs) | c2 (95% CIs) | e2 (95% CIs) | N total | N MZ | N DZ |
| Preschool hyperactivity poly-E | 0.30 (0.27, 0.33) | 0.60 (0.58, 0.63) | 0.10 (0.09, 0.10) | 8100 | 2872 | 5228 |
| Preschool conduct problems poly-E | 0.37 (0.33, 0.41) | 0.50 (0.46, 0.53) | 0.13 (0.12, 0.14) | 8106 | 2874 | 5232 |
| Preschool emotional problems poly-E | 0.10 (0.09, 0.11) | 0.86 (0.85, 0.87) | 0.04 (0.04, 0.05) | 8103 | 2874 | 5229 |
| Preschool peer problems poly-E | 0.10 (0.09, 0.11) | 0.86 (0.85, 0.87) | 0.04 (0.04, 0.05) | 8103 | 2874 | 5229 |
| Childhood hyperactivity poly-E | 0.70 (0.64, 0.77) | 0.15 (0.08, 0.21) | 0.15 (0.13, 0.16) | 6924 | 2480 | 4444 |
| Childhood conduct problems poly-E | 0.65 (0.59, 0.72) | 0.20 (0.13, 0.26) | 0.15 (0.14, 0.17) | 6927 | 2480 | 4447 |
| Childhood emotional problems poly-E | 0.33 (0.26, 0.41) | 0.34 (0.28, 0.40) | 0.33 (0.30, 0.36) | 5826 | 2115 | 3711 |
| Childhood peer problems poly-E | 0.63 (0.55, 0.71) | 0.07 (0.00, 0.14) | 0.30 (0.27, 0.33) | 5826 | 2115 | 3711 |
| Adolescence hyperactivity poly-E | 0.46 (0.42, 0.50) | 0.40 (0.37, 0.44) | 0.14 (0.13, 0.15) | 5295 | 1896 | 3399 |
| Adolescence conduct problems poly-E | 0.43 (0.40, 0.47) | 0.43 (0.39, 0.46) | 0.14 (0.13, 0.15) | 5303 | 1898 | 3405 |
| Note. h2= genetic influences; c2= shared environmental influences; e2= nonshared environmental influences; CIs= confidence intervals; N= sample size; MZ= monozygotic twin pairs; DZ= dizygotic twin pairs. | | | | | | |

Supplementary Table 3. Genetic, shared and nonshared environmental influences on behaviour problem symptoms and poly-E composites (i.e., environmental measures) estimated for males.

| Behaviour problem symptoms | h2 (95% CIs) | c2 (95% CIs) | e2 (95% CIs) | N total | N MZ | N DZ |
|---|---|---|---|---|---|---|
| Preschool hyperactivity parent-rated | 0.55 (0.50, 0.59) | 0.00 (0.00, 0.01) | 0.45 (0.41, 0.50) | 2935 | 1419 | 1516 |
| Preschool conduct problems parent-rated | 0.72 (0.66, 0.75) | 0.00 (0.00, 0.06) | 0.28 (0.25, 0.30) | 2936 | 1419 | 1517 |
| Preschool emotional problems parent-rated | 0.59 (0.55, 0.62) | 0.00 (0.00, 0.02) | 0.41 (0.38, 0.45) | 2933 | 1417 | 1516 |
| Preschool peer problems parent-rated | 0.59 (0.55, 0.62) | 0.00 (0.00, 0.02) | 0.41 (0.38, 0.45) | 2933 | 1417 | 1516 |
| Childhood hyperactivity parent-rated | 0.59 (0.55, 0.62) | 0.00 (0.00, 0.01) | 0.41 (0.38, 0.45) | 2649 | 1351 | 1298 |
| Childhood hyperactivity teacher-rated | 0.72 (0.70, 0.75) | 0.00 (0.00, 0.04) | 0.28 (0.25, 0.30) | 2182 | 1118 | 1064 |
| Childhood hyperactivity child-rated | 0.41 (0.32, 0.48) | 0.00 (0.00, 0.06) | 0.59 (0.52, 0.66) | 1046 | 536 | 510 |
| Childhood conduct problems parent-rated | 0.63 (0.55, 0.72) | 0.15 (0.06, 0.23) | 0.22 (0.20, 0.24) | 2651 | 1351 | 1300 |
| Childhood conduct problems teacher-rated | 0.71 (0.61, 0.74) | 0.00 (0.00, 0.10) | 0.29 (0.26, 0.31) | 2182 | 1118 | 1064 |
| Childhood conduct problems child-rated | 0.34 (0.15, 0.52) | 0.13 (0.00, 0.29) | 0.53 (0.47, 0.59) | 1045 | 534 | 511 |
| Childhood emotional problems parent-rated | 0.52 (0.42, 0.62) | 0.12 (0.02, 0.20) | 0.36 (0.34, 0.39) | 2651 | 1351 | 1300 |
| Childhood emotional problems teacher-rated | 0.50 (0.46, 0.54) | 0.00 (0.00, 0.03) | 0.50 (0.46, 0.54) | 2174 | 1113 | 1061 |
| Childhood emotional problems child-rated | 0.08 (0.00, 0.29) | 0.26 (0.12, 0.37) | 0.66 (0.59, 0.73) | 1044 | 534 | 510 |
| Childhood peer problems parent-rated | 0.64 (0.61, 0.67) | 0.00 (0.00, 0.02) | 0.36 (0.33, 0.39) | 2651 | 1351 | 1300 |
| Childhood peer problems teacher-rated | 0.67 (0.59, 0.70) | 0.00 (0.00, 0.07) | 0.33 (0.30, 0.36) | 2174 | 1116 | 1058 |
| Childhood peer problems child-rated | 0.23 (0.02, 0.43) | 0.14 (0.00, 0.30) | 0.63 (0.56, 0.71) | 1031 | 526 | 505 |
| Adolescence hyperactivity parent-rated | 0.75 (0.72, 0.77) | 0.00 (0.00, 0.01) | 0.25 (0.23, 0.28) | 2156 | 1123 | 1033 |
| Adolescence hyperactivity teacher-rated | 0.64 (0.60, 0.68) | 0.00 (0.00, 0.06) | 0.36 (0.32, 0.40) | 1345 | 700 | 645 |
| Adolescence hyperactivity child-rated | 0.48 (0.42, 0.52) | 0.00 (0.00, 0.04) | 0.52 (0.48, 0.56) | 2136 | 1112 | 1024 |
| Adolescence conduct problems parent-rated | 0.77 (0.68, 0.79) | 0.00 (0.00, 0.09) | 0.23 (0.21, 0.25) | 2156 | 1123 | 1033 |
| Adolescence conduct problems teacher-rated | 0.66 (0.62, 0.69) | 0.00 (0.00, 0.10) | 0.34 (0.31, 0.38) | 1347 | 701 | 646 |
| Adolescence conduct problems child-rated | 0.48 (0.43, 0.52) | 0.00 (0.00, 0.07) | 0.52 (0.48, 0.57) | 2136 | 1112 | 1024 |
| Adolescence emotional problems parent-rated | 0.59 (0.48, 0.63) | 0.00 (0.00, 0.10) | 0.41 (0.37, 0.45) | 1837 | 956 | 881 |
| Adolescence emotional problems teacher-rated | 0.45 (0.34, 0.50) | 0.00 (0.00, 0.09) | 0.55 (0.50, 0.61) | 1341 | 701 | 640 |
| Adolescence emotional problems child-rated | 0.37 (0.24, 0.42) | 0.00 (0.00, 0.11) | 0.63 (0.58, 0.67) | 2136 | 1112 | 1024 |
| Adolescence peer problems parent-rated | 0.73 (0.68, 0.75) | 0.00 (0.00, 0.04) | 0.27 (0.25, 0.30) | 1838 | 956 | 882 |
| Adolescence peer problems teacher-rated | 0.58 (0.44, 0.62) | 0.00 (0.00, 0.12) | 0.42 (0.38, 0.47) | 1346 | 700 | 646 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Adolescence peer problems child-rated | 0.47 (0.34, 0.51) | 0.00 (0.00, 0.11) | 0.53 (0.49, 0.57) | 2136 | 1112 | 1024 |
| Adulthood hyperactivity parent-rated | 0.59 (0.54, 0.64) | 0.00 (0.00, 0.02) | 0.41 (0.36, 0.46) | 1530 | 788 | 742 |
| Adulthood hyperactivity child-rated | 0.34 (0.26, 0.41) | 0.00 (0.00, 0.15) | 0.66 (0.59, 0.74) | 920 | 497 | 423 |
| Adulthood conduct problems parent-rated | 0.52 (0.36, 0.57) | 0.01 (0.00, 0.14) | 0.47 (0.43, 0.53) | 1532 | 789 | 743 |
| Adulthood conduct problems child-rated | 0.26 (0.00, 0.35) | 0.02 (0.00, 0.24) | 0.72 (0.65, 0.80) | 921 | 497 | 424 |
| Adulthood emotional problems parent-rated | 0.53 (0.47, 0.58) | 0.00 (0.00, 0.04) | 0.47 (0.42, 0.52) | 1525 | 785 | 740 |
| Adulthood emotional problems child-rated | 0.06 (0.00, 0.29) | 0.23 (0.04, 0.33) | 0.71 (0.63, 0.78) | 921 | 497 | 424 |
| Adulthood peer problems parent-rated | 0.68 (0.65, 0.72) | 0.00 (0.00, 0.03) | 0.32 (0.28, 0.35) | 1532 | 789 | 743 |
| Adulthood peer problems child-rated | 0.32 (0.08, 0.42) | 0.03 (0.00, 0.22) | 0.65 (0.58, 0.73) | 921 | 497 | 424 |
| | | | | | | |
| Poly-E composites | h2 (95% CIs) | c2 (95% CIs) | e2 (95% CIs) | N total | N MZ | N DZ |
| Preschool hyperactivity poly-E | 0.31 (0.26, 0.37) | 0.59 (0.54, 0.64) | 0.10 (0.09, 0.11) | 2649 | 1351 | 1298 |
| Preschool conduct problems poly-E | 0.39 (0.33, 0.47) | 0.48 (0.41, 0.54) | 0.13 (0.11, 0.14) | 2651 | 1351 | 1300 |
| Preschool emotional problems poly-E | 0.10 (0.08, 0.12) | 0.86 (0.84, 0.88) | 0.04 (0.04, 0.05) | 2651 | 1351 | 1300 |
| Preschool peer problems poly-E | 0.10 (0.08, 0.13) | 0.85 (0.83, 0.87) | 0.05 (0.04, 0.05) | 2651 | 1351 | 1300 |
| Childhood hyperactivity poly-E | 0.64 (0.52, 0.77) | 0.22 (0.10, 0.34) | 0.14 (0.12, 0.17) | 2156 | 1123 | 1033 |
| Childhood conduct problems poly-E | 0.58 (0.47, 0.71) | 0.27 (0.15, 0.38) | 0.15 (0.13, 0.17) | 2156 | 1123 | 1033 |
| Childhood emotional problems poly-E | 0.33 (0.20, 0.46) | 0.38 (0.26, 0.49) | 0.29 (0.26, 0.33) | 1837 | 956 | 881 |
| Childhood peer problems poly-E | 0.72 (0.60, 0.75) | 0.00 (0.00, 0.11) | 0.28 (0.25, 0.32) | 1838 | 956 | 882 |
| Adolescence hyperactivity poly-E | 0.51 (0.44, 0.60) | 0.34 (0.26, 0.42) | 0.14 (0.13, 0.16) | 1530 | 788 | 742 |
| Adolescence conduct problems poly-E | 0.47 (0.39, 0.55) | 0.39 (0.31, 0.46) | 0.15 (0.13, 0.16) | 1532 | 789 | 743 |
| Note. h2= genetic influences; c2= shared environmental influences; e2= nonshared environmental influences; CIs= confidence intervals; N= sample size; MZ= monozygotic twin pairs; DZ= dizygotic twin pairs. | | | | | | |

Supplementary Table 4. Genetic, shared and nonshared environmental influences on behaviour problem symptoms and poly-E composites (i.e., environmental measures) estimated for females.

| Behaviour problem symptoms | h2 (95% CIs) | c2 (95% CIs) | e2 (95% CIs) | N total | N MZ | N DZ |
|---|---|---|---|---|---|---|
| Preschool hyperactivity parent-rated | 0.50 (0.46, 0.54) | 0.00 (0.00, 0.01) | 0.50 (0.46, 0.54) | 3127 | 1642 | 1485 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Preschool conduct problems parent-rated | 0.57 (0.48, 0.66) | 0.11 (0.03, 0.19) | 0.32 (0.30, 0.34) | 3126 | 1642 | 1484 |
| Preschool emotional problems parent-rated | 0.59 (0.53, 0.62) | 0.00 (0.00, 0.05) | 0.41 (0.38, 0.44) | 3129 | 1642 | 1487 |
| Preschool peer problems parent-rated | 0.59 (0.53, 0.62) | 0.00 (0.00, 0.05) | 0.41 (0.38, 0.44) | 3129 | 1642 | 1485 |
| Childhood hyperactivity parent-rated | 0.58 (0.54, 0.62) | 0.00 (0.00, 0.01) | 0.42 (0.38, 0.46) | 2863 | 1521 | 1342 |
| Childhood hyperactivity teacher-rated | 0.71 (0.66, 0.73) | 0.00 (0.00, 0.04) | 0.29 (0.27, 0.32) | 2387 | 1269 | 1118 |
| Childhood hyperactivity child-rated | 0.40 (0.29, 0.46) | 0.00 (0.00, 0.09) | 0.60 (0.54, 0.66) | 1240 | 684 | 556 |
| Childhood conduct parent-rated | 0.59 (0.51, 0.67) | 0.16 (0.08, 0.24) | 0.25 (0.23, 0.27) | 2866 | 1523 | 1343 |
| Childhood conduct teacher-rated | 0.58 (0.48, 0.69) | 0.10 (0.00, 0.19) | 0.32 (0.29, 0.35) | 2387 | 1269 | 1118 |
| Childhood conduct child-rated | 0.44 (0.26, 0.53) | 0.04 (0.00, 0.18) | 0.52 (0.47, 0.58) | 1240 | 684 | 556 |
| Childhood emotional problems parent-rated | 0.50 (0.40, 0.60) | 0.15 (0.05, 0.23) | 0.36 (0.33, 0.39) | 2864 | 1523 | 1341 |
| Childhood emotional problems teacher-rated | 0.55 (0.50, 0.58) | 0.00 (0.00, 0.04) | 0.45 (0.42, 0.49) | 2376 | 1262 | 1114 |
| Childhood emotional problems child-rated | 0.49 (0.39, 0.54) | 0.00 (0.00, 0.08) | 0.51 (0.46, 0.56) | 1237 | 683 | 554 |
| Childhood peer problems parent-rated | 0.67 (0.64, 0.69) | 0.00 (0.00, 0.04) | 0.33 (0.31, 0.36) | 2864 | 1523 | 1341 |
| Childhood peer problems teacher-rated | 0.49 (0.38, 0.60) | 0.15 (0.05, 0.25) | 0.36 (0.33, 0.39) | 2383 | 1266 | 1117 |
| Childhood peer problems child-rated | 0.41 (0.22, 0.48) | 0.01 (0.00, 0.17) | 0.58 (0.52, 0.64) | 1239 | 684 | 555 |
| Adolescence hyperactivity parent-rated | 0.75 (0.72, 0.77) | 0.00 (0.00, 0.01) | 0.25 (0.23, 0.28) | 2562 | 1357 | 1205 |
| Adolescence hyperactivity teacher-rated | 0.59 (0.47, 0.63) | 0.00 (0.00, 0.11) | 0.41 (0.37, 0.45) | 1635 | 865 | 770 |
| Adolescence hyperactivity child-rated | 0.48 (0.43, 0.52) | 0.00 (0.00, 0.02) | 0.52 (0.48, 0.57) | 2545 | 1348 | 1197 |
| Adolescence conduct parent-rated | 0.73 (0.65, 0.81) | 0.06 (0.00, 0.14) | 0.21 (0.19, 0.23) | 2563 | 1357 | 1206 |
| Adolescence conduct teacher-rated | 0.43 (0.28, 0.56) | 0.08 (0.00, 0.20) | 0.49 (0.44, 0.55) | 1636 | 865 | 771 |
| Adolescence conduct child-rated | 0.47 (0.40, 0.51) | 0.00 (0.00, 0.05) | 0.53 (0.49, 0.58) | 2546 | 1348 | 1198 |
| Adolescence emotional problems parent-rated | 0.54 (0.42, 0.63) | 0.06 (0.00, 0.17) | 0.40 (0.36, 0.43) | 2161 | 1159 | 1002 |
| Adolescence emotional problems teacher-rated | 0.44 (0.39, 0.49) | 0.00 (0.00, 0.07) | 0.56 (0.51, 0.61) | 1635 | 865 | 770 |
| Adolescence emotional problems child-rated | 0.44 (0.40, 0.48) | 0.00 (0.00, 0.09) | 0.56 (0.52, 0.60) | 2546 | 1348 | 1198 |
| Adolescence peer problems parent-rated | 0.71 (0.61, 0.76) | 0.03 (0.00, 0.13) | 0.26 (0.23, 0.28) | 2161 | 1341 | 1002 |
| Adolescence peer problems teacher-rated | 0.52 (0.38, 0.60) | 0.03 (0.00, 0.16) | 0.44 (0.40, 0.49) | 1634 | 865 | 769 |
| Adolescence peer problems child-rated | 0.52 (0.41, 0.55) | 0.00 (0.00, 0.09) | 0.48 (0.45, 0.52) | 2546 | 1348 | 1198 |
| Adulthood hyperactivity parent-rated | 0.58 (0.54, 0.62) | 0.00 (0.00, 0.03) | 0.42 (0.38, 0.46) | 2088 | 1108 | 980 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Adulthood hyperactivity child-rated | 0.34 (0.18, 0.40) | 0.01 (0.00, 0.15) | 0.65 (0.60, 0.70) | 1817 | 1004 | 813 |
| Adulthood conduct parent-rated | 0.54 (0.42, 0.60) | 0.02 (0.00, 0.13) | 0.43 (0.40, 0.47) | 2090 | 1109 | 981 |
| Adulthood conduct child-rated | 0.19 (0.01, 0.33) | 0.08 (0.00, 0.22) | 0.73 (0.67, 0.80) | 1817 | 1004 | 813 |
| Adulthood emotional problems parent-rated | 0.54 (0.46, 0.58) | 0.00 (0.00, 0.07) | 0.46 (0.42, 0.50) | 2086 | 1106 | 980 |
| Adulthood emotional problems child-rated | 0.31 (0.15, 0.42) | 0.06 (0.00, 0.19) | 0.63 (0.58, 0.69) | 1817 | 1004 | 813 |
| Adulthood peer problems parent-rated | 0.68 (0.57, 0.71) | 0.00 (0.00, 0.10) | 0.32 (0.29, 0.35) | 2087 | 1107 | 980 |
| Adulthood peer problems child-rated | 0.41 (0.37, 0.46) | 0.00 (0.00, 0.13) | 0.59 (0.54, 0.63) | 1817 | 1004 | 813 |
| | | | | | | |
| Poly-E composites | h2 (95% CIs) | c2 (95% CIs) | e2 (95% CIs) | N total | N MZ | N DZ |
| Preschool hyperactivity poly-E | 0.26 (0.21, 0.32) | 0.64 (0.58, 0.68) | 0.10 (0.09, 0.11) | 2863 | 1521 | 1342 |
| Preschool conduct problems poly-E | 0.30 (0.24, 0.37) | 0.56 (0.50, 0.62) | 0.14 (0.12, 0.15) | 2866 | 1523 | 1343 |
| Preschool emotional problems poly-E | 0.07 (0.05, 0.09) | 0.88 (0.86, 0.90) | 0.04 (0.04, 0.05) | 2864 | 1523 | 1341 |
| Preschool peer problems poly-E | 0.07 (0.05, 0.09) | 0.88 (0.86, 0.90) | 0.05 (0.04, 0.05) | 2864 | 1523 | 1341 |
| Childhood hyperactivity poly-E | 0.53 (0.43, 0.65) | 0.32 (0.20, 0.42) | 0.15 (0.13, 0.17) | 2562 | 1357 | 1205 |
| Childhood conduct problems poly-E | 0.58 (0.47, 0.70) | 0.26 (0.14, 0.36) | 0.16 (0.14, 0.19) | 2563 | 1357 | 1206 |
| Childhood emotional problems poly-E | 0.34 (0.21, 0.48) | 0.31 (0.19, 0.43) | 0.35 (0.31, 0.39) | 2161 | 1159 | 1002 |
| Childhood peer problems poly-E | 0.62 (0.48, 0.72) | 0.07 (0.00, 0.20) | 0.31 (0.28, 0.35) | 2161 | 1341 | 1002 |
| Adolescence hyperactivity poly-E | 0.40 (0.33, 0.46) | 0.46 (0.4, 0.52) | 0.14 (0.13, 0.15) | 2088 | 1108 | 980 |
| Adolescence conduct problems poly-E | 0.36 (0.30, 0.43) | 0.5 (0.44, 0.55) | 0.14 (0.13, 0.15) | 2090 | 1109 | 981 |
| Note. h2= genetic influences; c2= shared environmental influences; e2= nonshared environmental influences; CIs= confidence intervals; N= sample size; MZ= monozygotic twin pairs; DZ= dizygotic twin pairs. | | | | | | |

Supplementary Table 5. Genetic, shared and nonshared environmental standardised squared bivariate path estimates calculated for the total sample.

| Genetic paths | | | | | | |
|---|---|---|---|---|---|---|
| Poly-E & behaviour problem symptoms | a11 (95% CIs) | a21 (95% CIs) | a22 (95% CIs) | N total | N MZ | N DZ |
| Preschool poly-E parent-rated & childhood hyperactivity parent-rated | 0.30 (0.27, 0.33) | 0.16 (0.12, 0.21) | 0.33 (0.28, 0.38) | 3947 | 1434 | 2513 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Preschool poly-E parent-rated & childhood conduct parent-rated | 0.36 (0.32, 0.40) | 0.21 (0.17, 0.27) | 0.41 (0.35, 0.47) | 3833 | 1387 | 2446 |
| Preschool poly-E parent-rated & childhood emotional problems parent-rated | 0.09 (0.08, 0.11) | 0.01 (0.00, 0.02) | 0.48 (0.42, 0.53) | 3991 | 1451 | 2540 |
| Preschool poly-E parent-rated & childhood peer problems parent-rated | 0.10 (0.08, 0.11) | 0.00 (0.00, 0.02) | 0.60 (0.58, 0.62) | 3991 | 1451 | 2540 |
| Preschool poly-E parent-rated & childhood hyperactivity teacher-rated | 0.30 (0.27, 0.33) | 0.08 (0.05, 0.12) | 0.61 (0.56, 0.64) | 3461 | 1262 | 2199 |
| Preschool poly-E parent-rated & childhood conduct teacher-rated | 0.37 (0.33, 0.41) | 0.08 (0.05, 0.13) | 0.60 (0.55, 0.64) | 3361 | 1221 | 2140 |
| Preschool poly-E parent-rated & childhood emotional problems teacher-rated | 0.10 (0.08, 0.11) | 0.00 (0.00, 0.01) | 0.51 (0.48, 0.53) | 3494 | 1272 | 2222 |
| Preschool poly-E parent-rated & childhood peer problems teacher-rated | 0.10 (0.09, 0.11) | 0.01 (0.00, 0.03) | 0.64 (0.61, 0.66) | 3496 | 1275 | 2221 |
| Preschool poly-E parent-rated & childhood hyperactivity child-rated | 0.30 (0.27, 0.33) | 0.07 (0.03, 0.12) | 0.31 (0.25, 0.37) | 2588 | 969 | 1619 |
| Preschool poly-E parent-rated & childhood conduct child-rated | 0.37 (0.33, 0.41) | 0.07 (0.03, 0.13) | 0.38 (0.26, 0.43) | 2509 | 937 | 1572 |
| Preschool poly-E parent-rated & childhood emotional problems child-rated | 0.10 (0.08, 0.11) | 0.01 (0.00, 0.04) | 0.38 (0.26, 0.42) | 2609 | 975 | 1634 |
| Preschool poly-E parent-rated & childhood peer problems child-rated | 0.10 (0.08, 0.11) | 0.01 (0.00, 0.04) | 0.30 (0.18, 0.41) | 2587 | 971 | 1616 |
| Childhood poly-E parent-rated & adolescence hyperactivity parent-rated | 0.68 (0.61, 0.75) | 0.25 (0.22, 0.29) | 0.45 (0.41, 0.49) | 2474 | 958 | 1516 |
| Childhood poly-E parent-rated & adolescence conduct parent-rated | 0.64 (0.57, 0.71) | 0.21 (0.16, 0.26) | 0.50 (0.43, 0.56) | 2558 | 976 | 1582 |
| Childhood poly-E parent-rated & adolescence emotional problems parent-rated | 0.33 (0.26, 0.41) | 0.11 (0.04, 0.19) | 0.45 (0.35, 0.52) | 2663 | 1015 | 1648 |
| Childhood poly-E parent-rated & adolescence peer problems parent-rated | 0.60 (0.52, 0.67) | 0.24 (0.19, 0.30) | 0.48 (0.42, 0.54) | 2630 | 1007 | 1623 |
| Childhood poly-E parent-rated & adolescence hyperactivity teacher-rated | 0.70 (0.62, 0.78) | 0.08 (0.05, 0.13) | 0.54 (0.48, 0.58) | 1379 | 547 | 832 |
| Childhood poly-E parent-rated & adolescence conduct teacher-rated | 0.64 (0.57, 0.72) | 0.03 (0.01, 0.06) | 0.59 (0.53, 0.62) | 1423 | 554 | 869 |
| Childhood poly-E parent-rated & adolescence emotional problems teacher-rated | 0.33 (0.25, 0.41) | 0.03 (0.00, 0.11) | 0.39 (0.32, 0.44) | 1559 | 607 | 952 |
| Childhood poly-E parent-rated & adolescence peer problems teacher-rated | 0.62 (0.54, 0.71) | 0.10 (0.06, 0.15) | 0.46 (0.39, 0.50) | 1550 | 605 | 945 |
| Childhood poly-E parent-rated & adolescence hyperactivity child-rated | 0.71 (0.63, 0.79) | 0.09 (0.06, 0.12) | 0.37 (0.33, 0.40) | 2451 | 949 | 1502 |
| Childhood poly-E parent-rated & adolescence conduct child-rated | 0.65 (0.58, 0.73) | 0.05 (0.03, 0.09) | 0.39 (0.36, 0.42) | 2532 | 967 | 1565 |
| Childhood poly-E parent-rated & adolescence emotional problems child-rated | 0.33 (0.25, 0.41) | 0.02 (0.00, 0.07) | 0.37 (0.32, 0.40) | 2840 | 1084 | 1756 |
| Childhood poly-E parent-rated & adolescence peer problems child-rated | 0.63 (0.54, 0.71) | 0.12 (0.08, 0.18) | 0.37 (0.30, 0.41) | 2808 | 1076 | 1732 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Adolescence poly-E parent-rated & adulthood hyperactivity parent-rated | 0.45 (0.41, 0.49) | 0.08 (0.05, 0.11) | 0.49 (0.44, 0.52) | 4036 | 1477 | 2559 |
| Adolescence poly-E parent-rated & adulthood conduct parent-rated | 0.43 (0.39, 0.48) | 0.11 (0.07, 0.16) | 0.44 (0.37, 0.48) | 4039 | 1477 | 2562 |
| Adolescence poly-E parent-rated & adulthood hyperactivity child-rated | 0.45 (0.41, 0.50) | 0.01 (0.00, 0.04) | 0.33 (0.25, 0.37) | 2914 | 1141 | 1773 |
| Adolescence poly-E parent-rated & adulthood conduct child-rated | 0.43 (0.39, 0.48) | 0.04 (0.01, 0.08) | 0.23 (0.12, 0.28) | 2912 | 1140 | 1772 |
| Shared environmental paths | | | | | | |
| Poly-E & behaviour problem symptoms | c11 (95% CIs) | c21 (95% CIs) | c22 (95% CIs) | N total | N MZ | N DZ |
| Preschool poly-E parent-rated & childhood hyperactivity parent-rated | 0.60 (0.57, 0.62) | 0.01 (0.01, 0.02) | 0.00 (0.00, 0.00) | 3947 | 1434 | 2513 |
| Preschool poly-E parent-rated & childhood conduct parent-rated | 0.49 (0.46, 0.52) | 0.03 (0.01, 0.05) | 0.11 (0.07, 0.15) | 3833 | 1387 | 2446 |
| Preschool poly-E parent-rated & childhood emotional problems parent-rated | 0.85 (0.82, 0.88) | 0.08 (0.07, 0.10) | 0.07 (0.05, 0.12) | 3991 | 1451 | 2540 |
| Preschool poly-E parent-rated & childhood peer problems parent-rated | 0.85 (0.82, 0.88) | 0.05 (0.03, 0.06) | 0.00 (0.00, 0.01) | 3991 | 1451 | 2540 |
| Preschool poly-E parent-rated & childhood hyperactivity teacher-rated | 0.60 (0.57, 0.63) | 0.00 (0.00, 0.01) | 0.00 (0.00, 0.01) | 3461 | 1262 | 2199 |
| Preschool poly-E parent-rated & childhood conduct teacher-rated | 0.50 (0.46, 0.53) | 0.00 (0.00, 0.01) | 0.00 (0.00, 0.03) | 3361 | 1221 | 2140 |
| Preschool poly-E parent-rated & childhood emotional problems teacher-rated | 0.86 (0.83, 0.89) | 0.01 (0.00, 0.01) | 0.00 (0.00, 0.01) | 3494 | 1272 | 2222 |
| Preschool poly-E parent-rated & childhood peer problems teacher-rated | 0.86 (0.83, 0.89) | 0.01 (0.00, 0.01) | 0.00 (0.00, 0.02) | 3496 | 1275 | 2221 |
| Preschool poly-E parent-rated & childhood hyperactivity child-rated | 0.60 (0.58, 0.63) | 0.00 (0.00, 0.01) | 0.00 (0.00, 0.02) | 2588 | 969 | 1619 |
| Preschool poly-E parent-rated & childhood conduct child-rated | 0.50 (0.47, 0.53) | 0.02 (0.00, 0.04) | 0.01 (0.00, 0.09) | 2509 | 937 | 1572 |
| Preschool poly-E parent-rated & childhood emotional problems child-rated | 0.86 (0.83, 0.89) | 0.04 (0.03, 0.06) | 0.00 (0.00, 0.09) | 2609 | 975 | 1634 |
| Preschool poly-E parent-rated & childhood peer problems child-rated | 0.86 (0.83, 0.89) | 0.03 (0.01, 0.04) | 0.06 (0.00, 0.15) | 2587 | 971 | 1616 |
| Childhood poly-E & adolescence hyperactivity parent-rated | 0.15 (0.09, 0.20) | 0.00 (0.00, 0.01) | 0.00 (0.00, 0.00) | 2474 | 958 | 1516 |
| Childhood poly-E & adolescence conduct parent-rated | 0.19 (0.13, 0.25) | 0.01 (0.00, 0.03) | 0.07 (0.02, 0.11) | 2558 | 976 | 1582 |
| Childhood poly-E & adolescence emotional problems parent-rated | 0.34 (0.27, 0.40) | 0.02 (0.00, 0.05) | 0.03 (0.00, 0.09) | 2663 | 1015 | 1648 |
| Childhood poly-E & adolescence peer problems parent-rated | 0.09 (0.03, 0.15) | 0.00 (0.00, 0.02) | 0.00 (0.00, 0.02) | 2630 | 1007 | 1623 |
| Childhood poly-E & adolescence hyperactivity teacher-rated | 0.15 (0.08, 0.21) | 0.00 (0.00, 0.01) | 0.00 (0.00, 0.03) | 1379 | 547 | 832 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Childhood poly-E & adolescence conduct teacher-rated | 0.20 (0.13, 0.25) | 0.00 (0.00, 0.03) | 0.00 (0.00, 0.04) | 1423 | 554 | 869 |
| Childhood poly-E & adolescence emotional problems teacher-rated | 0.34 (0.28, 0.40) | 0.01 (0.00, 0.03) | 0.00 (0.00, 0.03) | 1559 | 607 | 952 |
| Childhood poly-E & adolescence peer problems teacher-rated | 0.07 (0.00, 0.14) | 0.00 (0.00, 0.02) | 0.00 (0.00, 0.02) | 1550 | 605 | 945 |
| Childhood poly-E & adolescence hyperactivity child-rated | 0.14 (0.08, 0.20) | 0.00 (0.00, 0.01) | 0.00 (0.00, 0.01) | 2451 | 949 | 1502 |
| Childhood poly-E & adolescence conduct child-rated | 0.19 (0.13, 0.25) | 0.01 (0.00, 0.04) | 0.00 (0.00, 0.02) | 2532 | 967 | 1565 |
| Childhood poly-E & adolescence emotional problems child-rated | 0.34 (0.28, 0.40) | 0.01 (0.00, 0.04) | 0.00 (0.00, 0.04) | 2840 | 1084 | 1756 |
| Childhood poly-E & adolescence peer problems child-rated | 0.07 (0.00, 0.14) | 0.00 (0.00, 0.03) | 0.00 (0.00, 0.03) | 2808 | 1076 | 1732 |
| Adolescence poly-E parent-rated & adulthood hyperactivity parent-rated | 0.41 (0.37, 0.44) | 0.00 (0.00, 0.01) | 0.00 (0.00, 0.01) | 4036 | 1477 | 2559 |
| Adolescence poly-E parent-rated & adulthood conduct parent-rated | 0.43 (0.39, 0.46) | 0.00 (0.00, 0.01) | 0.00 (0.00, 0.05) | 4039 | 1477 | 2562 |
| Adolescence poly-E parent-rated & adulthood hyperactivity child-rated | 0.40 (0.37, 0.44) | 0.00 (0.00, 0.02) | 0.00 (0.00, 0.06) | 2914 | 1141 | 1773 |
| Adolescence poly-E parent-rated & adulthood conduct child-rated | 0.43 (0.39, 0.46) | 0.00 (0.00, 0.01) | 0.00 (0.00, 0.09) | 2912 | 1140 | 1772 |
| Nonshared environmental paths | | | | | | |
| Poly-E & behaviour problem symptoms | e11 (95% CIs) | e21 (95% CIs) | e22 (95% CIs) | N total | N MZ | N DZ |
| Preschool poly-E parent-rated & childhood hyperactivity parent-rated | 0.10 (0.09, 0.10) | 0.01 (0.00, 0.02) | 0.47 (0.43, 0.50) | 3947 | 1434 | 2513 |
| Preschool poly-E parent-rated & childhood conduct parent-rated | 0.12 (0.11, 0.14) | 0.01 (0.00, 0.01) | 0.22 (0.21, 0.24) | 3833 | 1387 | 2446 |
| Preschool poly-E parent-rated & childhood emotional problems parent-rated | 0.04 (0.04, 0.05) | 0.00 (0.00, 0.01) | 0.36 (0.34, 0.38) | 3991 | 1451 | 2540 |
| Preschool poly-E parent-rated & childhood peer problems parent-rated | 0.04 (0.04, 0.05) | 0.00 (0.00, 0.01) | 0.33 (0.30, 0.35) | 3991 | 1451 | 2540 |
| Preschool poly-E parent-rated & childhood hyperactivity teacher-rated | 0.10 (0.09, 0.10) | 0.00 (0.00, 0.00) | 0.29 (0.27, 0.31) | 3461 | 1262 | 2199 |
| Preschool poly-E parent-rated & childhood conduct teacher-rated | 0.13 (0.12, 0.14) | 0.00 (0.00, 0.00) | 0.30 (0.28, 0.33) | 3361 | 1221 | 2140 |
| Preschool poly-E parent-rated & childhood emotional problems teacher-rated | 0.04 (0.04, 0.05) | 0.00 (0.00, 0.01) | 0.48 (0.45, 0.52) | 3494 | 1272 | 2222 |
| Preschool poly-E parent-rated & childhood peer problems teacher-rated | 0.04 (0.04, 0.05) | 0.00 (0.00, 0.00) | 0.34 (0.31, 0.36) | 3496 | 1275 | 2221 |
| Preschool poly-E parent-rated & childhood hyperactivity child-rated | 0.10 (0.09, 0.11) | 0.00 (0.00, 0.01) | 0.61 (0.56, 0.66) | 2588 | 969 | 1619 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Preschool poly-E parent-rated & childhood conduct child-rated | 0.13 (0.12, 0.14) | 0.00 (0.00, 0.01) | 0.52 (0.47, 0.57) | 2509 | 937 | 1572 |
| Preschool poly-E parent-rated & childhood emotional problems child-rated | 0.04 (0.04, 0.05) | 0.00 (0.00, 0.00) | 0.57 (0.52, 0.62) | 2609 | 975 | 1634 |
| Preschool poly-E parent-rated & childhood peer problems child-rated | 0.05 (0.04, 0.05) | 0.00 (0.00, 0.01) | 0.60 (0.55, 0.66) | 2587 | 971 | 1616 |
| Childhood poly-E & adolescence hyperactivity parent-rated | 0.14 (0.12, 0.16) | 0.02 (0.01, 0.03) | 0.23 (0.21, 0.25) | 2474 | 958 | 1516 |
| Childhood poly-E & adolescence conduct parent-rated | 0.15 (0.13, 0.16) | 0.01 (0.01, 0.02) | 0.20 (0.18, 0.21) | 2558 | 976 | 1582 |
| Childhood poly-E & adolescence emotional problems parent-rated | 0.33 (0.29, 0.36) | 0.02 (0.01, 0.03) | 0.38 (0.35, 0.41) | 2663 | 1015 | 1648 |
| Childhood poly-E & adolescence peer problems parent-rated | 0.30 (0.27, 0.33) | 0.02 (0.01, 0.03) | 0.24 (0.22, 0.26) | 2630 | 1007 | 1623 |
| Childhood poly-E & adolescence hyperactivity teacher-rated | 0.14 (0.13, 0.16) | 0.01 (0.00, 0.02) | 0.36 (0.33, 0.40) | 1379 | 547 | 832 |
| Childhood poly-E & adolescence conduct teacher-rated | 0.15 (0.13, 0.17) | 0.00 (0.00, 0.01) | 0.38 (0.34, 0.41) | 1423 | 554 | 869 |
| Childhood poly-E & adolescence emotional problems teacher-rated | 0.33 (0.30, 0.36) | 0.00 (0.00, 0.01) | 0.57 (0.53, 0.61) | 1559 | 607 | 952 |
| Childhood poly-E & adolescence peer problems teacher-rated | 0.30 (0.27, 0.33) | 0.00 (0.00, 0.01) | 0.44 (0.40, 0.48) | 1550 | 605 | 945 |
| Childhood poly-E & adolescence hyperactivity child-rated | 0.15 (0.13, 0.16) | 0.01 (0.00, 0.02) | 0.53 (0.49, 0.56) | 2451 | 949 | 1502 |
| Childhood poly-E & adolescence conduct child-rated | 0.15 (0.13, 0.17) | 0.02 (0.01, 0.03) | 0.52 (0.49, 0.56) | 2532 | 967 | 1565 |
| Childhood poly-E & adolescence emotional problems child-rated | 0.33 (0.29, 0.36) | 0.01 (0.00, 0.02) | 0.58 (0.55, 0.62) | 2840 | 1084 | 1756 |
| Childhood poly-E & adolescence peer problems child-rated | 0.29 (0.27, 0.33) | 0.00 (0.00, 0.01) | 0.50 (0.47, 0.53) | 2808 | 1076 | 1732 |
| Adolescence poly-E parent-rated & adulthood hyperactivity parent-rated | 0.14 (0.13, 0.15) | 0.00 (0.00, 0.01) | 0.41 (0.38, 0.45) | 4036 | 1477 | 2559 |
| Adolescence poly-E parent-rated & adulthood conduct parent-rated | 0.14 (0.13, 0.15) | 0.00 (0.00, 0.01) | 0.45 (0.41, 0.48) | 4039 | 1477 | 2562 |
| Adolescence poly-E parent-rated & adulthood hyperactivity child-rated | 0.14 (0.13, 0.15) | 0.00 (0.00, 0.00) | 0.65 (0.61, 0.70) | 2914 | 1141 | 1773 |
| Adolescence poly-E parent-rated & adulthood conduct child-rated | 0.14 (0.13, 0.15) | 0.00 (0.00, 0.01) | 0.73 (0.68, 0.78) | 2912 | 1140 | 1772 |

Note. a= genetic path; c= shared environmental path; e= nonshared environmental path; CIs= confidence intervals; N= sample size; MZ= monozygotic twin pairs; DZ= dizygotic twin pairs.

Supplementary Table 6. Genetic, shared and nonshared environmental squared bivariate path estimates calculated for males.

| Genetic paths | | | | | | |
|---|---|---|---|---|---|---|
| Poly-E & behaviour problem symptoms | a11 (95% CIs) | a21 (95% CIs) | a22 (95% CIs) | N total | N MZ | N DZ |
| Preschool poly-E parent-rated & childhood hyperactivity parent-rated | 0.31 (0.26, 0.38) | 0.16 (0.10, 0.24) | 0.34 (0.27, 0.40) | 1301 | 658 | 643 |
| Preschool poly-E parent-rated & childhood conduct parent-rated | 0.39 (0.32, 0.48) | 0.24 (0.15, 0.35) | 0.33 (0.24, 0.43) | 1269 | 638 | 631 |
| Preschool poly-E parent-rated & childhood emotional problems parent-rated | 0.10 (0.08, 0.12) | 0.00 (0.00, 0.02) | 0.53 (0.43, 0.58) | 1321 | 666 | 655 |
| Preschool poly-E parent-rated & childhood peer problems parent-rated | 0.11 (0.08, 0.13) | 0.01 (0.00, 0.05) | 0.51 (0.47, 0.54) | 1321 | 666 | 655 |
| Preschool poly-E parent-rated & childhood hyperactivity teacher-rated | 0.31 (0.25, 0.37) | 0.08 (0.03, 0.16) | 0.50 (0.44, 0.54) | 1138 | 573 | 565 |
| Preschool poly-E parent-rated & childhood conduct teacher-rated | 0.39 (0.32, 0.48) | 0.11 (0.05, 0.20) | 0.41 (0.33, 0.46) | 1107 | 555 | 552 |
| Preschool poly-E parent-rated & childhood emotional problems teacher-rated | 0.10 (0.08, 0.13) | 0.00 (0.00, 0.05) | 0.49 (0.44, 0.53) | 1151 | 577 | 574 |
| Preschool poly-E parent-rated & childhood peer problems teacher-rated | 0.11 (0.08, 0.13) | 0.01 (0.00, 0.05) | 0.57 (0.50, 0.60) | 1151 | 579 | 572 |
| Preschool poly-E parent-rated & childhood hyperactivity child-rated | 0.31 (0.25, 0.37) | 0.07 (0.01, 0.17) | 0.32 (0.20, 0.39) | 831 | 433 | 398 |
| Preschool poly-E parent-rated & childhood conduct child-rated | 0.40 (0.32, 0.48) | 0.05 (0.00, 0.14) | 0.27 (0.10, 0.40) | 809 | 419 | 390 |
| Preschool poly-E parent-rated & childhood emotional problems child-rated | 0.10 (0.08, 0.13) | 0.06 (0.00, 0.18) | 0.03 (0.00, 0.24) | 841 | 435 | 406 |
| Preschool poly-E parent-rated & childhood peer problems child-rated | 0.10 (0.08, 0.13) | 0.00 (0.00, 0.07) | 0.22 (0.02, 0.39) | 833 | 432 | 401 |
| Childhood poly-E parent-rated & adolescence hyperactivity parent-rated | 0.56 (0.45, 0.67) | 0.27 (0.21, 0.34) | 0.37 (0.33, 0.44) | 762 | 417 | 345 |
| Childhood poly-E parent-rated & adolescence conduct parent-rated | 0.54 (0.43, 0.68) | 0.25 (0.15, 0.36) | 0.47 (0.36, 0.54) | 781 | 420 | 361 |
| Childhood poly-E parent-rated & adolescence emotional problems parent-rated | 0.32 (0.20, 0.46) | 0.03 (0.00, 0.12) | 0.53 (0.46, 0.58) | 824 | 435 | 389 |
| Childhood poly-E parent-rated & adolescence peer problems parent-rated | 0.63 (0.52, 0.69) | 0.22 (0.17, 0.30) | 0.42 (0.33, 0.47) | 813 | 432 | 381 |
| Childhood poly-E parent-rated & adolescence hyperactivity teacher-rated | 0.57 (0.46, 0.71) | 0.12 (0.05, 0.22) | 0.38 (0.27, 0.45) | 397 | 220 | 177 |
| Childhood poly-E parent-rated & adolescence conduct teacher-rated | 0.57 (0.45, 0.71) | 0.08 (0.01, 0.19) | 0.42 (0.30, 0.47) | 407 | 222 | 185 |
| Childhood poly-E parent-rated & adolescence emotional problems teacher-rated | 0.31 (0.19, 0.44) | 0.07 (0.00, 0.27) | 0.35 (0.13, 0.43) | 450 | 246 | 204 |
| Childhood poly-E parent-rated & adolescence peer problems teacher-rated | 0.63 (0.52, 0.70) | 0.14 (0.07, 0.26) | 0.33 (0.17, 0.44) | 452 | 246 | 206 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Childhood poly-E parent-rated & adolescence hyperactivity child-rated | 0.55 (0.44, 0.67) | 0.13 (0.07, 0.22) | 0.31 (0.19, 0.39) | 752 | 410 | 342 |
| Childhood poly-E parent-rated & adolescence conduct child-rated | 0.58 (0.45, 0.72) | 0.05 (0.01, 0.13) | 0.35 (0.28, 0.39) | 771 | 413 | 358 |
| Childhood poly-E parent-rated & adolescence emotional problems child-rated | 0.32 (0.20, 0.45) | 0.02 (0.00, 0.12) | 0.39 (0.24, 0.44) | 874 | 465 | 409 |
| Childhood poly-E parent-rated & adolescence peer problems child-rated | 0.66 (0.55, 0.70) | 0.10 (0.06, 0.14) | 0.35 (0.24, 0.40) | 865 | 462 | 403 |
| Adolescence poly-E parent-rated & adulthood hyperactivity parent-rated | 0.49 (0.41, 0.58) | 0.09 (0.04, 0.15) | 0.48 (0.40, 0.54) | 1156 | 598 | 558 |
| Adolescence poly-E parent-rated & adulthood conduct parent-rated | 0.46 (0.38, 0.55) | 0.14 (0.06, 0.25) | 0.44 (0.25, 0.53) | 1156 | 597 | 559 |
| Adolescence poly-E parent-rated & adulthood hyperactivity child-rated | 0.50 (0.41, 0.59) | 0.05 (0.00, 0.14) | 0.29 (0.20, 0.38) | 706 | 380 | 326 |
| Adolescence poly-E parent-rated & adulthood conduct child-rated | 0.46 (0.38, 0.55) | 0.02 (0.00, 0.12) | 0.24 (0.00, 0.32) | 706 | 379 | 327 |
| Shared environmental paths | | | | | | |
| Poly-E & behaviour problem symptoms | c11 (95% CIs) | c21 (95% CIs) | c22 (95% CIs) | N total | N MZ | N DZ |
| Preschool poly-E parent-rated & childhood hyperactivity parent-rated | 0.58 (0.53, 0.63) | 0.03 (0.01, 0.05) | 0.00 (0.00, 0.01) | 1301 | 658 | 643 |
| Preschool poly-E parent-rated & childhood conduct parent-rated | 0.47 (0.40, 0.53) | 0.03 (0.00, 0.07) | 0.10 (0.03, 0.16) | 1269 | 638 | 631 |
| Preschool poly-E parent-rated & childhood emotional problems parent-rated | 0.86 (0.81, 0.91) | 0.12 (0.08, 0.16) | 0.00 (0.00, 0.10) | 1321 | 666 | 655 |
| Preschool poly-E parent-rated & childhood peer problems parent-rated | 0.86 (0.81, 0.91) | 0.04 (0.02, 0.07) | 0.00 (0.00, 0.01) | 1321 | 666 | 655 |
| Preschool poly-E parent-rated & childhood hyperactivity teacher-rated | 0.59 (0.54, 0.64) | 0.00 (0.00, 0.02) | 0.00 (0.00, 0.03) | 1138 | 573 | 565 |
| Preschool poly-E parent-rated & childhood conduct teacher-rated | 0.48 (0.41, 0.54) | 0.00 (0.00, 0.01) | 0.00 (0.00, 0.07) | 1107 | 555 | 552 |
| Preschool poly-E parent-rated & childhood emotional problems teacher-rated | 0.87 (0.82, 0.92) | 0.01 (0.00, 0.02) | 0.00 (0.00, 0.03) | 1151 | 577 | 574 |
| Preschool poly-E parent-rated & childhood peer problems teacher-rated | 0.86 (0.81, 0.91) | 0.01 (0.00, 0.02) | 0.00 (0.00, 0.06) | 1151 | 579 | 572 |
| Preschool poly-E parent-rated & childhood hyperactivity child-rated | 0.59 (0.54, 0.64) | 0.00 (0.00, 0.03) | 0.00 (0.00, 0.05) | 831 | 433 | 398 |
| Preschool poly-E parent-rated & childhood conduct child-rated | 0.48 (0.41, 0.54) | 0.04 (0.00, 0.11) | 0.08 (0.00, 0.21) | 809 | 419 | 390 |
| Preschool poly-E parent-rated & childhood emotional problems child-rated | 0.87 (0.82, 0.92) | 0.03 (0.01, 0.06) | 0.24 (0.07, 0.32) | 841 | 435 | 406 |
| Preschool poly-E parent-rated & childhood peer problems child-rated | 0.86 (0.81, 0.91) | 0.04 (0.02, 0.08) | 0.10 (0.00, 0.26) | 833 | 432 | 401 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Childhood poly-E & adolescence hyperactivity parent-rated | 0.20 (0.10, 0.28) | 0.00 (0.00, 0.01) | 0.00 (0.00, 0.01) | 762 | 417 | 345 |
| Childhood poly-E & adolescence conduct parent-rated | 0.28 (0.17, 0.38) | 0.01 (0.00, 0.06) | 0.00 (0.00, 0.07) | 781 | 420 | 361 |
| Childhood poly-E & adolescence emotional problems parent-rated | 0.37 (0.25, 0.48) | 0.06 (0.01, 0.14) | 0.00 (0.00, 0.06) | 824 | 435 | 389 |
| Childhood poly-E & adolescence peer problems parent-rated | 0.01 (0.00, 0.11) | 0.00 (0.00, 0.03) | 0.00 (0.00, 0.03) | 813 | 432 | 381 |
| Childhood poly-E & adolescence hyperactivity teacher-rated | 0.20 (0.09, 0.30) | 0.00 (0.00, 0.04) | 0.00 (0.00, 0.04) | 397 | 220 | 177 |
| Childhood poly-E & adolescence conduct teacher-rated | 0.27 (0.24, 0.38) | 0.00 (0.00, 0.06) | 0.00 (0.00, 0.07) | 407 | 222 | 185 |
| Childhood poly-E & adolescence emotional problems teacher-rated | 0.38 (0.26, 0.48) | 0.00 (0.00, 0.06) | 0.00 (0.00, 0.08) | 450 | 246 | 204 |
| Childhood poly-E & adolescence peer problems teacher-rated | 0.02 (0.00, 0.12) | 0.03 (0.00, 0.13) | 0.00 (0.00, 0.11) | 452 | 246 | 206 |
| Childhood poly-E & adolescence hyperactivity child-rated | 0.22 (0.12, 0.32) | 0.00 (0.00, 0.04) | 0.00 (0.00, 0.04) | 752 | 410 | 342 |
| Childhood poly-E & adolescence conduct child-rated | 0.27 (0.14, 0.37) | 0.02 (0.00, 0.08) | 0.00 (0.00, 0.05) | 771 | 413 | 358 |
| Childhood poly-E & adolescence emotional problems child-rated | 0.37 (0.26, 0.48) | 0.02 (0.00, 0.08) | 0.00 (0.00, 0.11) | 874 | 465 | 409 |
| Childhood poly-E & adolescence peer problems child-rated | 0.00 (0.00, 0.09) | 0.00 (0.00, 0.10) | 0.00 (0.00, 0.09) | 865 | 462 | 403 |
| Adolescence poly-E parent-rated & adulthood hyperactivity parent-rated | 0.35 (0.27, 0.41) | 0.00 (0.00, 0.01) | 0.00 (0.00, 0.02) | 1156 | 598 | 558 |
| Adolescence poly-E parent-rated & adulthood conduct parent-rated | 0.39 (0.31, 0.45) | 0.00 (0.00, 0.02) | 0.00 (0.00, 0.14) | 1156 | 597 | 559 |
| Adolescence poly-E parent-rated & adulthood hyperactivity child-rated | 0.34 (0.26, 0.41) | 0.00 (0.00, 0.06) | 0.00 (0.00, 0.13) | 706 | 380 | 326 |
| Adolescence poly-E parent-rated & adulthood conduct child-rated | 0.38 (0.31, 0.45) | 0.00 (0.00, 0.06) | 0.01 (0.00, 0.21) | 706 | 379 | 327 |
| Nonshared environmental paths | | | | | | |
| Poly-E & behaviour problem symptoms | e11 (95% CIs) | e21 (95% CIs) | e22 (95% CIs) | N total | N MZ | N DZ |
| Preschool poly-E parent-rated & childhood hyperactivity parent-rated | 0.10 (0.08, 0.11) | 0.01 (0.00, 0.03) | 0.36 (0.32, 0.41) | 1301 | 658 | 643 |
| Preschool poly-E parent-rated & childhood conduct parent-rated | 0.12 (0.10, 0.14) | 0.00 (0.00, 0.01) | 0.18 (0.16, 0.21) | 1269 | 638 | 631 |
| Preschool poly-E parent-rated & childhood emotional problems parent-rated | 0.04 (0.04, 0.05) | 0.00 (0.00, 0.01) | 0.37 (0.33, 0.41) | 1321 | 666 | 655 |
| Preschool poly-E parent-rated & childhood peer problems parent-rated | 0.05 (0.04, 0.05) | 0.00 (0.00, 0.01) | 0.31 (0.28, 0.35) | 1321 | 666 | 655 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Preschool poly-E parent-rated & childhood hyperactivity teacher-rated | 0.10 (0.08, 0.11) | 0.00 (0.00, 0.00) | 0.22 (0.19, 0.24) | 1138 | 573 | 565 |
| Preschool poly-E parent-rated & childhood conduct teacher-rated | 0.13 (0.11, 0.15) | 0.00 (0.00, 0.00) | 0.20 (0.17, 0.22) | 1107 | 555 | 552 |
| Preschool poly-E parent-rated & childhood emotional problems teacher-rated | 0.04 (0.04, 0.05) | 0.00 (0.00, 0.01) | 0.49 (0.44, 0.55) | 1151 | 577 | 574 |
| Preschool poly-E parent-rated & childhood peer problems teacher-rated | 0.05 (0.04, 0.05) | 0.00 (0.00, 0.00) | 0.28 (0.25, 0.32) | 1151 | 579 | 572 |
| Preschool poly-E parent-rated & childhood hyperactivity child-rated | 0.10 (0.08, 0.11) | 0.00 (0.00, 0.01) | 0.54 (0.47, 0.63) | 831 | 433 | 398 |
| Preschool poly-E parent-rated & childhood conduct child-rated | 0.13 (0.11, 0.15) | 0.00 (0.00, 0.01) | 0.46 (0.39, 0.53) | 809 | 419 | 390 |
| Preschool poly-E parent-rated & childhood emotional problems child-rated | 0.04 (0.04, 0.05) | 0.00 (0.00, 0.01) | 0.68 (0.58, 0.77) | 841 | 435 | 406 |
| Preschool poly-E parent-rated & childhood peer problems child-rated | 0.05 (0.04, 0.05) | 0.00 (0.00, 0.01) | 0.61 (0.52, 0.70) | 833 | 432 | 401 |
| Childhood poly-E & adolescence hyperactivity parent-rated | 0.12 (0.10, 0.15) | 0.03 (0.01, 0.04) | 0.19 (0.16, 0.22) | 762 | 417 | 345 |
| Childhood poly-E & adolescence conduct parent-rated | 0.14 (0.11, 0.17) | 0.01 (0.00, 0.02) | 0.20 (0.18, 0.23) | 781 | 420 | 361 |
| Childhood poly-E & adolescence emotional problems parent-rated | 0.29 (0.24, 0.34) | 0.02 (0.01, 0.05) | 0.42 (0.36, 0.47) | 824 | 435 | 389 |
| Childhood poly-E & adolescence peer problems parent-rated | 0.26 (0.22, 0.31) | 0.03 (0.02, 0.05) | 0.20 (0.17, 0.23) | 813 | 432 | 381 |
| Childhood poly-E & adolescence hyperactivity teacher-rated | 0.13 (0.11, 0.16) | 0.01 (0.00, 0.03) | 0.26 (0.22, 0.30) | 397 | 220 | 177 |
| Childhood poly-E & adolescence conduct teacher-rated | 0.15 (0.12, 0.18) | 0.00 (0.00, 0.02) | 0.25 (0.21, 0.28) | 407 | 222 | 185 |
| Childhood poly-E & adolescence emotional problems teacher-rated | 0.29 (0.24, 0.34) | 0.00 (0.00, 0.02) | 0.53 (0.47, 0.60) | 450 | 246 | 204 |
| Childhood poly-E & adolescence peer problems teacher-rated | 0.26 (0.22, 0.31) | 0.00 (0.00, 0.02) | 0.36 (0.31, 0.41) | 452 | 246 | 206 |
| Childhood poly-E & adolescence hyperactivity child-rated | 0.13 (0.11, 0.16) | 0.03 (0.01, 0.05) | 0.45 (0.40, 0.50) | 752 | 410 | 342 |
| Childhood poly-E & adolescence conduct child-rated | 0.15 (0.12, 0.18) | 0.02 (0.01, 0.04) | 0.44 (0.39, 0.49) | 771 | 413 | 358 |
| Childhood poly-E & adolescence emotional problems child-rated | 0.29 (0.24, 0.34) | 0.00 (0.00, 0.01) | 0.72 (0.65, 0.79) | 874 | 465 | 409 |
| Childhood poly-E & adolescence peer problems child-rated | 0.26 (0.22, 0.31) | 0.01 (0.00, 0.02) | 0.50 (0.45, 0.55) | 865 | 462 | 403 |
| Adolescence poly-E parent-rated & adulthood hyperactivity parent-rated | 0.14 (0.12, 0.16) | 0.00 (0.00, 0.01) | 0.39 (0.33, 0.45) | 1156 | 598 | 558 |
| Adolescence poly-E parent-rated & adulthood conduct parent-rated | 0.14 (0.12, 0.16) | 0.00 (0.00, 0.01) | 0.53 (0.47, 0.60) | 1156 | 597 | 559 |
| Adolescence poly-E parent-rated & adulthood hyperactivity child-rated | 0.14 (0.12, 0.16) | 0.00 (0.00, 0.01) | 0.66 (0.57, 0.75) | 706 | 380 | 326 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Adolescence poly-E parent-rated & adulthood conduct child-rated | 0.14 (0.12, 0.17) | 0.01 (0.00, 0.02) | 0.68 (0.59, 0.77) | 706 | 379 | 327 |

Note. a= genetic path; c= shared environmental path; e= nonshared environmental path; CIs= confidence intervals; N= sample size; MZ= monozygotic twin pairs; DZ= dizygotic twin pairs.

Supplementary Table 7. Genetic, shared and nonshared environmental squared bivariate path estimates calculated for females.

| Genetic paths | | | | | | |
|---|---|---|---|---|---|---|
| Poly-E & behaviour problem symptoms | a11 (95% CIs) | a21 (95% CIs) | a22 (95% CIs) | N total | N MZ | N DZ |
| Preschool poly-E parent-rated & childhood hyperactivity parent-rated | 0.28 (0.22, 0.34) | 0.16 (0.09, 0.24) | 0.45 (0.37, 0.52) | 1432 | 776 | 656 |
| Preschool poly-E parent-rated & childhood conduct parent-rated | 0.30 (0.24, 0.38) | 0.24 (0.15, 0.35) | 0.42 (0.29, 0.54) | 1388 | 749 | 639 |
| Preschool poly-E parent-rated & childhood emotional problems parent-rated | 0.07 (0.05, 0.10) | 0.00 (0.00, 0.03) | 0.49 (0.39, 0.58) | 1446 | 785 | 661 |
| Preschool poly-E parent-rated & childhood peer problems parent-rated | 0.07 (0.05, 0.09) | 0.01 (0.00, 0.05) | 0.76 (0.71, 0.81) | 1446 | 785 | 661 |
| Preschool poly-E parent-rated & childhood hyperactivity teacher-rated | 0.28 (0.22, 0.34) | 0.10 (0.04, 0.19) | 0.79 (0.67, 0.88) | 1265 | 689 | 576 |
| Preschool poly-E parent-rated & childhood conduct teacher-rated | 0.31 (0.24, 0.39) | 0.08 (0.02, 0.18) | 0.75 (0.57, 0.93) | 1227 | 666 | 561 |
| Preschool poly-E parent-rated & childhood emotional problems teacher-rated | 0.07 (0.06, 0.10) | 0.00 (0.00, 0.05) | 0.50 (0.44, 0.53) | 1273 | 695 | 578 |
| Preschool poly-E parent-rated & childhood peer problems teacher-rated | 0.07 (0.05, 0.10) | 0.00 (0.00, 0.04) | 0.57 (0.44, 0.71) | 1276 | 696 | 580 |
| Preschool poly-E parent-rated & childhood hyperactivity child-rated | 0.28 (0.22, 0.35) | 0.10 (0.02, 0.22) | 0.33 (0.17, 0.44) | 958 | 536 | 422 |
| Preschool poly-E parent-rated & childhood conduct child-rated | 0.31 (0.24, 0.39) | 0.07 (0.01, 0.19) | 0.40 (0.19, 0.51) | 927 | 518 | 409 |
| Preschool poly-E parent-rated & childhood emotional problems child-rated | 0.07 (0.06, 0.10) | 0.02 (0.00, 0.10) | 0.37 (0.26, 0.44) | 964 | 540 | 424 |
| Preschool poly-E parent-rated & childhood peer problems child-rated | 0.07 (0.05, 0.10) | 0.02 (0.00, 0.11) | 0.38 (0.19, 0.44) | 962 | 539 | 423 |
| Childhood poly-E parent-rated & adolescence hyperactivity parent-rated | 0.59 (0.48, 0.72) | 0.28 (0.20, 0.37) | 0.53 (0.44, 0.61) | 972 | 541 | 431 |
| Childhood poly-E parent-rated & adolescence conduct parent-rated | 0.59 (0.47, 0.73) | 0.14 (0.07, 0.24) | 0.65 (0.54, 0.73) | 1004 | 556 | 448 |
| Childhood poly-E parent-rated & adolescence emotional problems parent-rated | 0.35 (0.22, 0.49) | 0.26 (0.10, 0.49) | 0.27 (0.08, 0.44) | 1043 | 580 | 463 |
| Childhood poly-E parent-rated & adolescence peer problems parent-rated | 0.65 (0.50, 0.75) | 0.27 (0.15, 0.38) | 0.52 (0.36, 0.68) | 1029 | 575 | 454 |
| Childhood poly-E parent-rated & adolescence hyperactivity teacher-rated | 0.59 (0.47, 0.73) | 0.05 (0.00, 0.15) | 0.79 (0.58, 0.86) | 570 | 327 | 243 |
| Childhood poly-E parent-rated & adolescence conduct teacher-rated | 0.61 (0.48, 0.75) | 0.00 (0.00, 0.03) | 0.69 (0.44, 0.87) | 587 | 332 | 255 |
| Childhood poly-E parent-rated & adolescence emotional problems teacher-rated | 0.34 (0.21, 0.49) | 0.03 (0.00, 0.15) | 0.42 (0.27, 0.48) | 637 | 361 | 276 |
| Childhood poly-E parent-rated & adolescence peer problems teacher-rated | 0.66 (0.50, 0.77) | 0.07 (0.01, 0.19) | 0.56 (0.35, 0.67) | 627 | 359 | 268 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Childhood poly-E parent-rated & adolescence hyperactivity child-rated | 0.61 (0.48, 0.75) | 0.10 (0.04, 0.18) | 0.40 (0.32, 0.46) | 967 | 539 | 428 |
| Childhood poly-E parent-rated & adolescence conduct child-rated | 0.61 (0.48, 0.75) | 0.05 (0.01, 0.12) | 0.43 (0.36, 0.48) | 998 | 554 | 444 |
| Childhood poly-E parent-rated & adolescence emotional problems child-rated | 0.34 (0.21, 0.49) | 0.02 (0.00, 0.12) | 0.36 (0.26, 0.40) | 1115 | 619 | 496 |
| Childhood poly-E parent-rated & adolescence peer problems child-rated | 0.64 (0.50, 0.75) | 0.21 (0.11, 0.34) | 0.32 (0.14, 0.44) | 1100 | 614 | 486 |
| Adolescence poly-E parent-rated & adulthood hyperactivity parent-rated | 0.41 (0.34, 0.49) | 0.06 (0.02, 0.11) | 0.56 (0.50, 0.61) | 1625 | 879 | 746 |
| Adolescence poly-E parent-rated & adulthood conduct parent-rated | 0.38 (0.31, 0.45) | 0.07 (0.02, 0.15) | 0.44 (0.32, 0.49) | 1625 | 880 | 745 |
| Adolescence poly-E parent-rated & adulthood hyperactivity child-rated | 0.41 (0.34, 0.49) | 0.02 (0.00, 0.09) | 0.32 (0.15, 0.39) | 1359 | 761 | 598 |
| Adolescence poly-E parent-rated & adulthood conduct child-rated | 0.38 (0.31, 0.46) | 0.05 (0.01, 0.14) | 0.14 (0.00, 0.30) | 1358 | 761 | 597 |
| Shared environmental paths | | | | | | |
| Poly-E & behaviour problem symptoms | c11 (95% CIs) | c21 (95% CIs) | c22 (95% CIs) | N total | N MZ | N DZ |
| Preschool poly-E parent-rated & childhood hyperactivity parent-rated | 0.67 (0.62, 0.73) | 0.01 (0.00, 0.03) | 0.00 (0.00, 0.01) | 1432 | 776 | 656 |
| Preschool poly-E parent-rated & childhood conduct parent-rated | 0.58 (0.52, 0.64) | 0.02 (0.00, 0.05) | 0.18 (0.09, 0.26) | 1388 | 749 | 639 |
| Preschool poly-E parent-rated & childhood emotional problems parent-rated | 0.92 (0.86, 0.98) | 0.08 (0.05, 0.11) | 0.06 (0.00, 0.15) | 1446 | 785 | 661 |
| Preschool poly-E parent-rated & childhood peer problems parent-rated | 0.92 (0.86, 0.97) | 0.05 (0.03, 0.08) | 0.00 (0.00, 0.03) | 1446 | 785 | 661 |
| Preschool poly-E parent-rated & childhood hyperactivity teacher-rated | 0.67 (0.62, 0.73) | 0.00 (0.00, 0.01) | 0.00 (0.00, 0.05) | 1265 | 689 | 576 |
| Preschool poly-E parent-rated & childhood conduct teacher-rated | 0.58 (0.52, 0.64) | 0.00 (0.00, 0.03) | 0.14 (0.00, 0.28) | 1227 | 666 | 561 |
| Preschool poly-E parent-rated & childhood emotional problems teacher-rated | 0.93 (0.87, 0.98) | 0.01 (0.00, 0.02) | 0.00 (0.00, 0.04) | 1273 | 695 | 578 |
| Preschool poly-E parent-rated & childhood peer problems teacher-rated | 0.92 (0.87, 0.98) | 0.01 (0.00, 0.02) | 0.17 (0.06, 0.29) | 1276 | 696 | 580 |
| Preschool poly-E parent-rated & childhood hyperactivity child-rated | 0.67 (0.62, 0.73) | 0.00 (0.00, 0.02) | 0.00 (0.00, 0.11) | 958 | 536 | 422 |
| Preschool poly-E parent-rated & childhood conduct child-rated | 0.58 (0.52, 0.64) | 0.02 (0.00, 0.07) | 0.04 (0.00, 0.19) | 927 | 518 | 409 |
| Preschool poly-E parent-rated & childhood emotional problems child-rated | 0.93 (0.87, 0.98) | 0.07 (0.04, 0.11) | 0.00 (0.00, 0.05) | 964 | 540 | 424 |
| Preschool poly-E parent-rated & childhood peer problems child-rated | 0.92 (0.87, 0.98) | 0.02 (0.01, 0.05) | 0.00 (0.00, 0.15) | 962 | 539 | 423 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Childhood poly-E & adolescence hyperactivity parent-rated | 0.32 (0.21, 0.41) | 0.00 (0.00, 0.02) | 0.00 (0.00, 0.01) | 972 | 541 | 431 |
| Childhood poly-E & adolescence conduct parent-rated | 0.27 (0.16, 0.38) | 0.04 (0.00, 0.12) | 0.03 (0.00, 0.11) | 1004 | 556 | 448 |
| Childhood poly-E & adolescence emotional problems parent-rated | 0.29 (0.17, 0.41) | 0.01 (0.00, 0.08) | 0.05 (0.00, 0.16) | 1043 | 580 | 463 |
| Childhood poly-E & adolescence peer problems parent-rated | 0.07 (0.00, 0.20) | 0.04 (0.00, 0.13) | 0.00 (0.00, 0.14) | 1029 | 575 | 454 |
| Childhood poly-E & adolescence hyperactivity teacher-rated | 0.34 (0.22, 0.45) | 0.00 (0.00, 0.07) | 0.00 (0.00, 0.16) | 570 | 327 | 243 |
| Childhood poly-E & adolescence conduct teacher-rated | 0.27 (0.15, 0.38) | 0.04 (0.00, 0.16) | 0.07 (0.00, 0.28) | 587 | 332 | 255 |
| Childhood poly-E & adolescence emotional problems teacher-rated | 0.30 (0.18, 0.42) | 0.00 (0.00, 0.04) | 0.00 (0.00, 0.07) | 637 | 361 | 276 |
| Childhood poly-E & adolescence peer problems teacher-rated | 0.07 (0.00, 0.20) | 0.00 (0.00, 0.15) | 0.03 (0.00, 0.19) | 627 | 359 | 268 |
| Childhood poly-E & adolescence hyperactivity child-rated | 0.33 (0.20, 0.43) | 0.01 (0.00, 0.04) | 0.00 (0.00, 0.02) | 967 | 539 | 428 |
| Childhood poly-E & adolescence conduct child-rated | 0.27 (0.15, 0.37) | 0.02 (0.00, 0.08) | 0.00 (0.00, 0.05) | 998 | 554 | 444 |
| Childhood poly-E & adolescence emotional problems child-rated | 0.30 (0.18, 0.42) | 0.01 (0.00, 0.06) | 0.00 (0.00, 0.07) | 1115 | 619 | 496 |
| Childhood poly-E & adolescence peer problems child-rated | 0.09 (0.00, 0.21) | 0.02 (0.00, 0.10) | 0.00 (0.00, 0.10) | 1100 | 614 | 486 |
| Adolescence poly-E parent-rated & adulthood hyperactivity parent-rated | 0.49 (0.42, 0.55) | 0.00 (0.00, 0.02) | 0.00 (0.00, 0.03) | 1625 | 879 | 746 |
| Adolescence poly-E parent-rated & adulthood conduct parent-rated | 0.52 (0.46, 0.57) | 0.02 (0.00, 0.06) | 0.01 (0.00, 0.10) | 1625 | 880 | 745 |
| Adolescence poly-E parent-rated & adulthood hyperactivity child-rated | 0.49 (0.42, 0.55) | 0.00 (0.00, 0.02) | 0.01 (0.00, 0.15) | 1359 | 761 | 598 |
| Adolescence poly-E parent-rated & adulthood conduct child-rated | 0.52 (0.46, 0.57) | 0.00 (0.00, 0.02) | 0.09 (0.00, 0.23) | 1358 | 761 | 597 |
| Nonshared environmental paths | | | | | | |
| Poly-E & behaviour problem symptoms | e11 (95% CIs) | e21 (95% CIs) | e22 (95% CIs) | N total | N MZ | N DZ |
| Preschool poly-E parent-rated & childhood hyperactivity parent-rated | 0.11 (0.09, 0.13) | 0.01 (0.00, 0.02) | 0.46 (0.41, 0.51) | 1432 | 776 | 656 |
| Preschool poly-E parent-rated & childhood conduct parent-rated | 0.14 (0.12, 0.16) | 0.01 (0.00, 0.02) | 0.29 (0.26, 0.32) | 1388 | 749 | 639 |
| Preschool poly-E parent-rated & childhood emotional problems parent-rated | 0.05 (0.04, 0.05) | 0.00 (0.00, 0.01) | 0.35 (0.32, 0.39) | 1446 | 785 | 661 |
| Preschool poly-E parent-rated & childhood peer problems parent-rated | 0.05 (0.04, 0.06) | 0.01 (0.00, 0.02) | 0.42 (0.37, 0.46) | 1446 | 785 | 661 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Preschool poly-E parent-rated & childhood hyperactivity teacher-rated | 0.11 (0.09, 0.13) | 0.00 (0.00, 0.00) | 0.38 (0.34, 0.43) | 1265 | 689 | 576 |
| Preschool poly-E parent-rated & childhood conduct teacher-rated | 0.14 (0.12, 0.17) | 0.00 (0.00, 0.00) | 0.48 (0.43, 0.54) | 1227 | 666 | 561 |
| Preschool poly-E parent-rated & childhood emotional problems teacher-rated | 0.05 (0.04, 0.05) | 0.00 (0.00, 0.01) | 0.42 (0.38, 0.46) | 1273 | 695 | 578 |
| Preschool poly-E parent-rated & childhood peer problems teacher-rated | 0.05 (0.04, 0.06) | 0.00 (0.00, 0.01) | 0.42 (0.37, 0.47) | 1276 | 696 | 580 |
| Preschool poly-E parent-rated & childhood hyperactivity child-rated | 0.11 (0.09, 0.13) | 0.00 (0.00, 0.02) | 0.65 (0.57, 0.73) | 958 | 536 | 422 |
| Preschool poly-E parent-rated & childhood conduct child-rated | 0.14 (0.12, 0.17) | 0.00 (0.00, 0.01) | 0.58 (0.50, 0.66) | 927 | 518 | 409 |
| Preschool poly-E parent-rated & childhood emotional problems child-rated | 0.05 (0.04, 0.05) | 0.00 (0.00, 0.02) | 0.48 (0.42, 0.55) | 964 | 540 | 424 |
| Preschool poly-E parent-rated & childhood peer problems child-rated | 0.05 (0.04, 0.06) | 0.00 (0.00, 0.01) | 0.58 (0.51, 0.66) | 962 | 539 | 423 |
| Childhood poly-E & adolescence hyperactivity parent-rated | 0.16 (0.13, 0.19) | 0.02 (0.00, 0.03) | 0.27 (0.23, 0.30) | 972 | 541 | 431 |
| Childhood poly-E & adolescence conduct parent-rated | 0.17 (0.14, 0.20) | 0.02 (0.01, 0.03) | 0.21 (0.19, 0.24) | 1004 | 556 | 448 |
| Childhood poly-E & adolescence emotional problems parent-rated | 0.35 (0.30, 0.41) | 0.01 (0.00, 0.02) | 0.36 (0.32, 0.41) | 1043 | 580 | 463 |
| Childhood poly-E & adolescence peer problems parent-rated | 0.32 (0.28, 0.38) | 0.01 (0.00, 0.02) | 0.29 (0.26, 0.33) | 1029 | 575 | 454 |
| Childhood poly-E & adolescence hyperactivity teacher-rated | 0.16 (0.14, 0.20) | 0.00 (0.00, 0.02) | 0.59 (0.52, 0.67) | 570 | 327 | 243 |
| Childhood poly-E & adolescence conduct teacher-rated | 0.18 (0.15, 0.21) | 0.01 (0.00, 0.02) | 0.78 (0.68, 0.90) | 587 | 332 | 255 |
| Childhood poly-E & adolescence emotional problems teacher-rated | 0.35 (0.30, 0.41) | 0.00 (0.00, 0.01) | 0.56 (0.50, 0.63) | 637 | 361 | 276 |
| Childhood poly-E & adolescence peer problems teacher-rated | 0.33 (0.29, 0.39) | 0.00 (0.00, 0.01) | 0.54 (0.48, 0.62) | 627 | 359 | 268 |
| Childhood poly-E & adolescence hyperactivity child-rated | 0.16 (0.14, 0.20) | 0.00 (0.00, 0.02) | 0.56 (0.50, 0.62) | 967 | 539 | 428 |
| Childhood poly-E & adolescence conduct child-rated | 0.17 (0.14, 0.21) | 0.01 (0.00, 0.03) | 0.59 (0.53, 0.65) | 998 | 554 | 444 |
| Childhood poly-E & adolescence emotional problems child-rated | 0.35 (0.30, 0.41) | 0.01 (0.00, 0.03) | 0.48 (0.43, 0.53) | 1115 | 619 | 496 |
| Childhood poly-E & adolescence peer problems child-rated | 0.32 (0.28, 0.38) | 0.00 (0.00, 0.01) | 0.51 (0.46, 0.57) | 1100 | 614 | 486 |
| Adolescence poly-E parent-rated & adulthood hyperactivity parent-rated | 0.15 (0.13, 0.17) | 0.01 (0.00, 0.01) | 0.44 (0.39, 0.50) | 1625 | 879 | 746 |
| Adolescence poly-E parent-rated & adulthood conduct parent-rated | 0.15 (0.13, 0.17) | 0.00 (0.00, 0.01) | 0.40 (0.36, 0.45) | 1625 | 880 | 745 |
| Adolescence poly-E parent-rated & adulthood hyperactivity child-rated | 0.15 (0.13, 0.17) | 0.00 (0.00, 0.01) | 0.64 (0.58, 0.71) | 1359 | 761 | 598 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Adolescence poly-E parent-rated & adulthood conduct child-rated | 0.15 (0.13, 0.17) | 0.00 (0.00, 0.01) | 0.75 (0.67, 0.83) | 1358 | 761 | 597 |

Note. a= genetic path; c= shared environmental path; e= nonshared environmental path; CIs= confidence intervals; N= sample size; MZ= monozygotic twin pairs; DZ= dizygotic twin pairs.

Supplementary Table 8. Genetic, shared and nonshared environmental standardised squared multivariate path estimates for the total sample for the cumulative NSE prediction of behaviour problem symptoms in adulthood from environmental measures in preschool, childhood and adolescence.

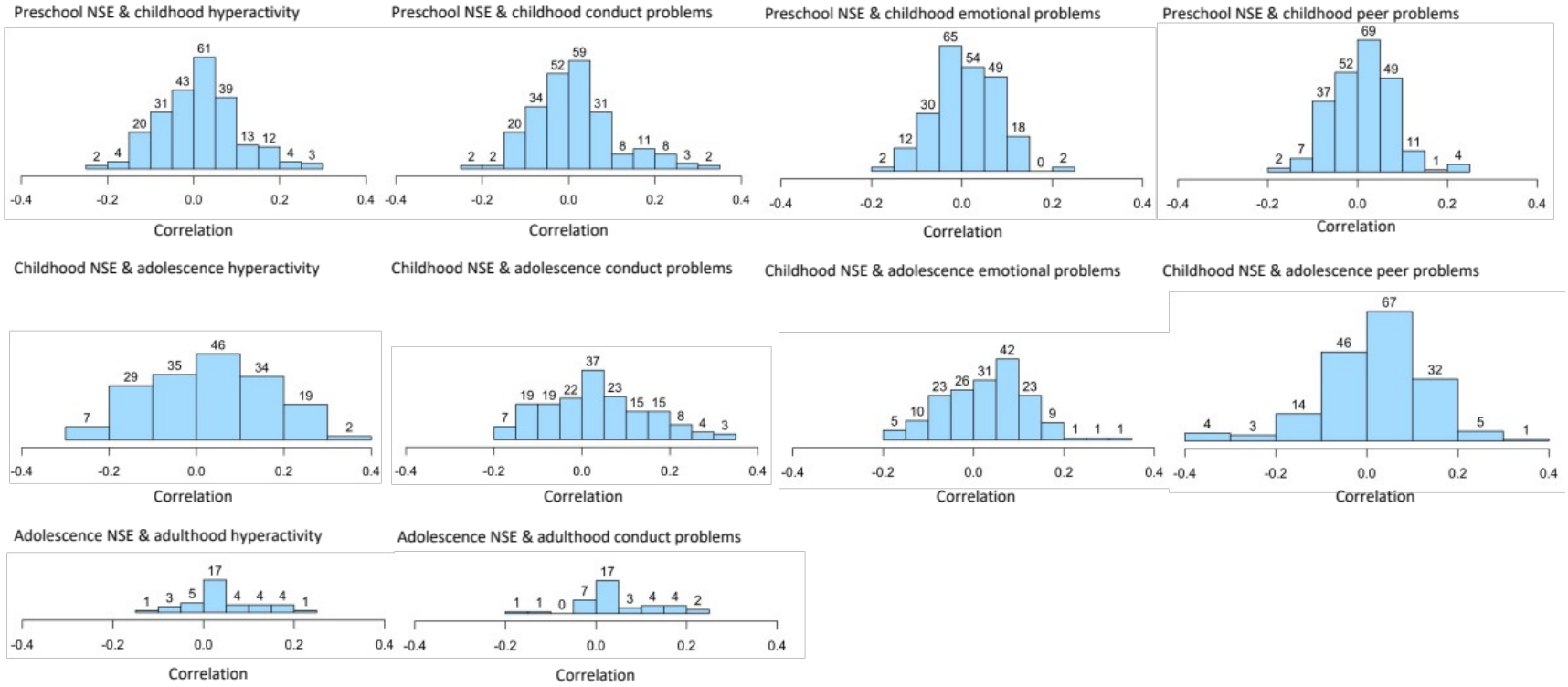
| Genetic paths | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Poly-E & behaviour problem symptoms | a11 (95% CIs) | a21 (95% CIs) | a31 (95% CIs) | a41 (95% CIs) | a22 (95% CIs) | a23 (95% CIs) | a24 (95% CIs) | a33 (95% CIs) | a34 (95% CIs) | a44 (95% CIs) | N total | MZ | DZ |
| Preschool, childhood and adolescence poly-E & adulthood hyperactivity parent-rated | 0.30 (0.27, 0.33) | 0.25 (0.19, 0.31) | 0.07 (0.04, 0.10) | 0.03 (0.01, 0.07) | 0.44 (0.37, 0.51) | 0.05 (0.03, 0.08) | 0.07 (0.04, 0.12) | 0.33 (0.29, 0.37) | 0.01 (0.00, 0.04) | 0.42 (0.38, 0.47) | 1441 | 563 | 878 |
| Preschool, childhood and adolescence poly-E & adulthood conduct parent-rated | 0.36 (0.32, 0.40) | 0.33 (0.27, 0.40) | 0.10 (0.07, 0.13) | 0.03 (0.01, 0.07) | 0.30 (0.24, 0.37) | 0.06 (0.03, 0.10) | 0.03 (0.00, 0.08) | 0.28 (0.24, 0.32) | 0.05 (0.02, 0.10) | 0.42 (0.36, 0.46) | 1450 | 561 | 889 |
| Preschool, childhood and adolescence poly-E & adulthood hyperactivity | 0.30 (0.26, 0.33) | 0.25 (0.19, 0.31) | 0.07 (0.05, 0.10) | 0.00 (0.00, 0.02) | 0.45 (0.38, 0.52) | 0.05 (0.03, 0.09) | 0.04 (0.01, 0.10) | 0.33 (0.29, 0.38) | 0.00 (0.00, 0.02) | 0.28 (0.19, 0.34) | 1057 | 451 | 606 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| child-rated | | | | | | | | | | | | | |
| Preschool, childhood and adolescence poly-E & adulthood conduct child-rated | 0.36 (0.32, 0.41) | 0.33 (0.26, 0.40) | 0.09 (0.07, 0.13) | 0.01 (0.00, 0.03) | 0.30 (0.24, 0.37) | 0.06 (0.03, 0.10) | 0.04 (0.00, 0.13) | 0.28 (0.24, 0.32) | 0.01 (0.00, 0.04) | 0.18 (0.06, 0.26) | 1051 | 446 | 605 |
| Shared environmental paths | | | | | | | | | | | | | |
| E & behaviour problem symptoms | c11 (95% CIs) | c21 (95% CIs) | c31 (95% CIs) | c41 (95% CIs) | c22 (95% CIs) | c23 (95% CIs) | c24 (95% CIs) | c33 (95% CIs) | c34 (95% CIs) | c44 (95% CIs) | N total | MZ | DZ |
| Preschool, childhood and adolescence poly-E & adulthood hyperactivity parent-rated | 0.60 (0.57, 0.63) | 0.04 (0.02, 0.06) | 0.02 (0.01, 0.04) | 0.01 (0.00, 0.02) | 0.12 (0.06, 0.17) | 0.06 (0.02, 0.13) | 0.00 (0.00, 0.01) | 0.32 (0.25, 0.37) | 0.00 (0.00, 0.01) | 0.00 (0.00, 0.01) | 1441 | 563 | 878 |
| Preschool, childhood and adolescence poly-E & adulthood conduct parent-rated | 0.50 (0.47, 0.53) | 0.03 (0.01, 0.05) | 0.04 (0.02, 0.07) | 0.01 (0.00, 0.04) | 0.17 (0.12, 0.22) | 0.14 (0.08, 0.21) | 0.00 (0.00, 0.01) | 0.24 (0.17, 0.30) | 0.00 (0.00, 0.02) | 0.00 (0.00, 0.04) | 1450 | 561 | 889 |
| Preschool, childhood and | 0.60 (0.58, 0.63) | 0.04 (0.02, | 0.02 (0.01, | 0.01 (0.00, | 0.11 (0.05, | 0.06 (0.01, | 0.00 (0.00, 0.03) | 0.32 (0.25, | 0.00 (0.00, | 0.00 (0.00, 0.05) | 1057 | 451 | 606 |

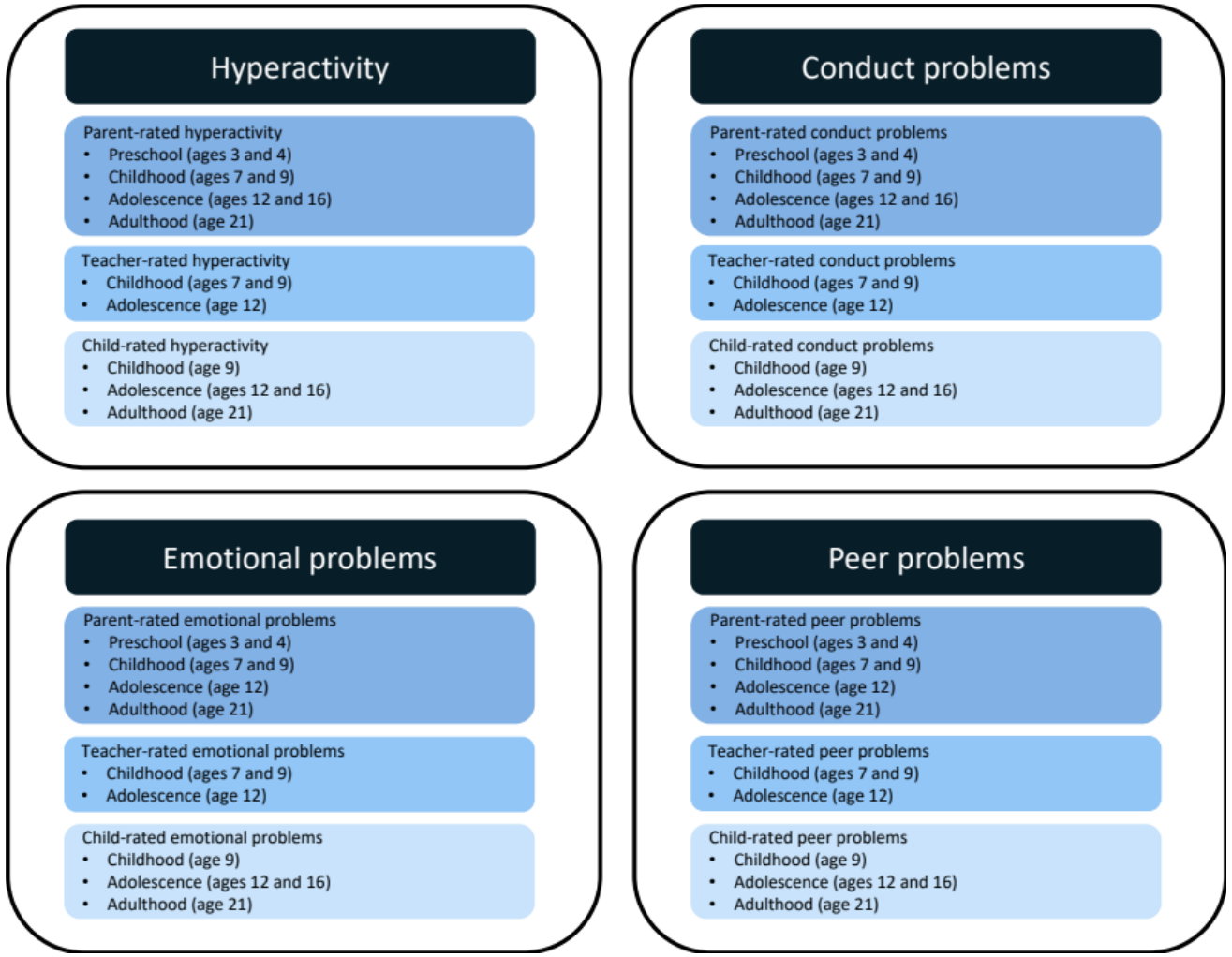
| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| adolescence poly-E & adulthood hyperactivity child-rated | | 0.07) | 0.04) | 0.03) | 0.16) | 0.11) | | 0.37) | 0.01) | | | | |
| Preschool, childhood and adolescence poly-E & adulthood conduct child-rated | 0.50 (0.47, 0.53) | 0.03 (0.01, 0.05) | 0.04 (0.03, 0.07) | 0.01 (0.00, 0.03) | 0.18 (0.13, 0.22) | 0.14 (0.08, 0.20) | 0.01 (0.00, 0.05) | 0.24 (0.17, 0.30) | 0.00 (0.00, 0.02) | 0.00 (0.00, 0.07) | 1051 | 446 | 605 |
| Nonshared environmental paths | | | | | | | | | | | | | |
| E & behaviour problem symptoms | e11 (95% CIs) | e21 (95% CIs) | e31 (95% CIs) | e41 (95% CIs) | e22 (95% CIs) | e23 (95% CIs) | e24 (95% CIs) | e33 (95% CIs) | e34 (95% CIs) | e44 (95% CIs) | N total | MZ | DZ |
| Preschool, childhood and adolescence poly-E & adulthood hyperactivity parent-rated | 0.10 (0.09, 0.10) | 0.01 (0.00, 0.01) | 0.00 (0.00, 0.00) | 0.01 (0.00, 0.02) | 0.14 (0.12, 0.15) | 0.01 (0.00, 0.01) | 0.01 (0.00, 0.03) | 0.13 (0.12, 0.14) | 0.00 (0.00, 0.00) | 0.40 (0.36, 0.44) | 1441 | 563 | 878 |
| Preschool, childhood and adolescence poly-E & adulthood conduct parent- | 0.13 (0.12, 0.14) | 0.01 (0.00, 0.01) | 0.00 (0.00, 0.00) | 0.01 (0.00, 0.01) | 0.14 (0.13, 0.16) | 0.01 (0.01, 0.01) | 0.02 (0.01, 0.03) | 0.13 (0.12, 0.14) | 0.00 (0.00, 0.00) | 0.43 (0.39, 0.46) | 1450 | 561 | 889 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| rated | | | | | | | | | | | | | |
| Preschool, childhood and adolescence poly-E & adulthood hyperactivity child-rated | 0.10 (0.09, 0.10) | 0.01 (0.00, 0.01) | 0.00 (0.00, 0.00) | 0.00 (0.00, 0.01) | 0.14 (0.12, 0.15) | 0.01 (0.00, 0.01) | 0.00 (0.00, 0.01) | 0.13 (0.12, 0.14) | 0.00 (0.00, 0.00) | 0.65 (0.61, 0.70) | 1057 | 451 | 606 |
| Preschool, childhood and adolescence poly-E & adulthood conduct child-rated | 0.13 (0.12, 0.14) | 0.01 (0.00, 0.01) | 0.00 (0.00, 0.00) | 0.00 (0.00, 0.01) | 0.14 (0.13, 0.16) | 0.01 (0.01, 0.02) | 0.00 (0.00, 0.01) | 0.13 (0.12, 0.14) | 0.00 (0.00, 0.01) | 0.73 (0.68, 0.78) | 1051 | 446 | 605 |
| Note. a= genetic path; c= shared environmental path; e= nonshared environmental path; CIs= confidence intervals; N= sample size; MZ= monozygotic twin pairs; DZ= dizygotic twin pairs. | | | | | | | | | | | | | |

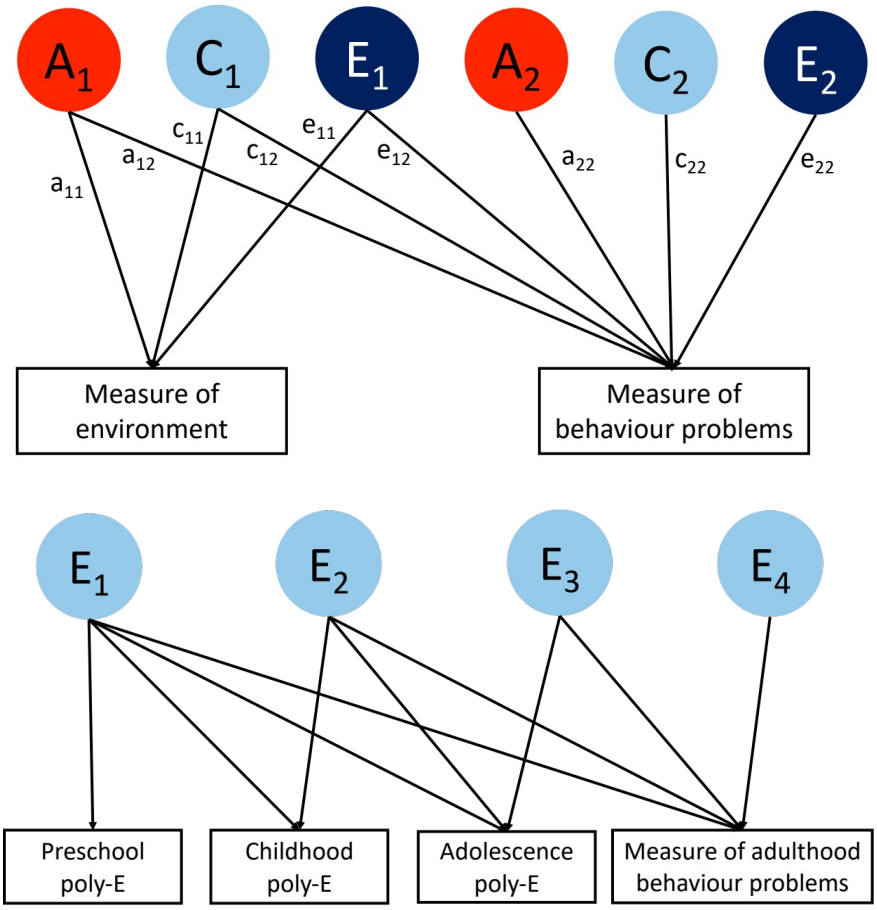
# Supplementary Figures




Supplementary Figure 1. Distribution of correlations between environmental measures and symptoms of behaviour problems. Histograms illustrating distributions of correlations between parent-rated environmental measures in preschool, childhood and adolescence and parent-rated behaviour problem symptoms measured at the subsequent age (e.g., environmental measures in preschool predicting behaviour problem symptoms in childhood). Numbers on top of the bars represent the number of environmental variables reaching the correlation with symptoms of behaviour problems as indicated on the x-axis.



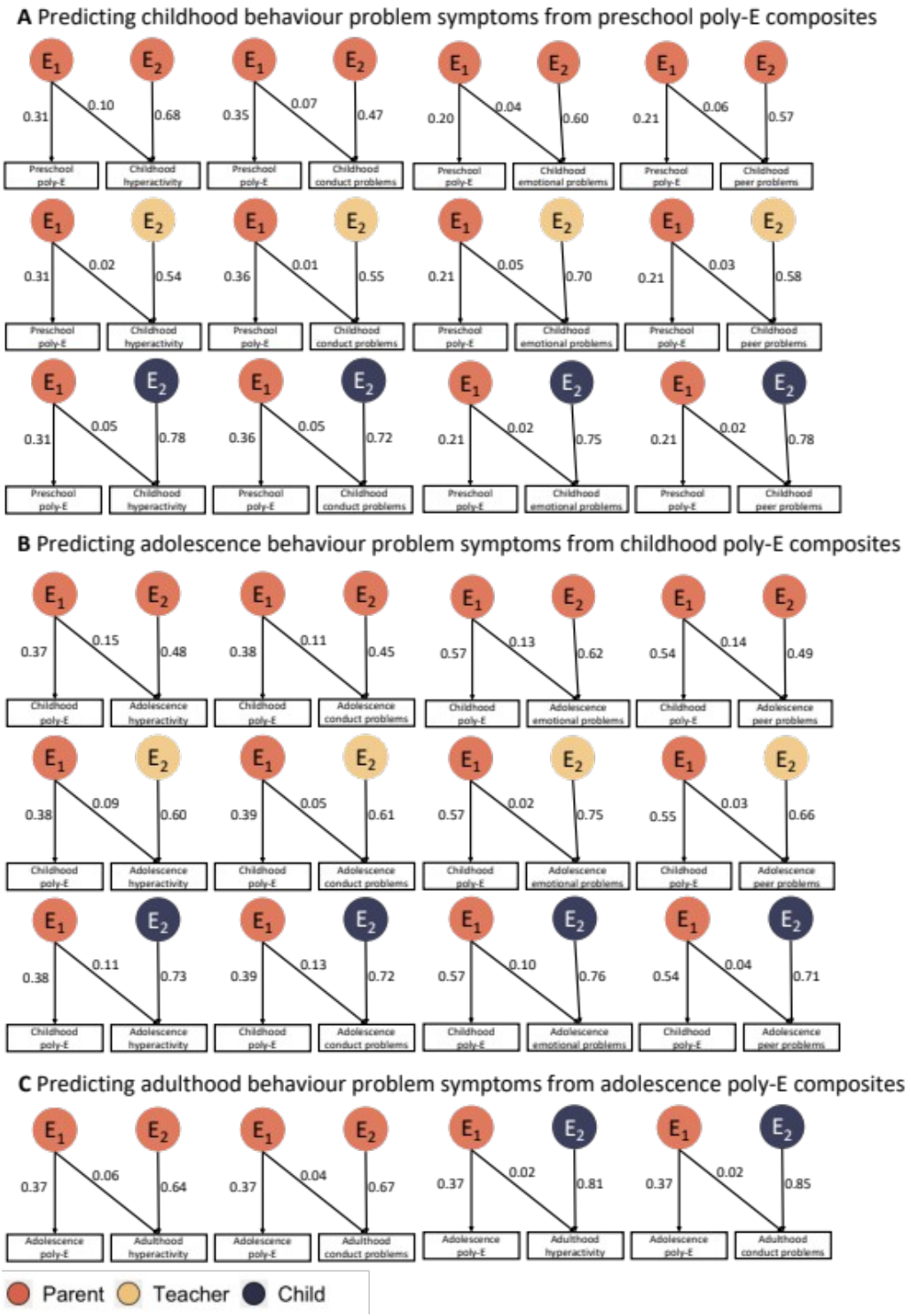

**Supplementary Figure 2. Behaviour problem measures and their composites across ages.**




Supplementary Figure 3. Cholesky decomposition models.

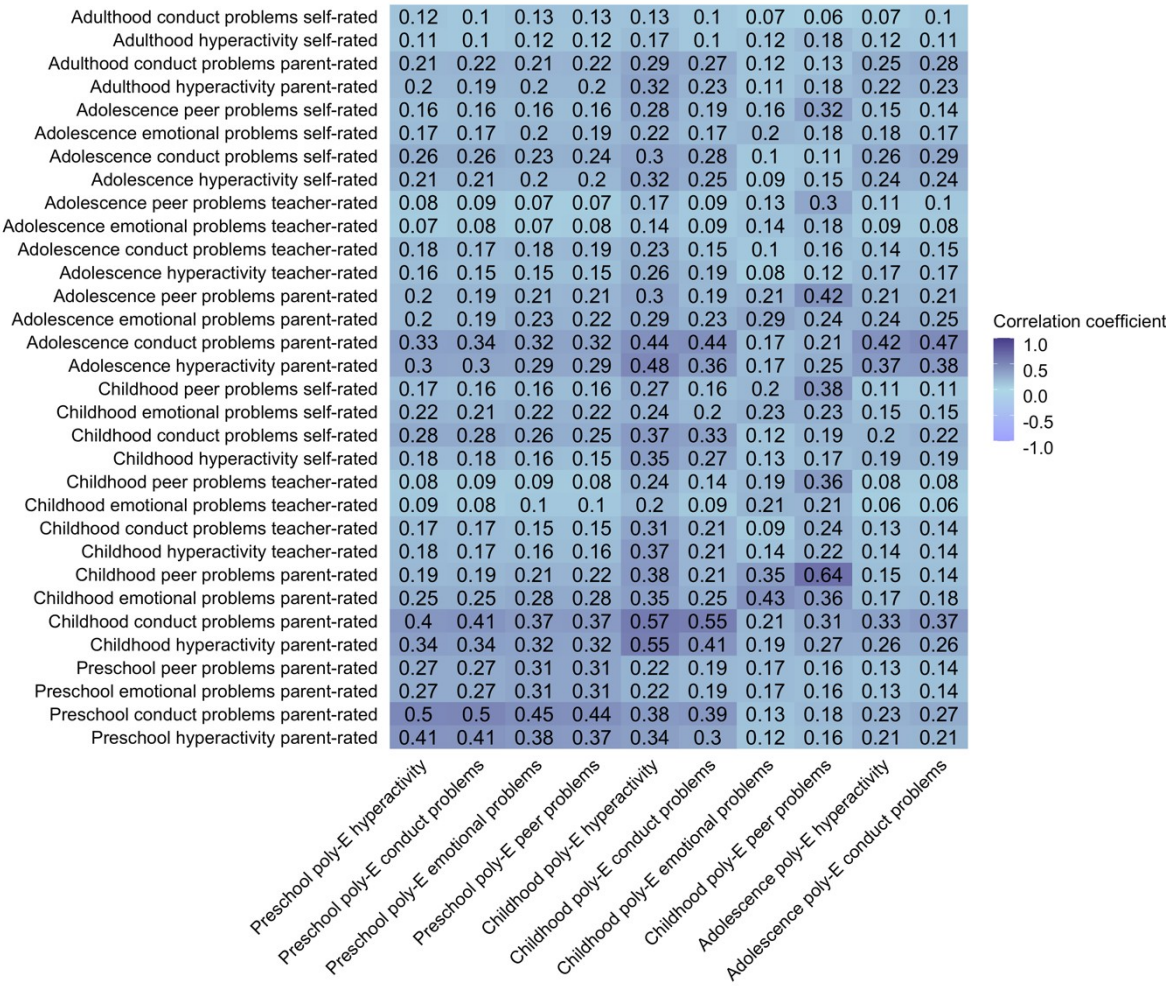
Panel A presents the bivariate genetic model (Cholesky decomposition) of a measure of environment and a measure of behaviour problem symptoms. A1, C1 and E1 are latent factors indexing genetic (A), common or shared environmental (C) and nonshared environmental (E) variance for the environmental measure . A2, C2 and E2 are latent factors indexing residual variance in the measure of behaviour problems independent of the environmental measure.

Panel B presents a multivariate Cholesky model of poly-E composites (i.e., environmental measures) in preschool, childhood and adolescence cumulatively predicting a measure of behaviour problem symptoms in adulthood. E1 is a latent factor indexing nonshared environmental factors influencing all four measures, while E4 is a latent factor indexing nonshared environmental factors specific to the measure of behaviour problems in adulthood after accounting for poly-E composites. For simplicity, this figure illustrates only the NSE components of variance and covariance.



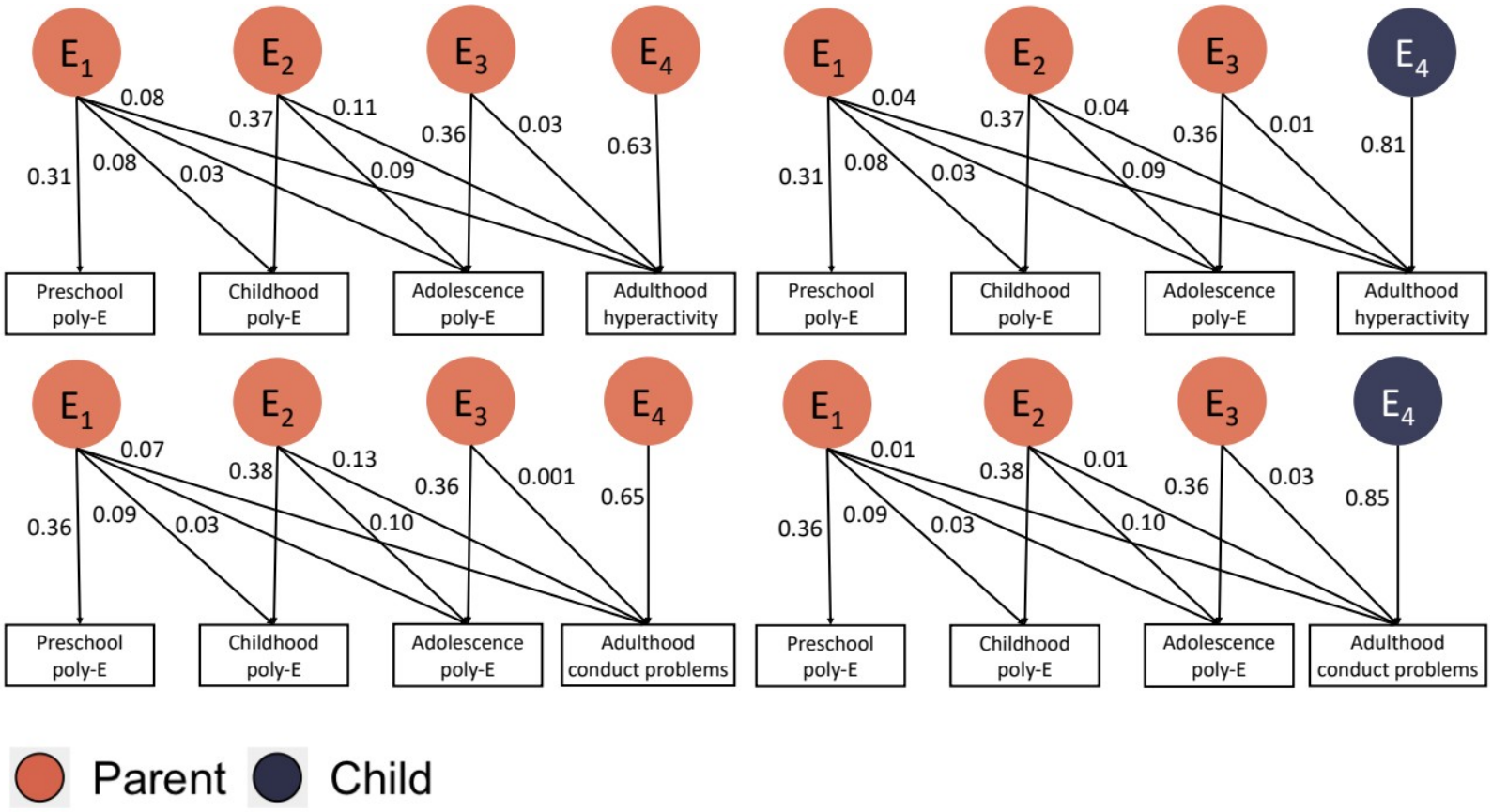

Supplementary Figure 4. Path diagrams of the bivariate Cholesky model.

Bivariate Cholesky model of poly-E composites (i.e., environmental measures) in preschool (A), childhood (B) and adolescence (C) and measures of behaviour problems in subsequent developmental stages. For simplicity, only the NSE components of variance and covariance are illustrated. Presented path estimates are standardised. Estimates in this figure are square roots of the path estimates in Supplementary Table 6.



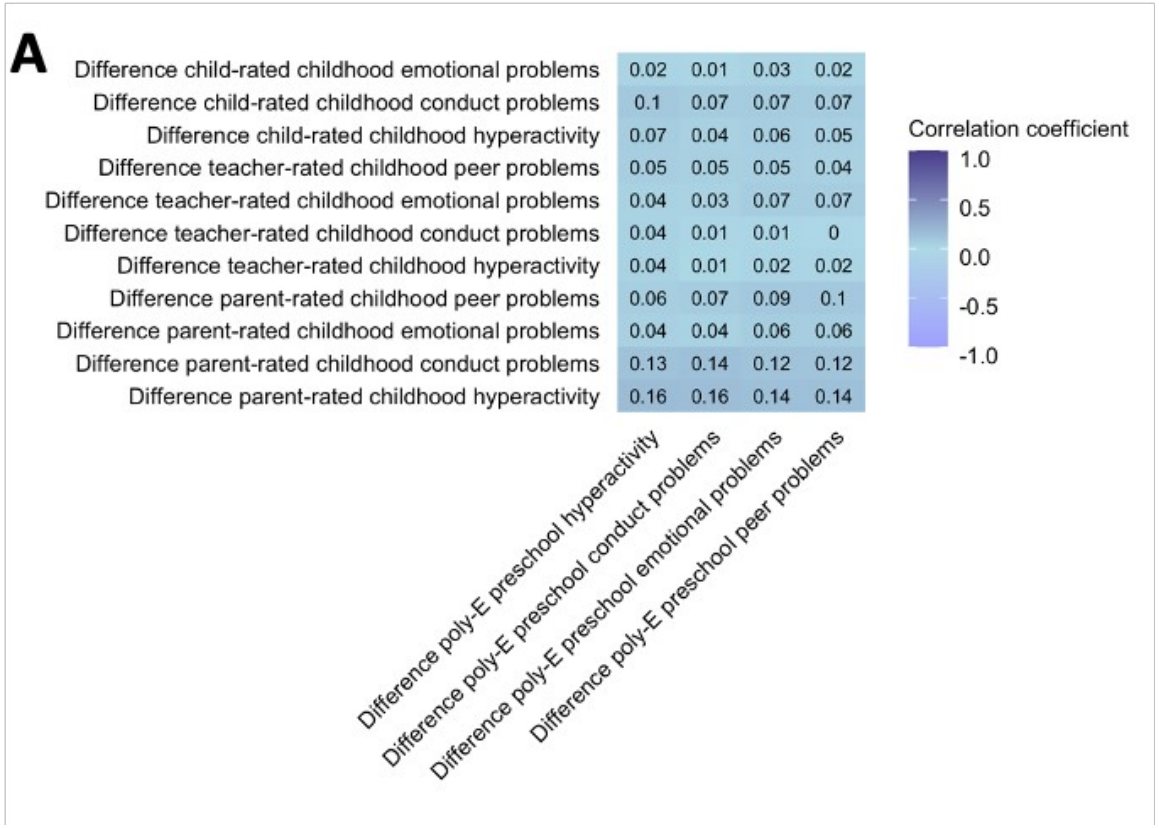

Supplementary Figure 5. Phenotypic correlations between poly-E composites (i.e., environmental measures) and behaviour problem symptoms.

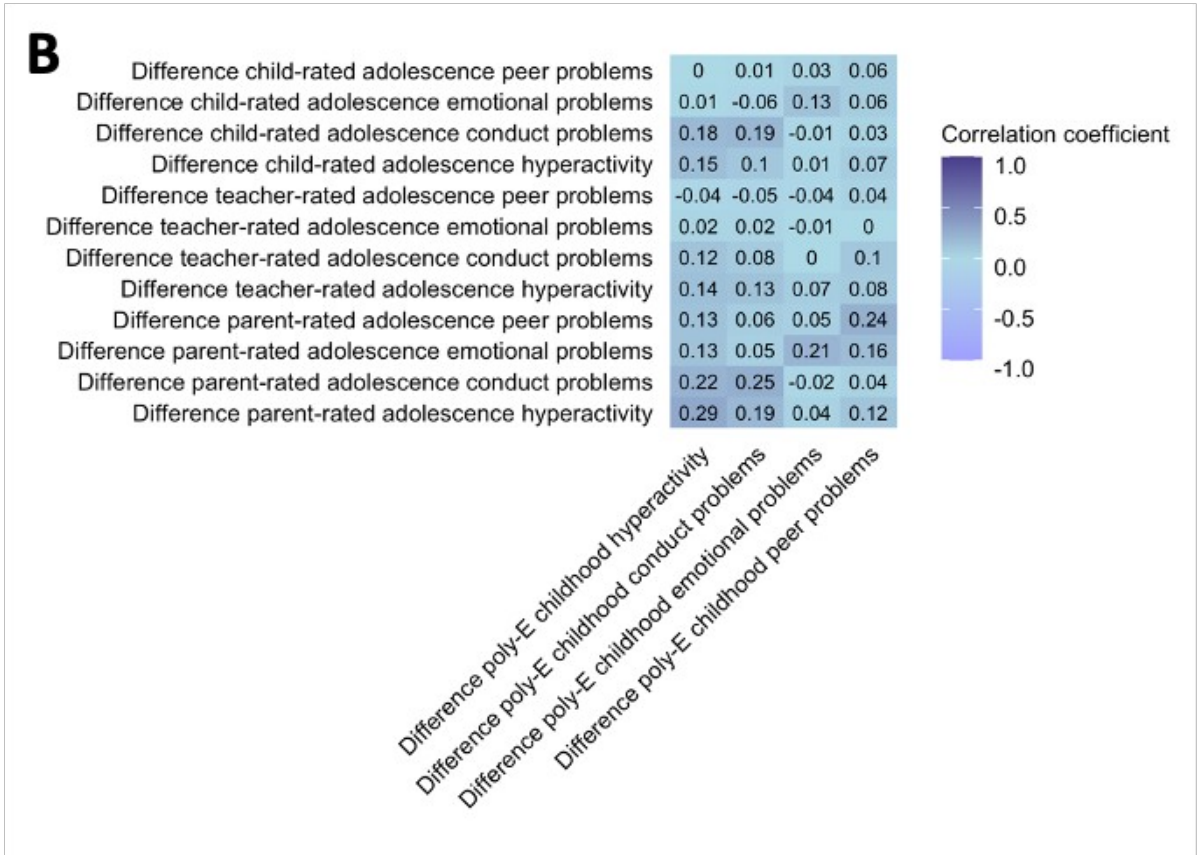
Correlations between poly-E composites (constructed for hyperactivity, conduct, emotional problems and peer problems) and behaviour problem symptoms (i.e., correlations between poly-E composites in preschool, childhood and adolescence and hyperactivity, conduct, emotional problems and peer problems at the same age, as well as subsequent ages).

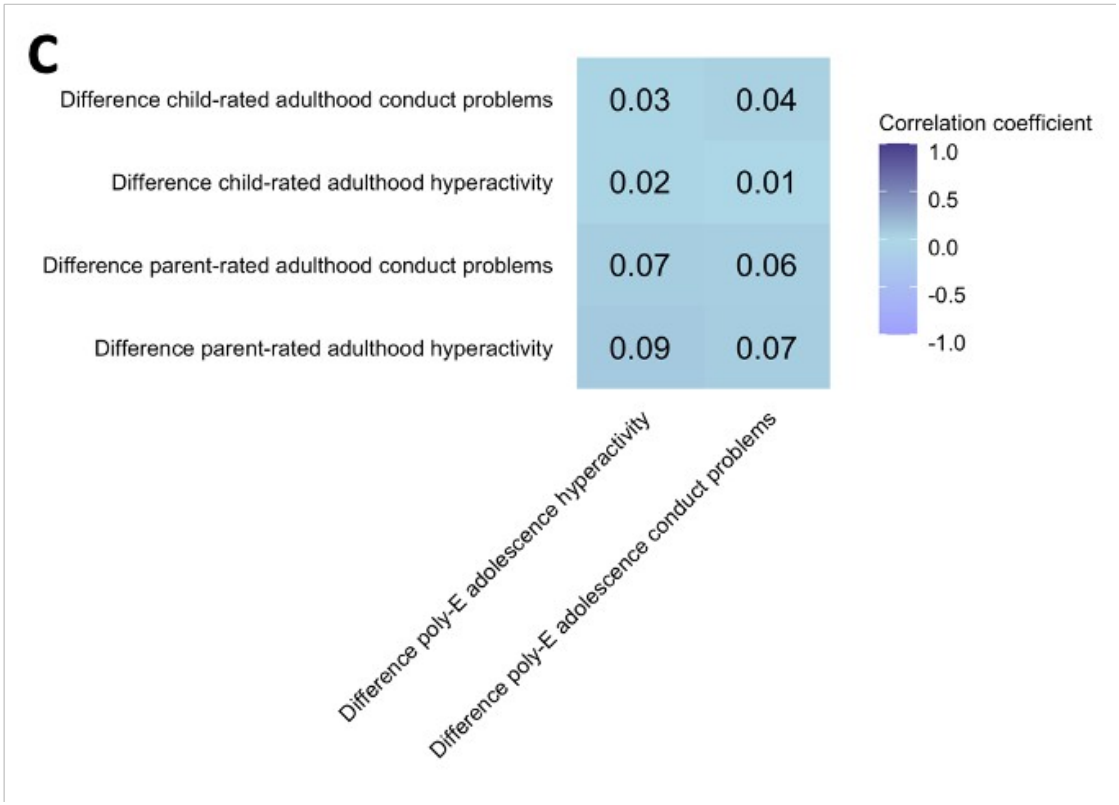



Supplementary Figure 6. Path diagrams of the multivariate Cholesky model.

Multivariate Cholesky analysis of poly-E composites (i.e., environmental measures) in preschool, childhood and adolescence cumulatively predicting hyperactivity and conduct in adulthood. E1 is a latent factor indexing nonshared environmental factors influencing all traits while E4 is a latent factor indexing nonshared environmental factors specific to behaviour problems measure. For simplicity, only the NSE components of variance and covariance are illustrated. Presented path estimates are standardised. Estimates in this figure are square roots of the path estimates in Supplementary Table 9.

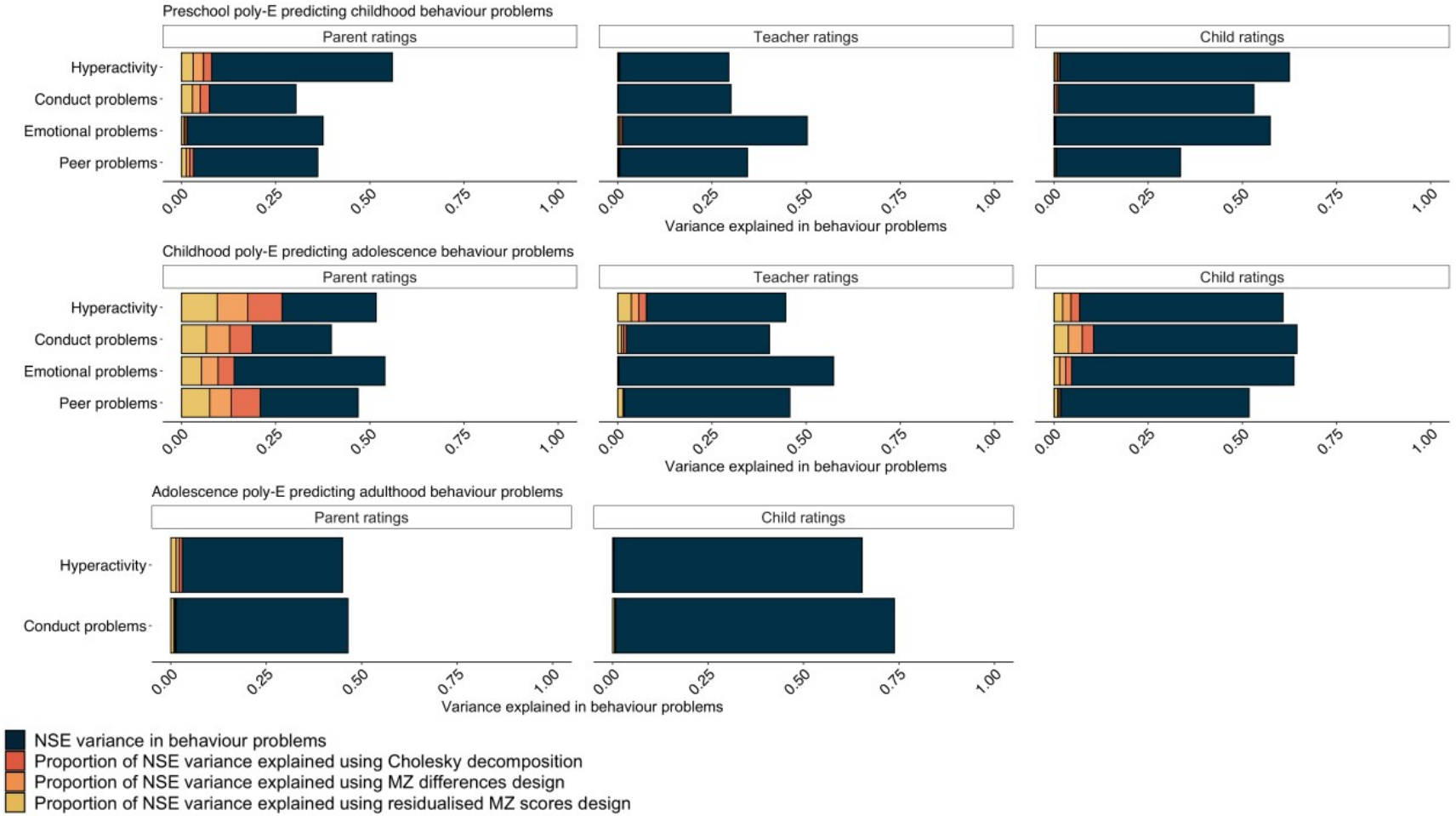

A
Difference child-rated childhood emotional problems
Difference child-rated childhood conduct problems
Difference child-rated childhood hyperactivity
Difference teacher-rated childhood peer problems
Difference teacher-rated childhood emotional problems
Difference teacher-rated childhood conduct problems
Difference teacher-rated childhood hyperactivity
Difference parent-rated childhood peer problems
Difference parent-rated childhood emotional problems
Difference parent-rated childhood conduct problems
Difference parent-rated childhood hyperactivity
0.02 0.01 0.03 0.02
0.1 0.07 0.07 0.07
0.07 0.04 0.06 0.05
0.05 0.05 0.05 0.04
0.04 0.03 0.07 0.07
0.04 0.01 0.01 0
0.04 0.01 0.02 0.02
0.06 0.07 0.09 0.1
0.04 0.04 0.06 0.06
0.13 0.14 0.12 0.12
0.16 0.16 0.14 0.14
Difference poly-E preschool hyperactivity
Difference poly-E preschool conduct problems
Difference poly-E preschool emotional problems
Difference poly-E preschool peer problems
Correlation coefficient
1.0
0.5
0.0
-0.5
-1.0


B
Difference child-rated adolescence peer problems
Difference child-rated adolescence emotional problems
Difference child-rated adolescence conduct problems
Difference child-rated adolescence hyperactivity
Difference teacher-rated adolescence peer problems
Difference teacher-rated adolescence emotional problems
Difference teacher-rated adolescence conduct problems
Difference teacher-rated adolescence hyperactivity
Difference parent-rated adolescence peer problems
Difference parent-rated adolescence emotional problems
Difference parent-rated adolescence conduct problems
Difference parent-rated adolescence hyperactivity
0 0.01 0.03 0.06
0.01 -0.06 0.13 0.06
0.18 0.19 -0.01 0.03
0.15 0.1 0.01 0.07
-0.04 -0.05 -0.04 0.04
0.02 0.02 -0.01 0
0.12 0.08 0 0.1
0.14 0.13 0.07 0.08
0.13 0.06 0.05 0.24
0.13 0.05 0.21 0.16
0.22 0.25 -0.02 0.04
0.29 0.19 0.04 0.12
Difference poly-E childhood hyperactivity
Difference poly-E childhood conduct problems
Difference poly-E childhood emotional problems
Difference poly-E childhood peer problems
Correlation coefficient
1.0
0.5
0.0
-0.5
-1.0



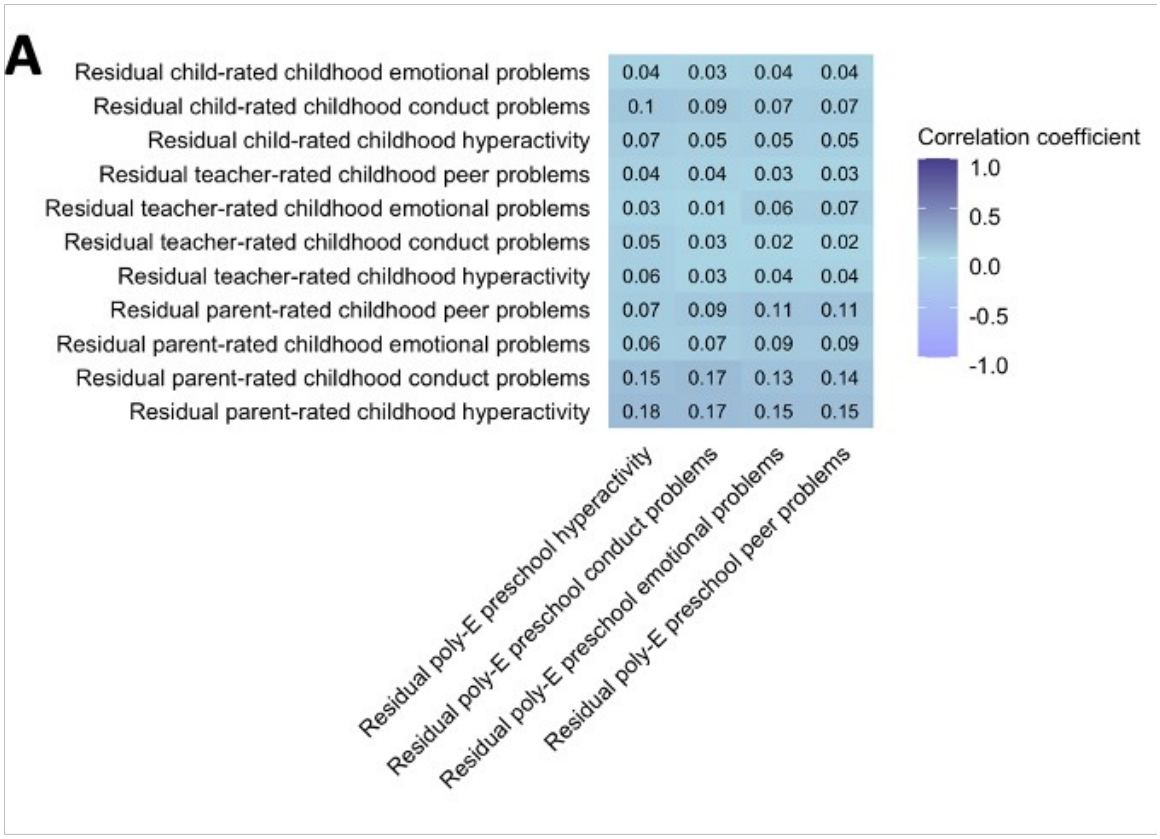

Supporting figure 7. Correlations between MZ difference scores.

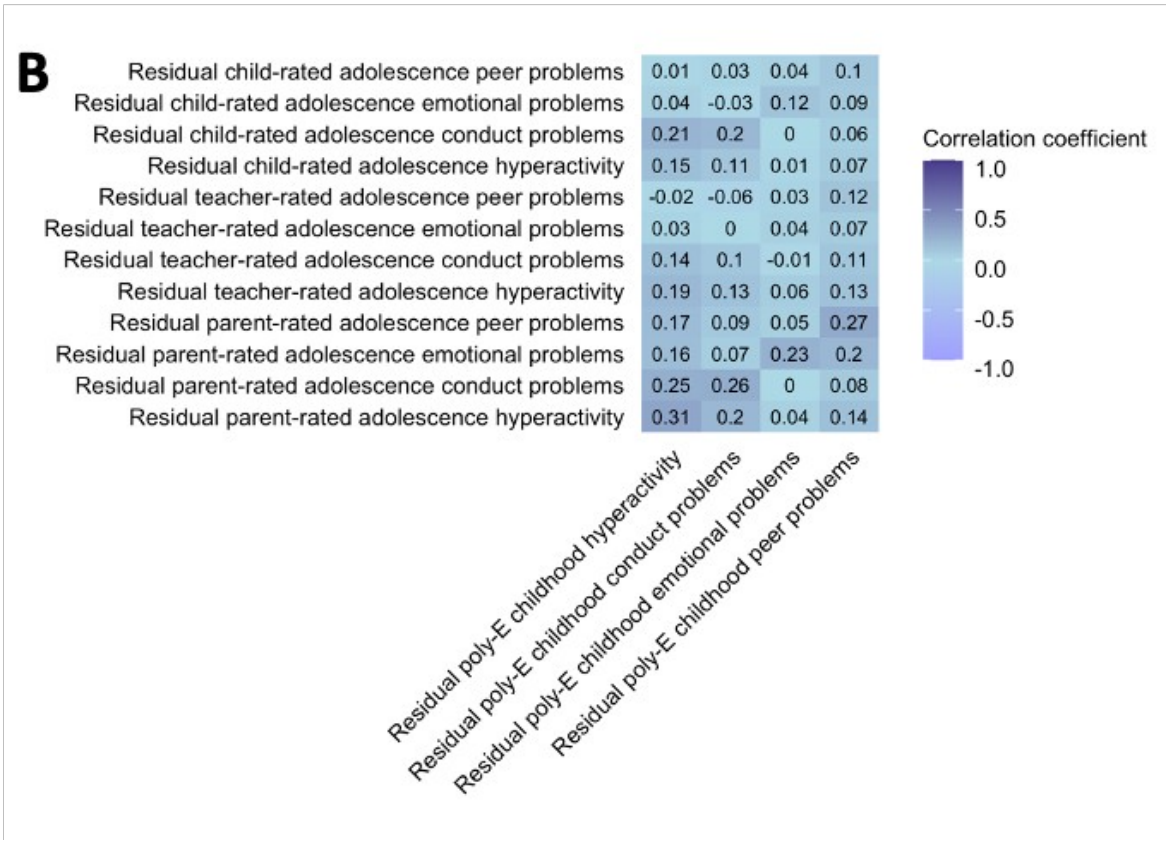
Correlations between MZ poly-E differences (i.e., environmental measures constructed for hyperactivity, conduct, emotional problems and peer problems) and MZ behaviour problem symptom differences in childhood (A), adolescence (B) and adulthood (C).

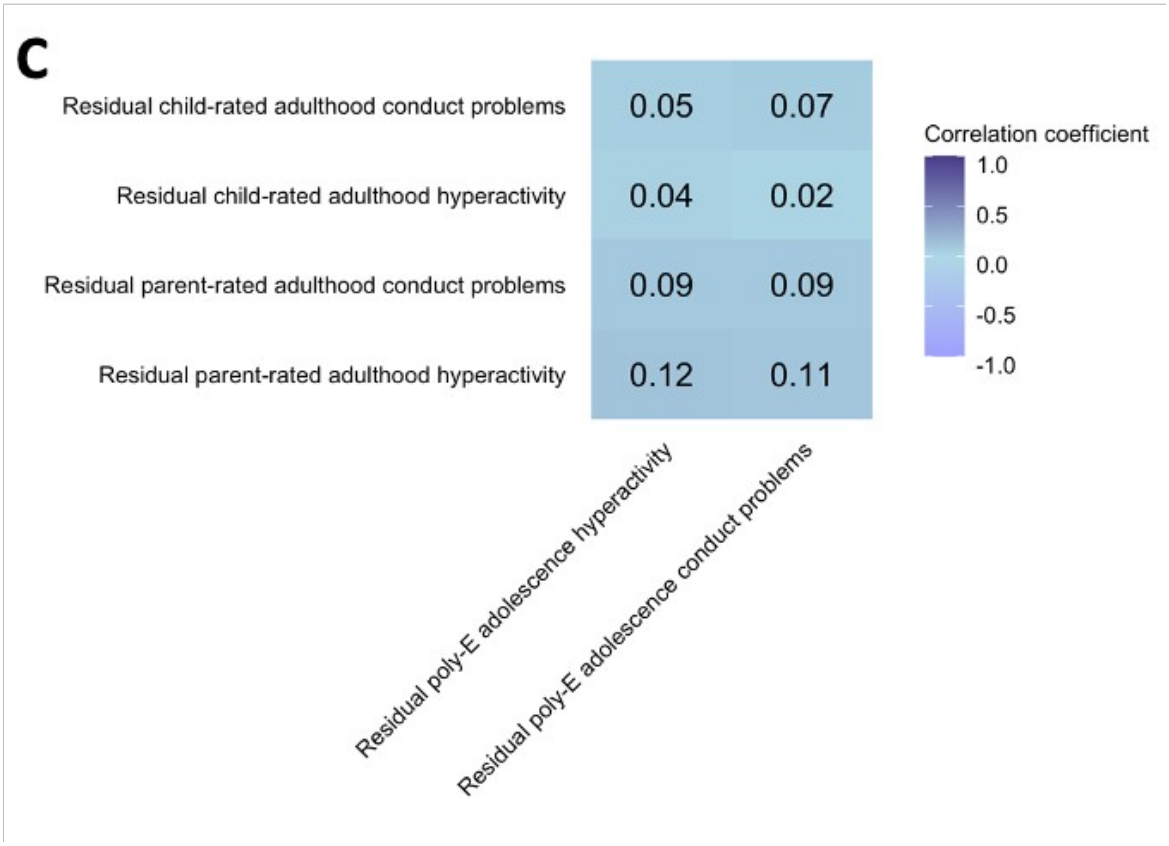



Supplementary Figure 8. Comparison of results obtained from MZ differences, residualised scores and Cholesky analyses.

Note. Variance explained in behaviour problems refers to the proportion of NSE variance explained by poly-E composites, not the total variance. For a detailed description, see Supplementary Note 5.


A
Residual child-rated childhood emotional problems 0.04 0.03 0.04 0.04
Residual child-rated childhood conduct problems 0.1 0.09 0.07 0.07
Residual child-rated childhood hyperactivity 0.07 0.05 0.05 0.05
Residual teacher-rated childhood peer problems 0.04 0.04 0.03 0.03
Residual teacher-rated childhood emotional problems 0.03 0.01 0.06 0.07
Residual teacher-rated childhood conduct problems 0.05 0.03 0.02 0.02
Residual teacher-rated childhood hyperactivity 0.06 0.03 0.04 0.04
Residual parent-rated childhood peer problems 0.07 0.09 0.11 0.11
Residual parent-rated childhood emotional problems 0.06 0.07 0.09 0.09
Residual parent-rated childhood conduct problems 0.15 0.17 0.13 0.14
Residual parent-rated childhood hyperactivity 0.18 0.17 0.15 0.15
Residual poly-E preschool hyperactivity
Residual poly-E preschool conduct problems
Residual poly-E preschool emotional problems
Residual poly-E preschool peer problems
Correlation coefficient
1.0
0.5
0.0
-0.5
-1.0


B
Residual child-rated adolescence peer problems 0.01 0.03 0.04 0.1
Residual child-rated adolescence emotional problems 0.04 -0.03 0.12 0.09
Residual child-rated adolescence conduct problems 0.21 0.2 0 0.06
Residual child-rated adolescence hyperactivity 0.15 0.11 0.01 0.07
Residual teacher-rated adolescence peer problems -0.02 -0.06 0.03 0.12
Residual teacher-rated adolescence emotional problems 0.03 0 0.04 0.07
Residual teacher-rated adolescence conduct problems 0.14 0.1 -0.01 0.11
Residual teacher-rated adolescence hyperactivity 0.19 0.13 0.06 0.13
Residual parent-rated adolescence peer problems 0.17 0.09 0.05 0.27
Residual parent-rated adolescence emotional problems 0.16 0.07 0.23 0.2
Residual parent-rated adolescence conduct problems 0.25 0.26 0 0.08
Residual parent-rated adolescence hyperactivity 0.31 0.2 0.04 0.14
Residual poly-E childhood hyperactivity
Residual poly-E childhood conduct problems
Residual poly-E childhood emotional problems
Residual poly-E childhood peer problems
Correlation coefficient
1.0
0.5
0.0
-0.5
-1.0




Supplementary Figure 9. Correlations between residual MZ scores.

Correlations between residual MZ poly-E scores (i.e., environmental measures constructed for hyperactivity, conduct, emotional problems and peer problems) and residual MZ behaviour problem symptom scores in childhood (A), adolescence (B) and adulthood (C

# Appendix 4

## Supplementary Notes

Supplementary Note 1: Hypotheses pre-registered with the Open Science Framework (OSF).

The following hypotheses were preregistered with the Open Science Framework (OSF) (https://osf.io/dzqnu/).

Hypothesis 1: Overall, environmental measures will predict more variance in developmental psychopathology symptoms than polygenic scores.
Hypothesis 2: The proportion of variance in symptoms of developmental psychopathology explained by G×E will be modest, generally less than 1%.
Hypothesis 3: Effects are likely to be stronger when the same person (parent or child) rates the environment and symptoms of developmental psychopathology as compared to cross-rater analyses.
Hypothesis 4: Stronger prediction will be achieved for externalizing (ADHD, conduct problems), rather than internalizing (anxiety, mood disorders) measures of developmental psychopathology.
Hypothesis 5: Effects will not differ substantially between males and females.

Although we expected to see differences in patterns of results across measures and raters, we focused on comparing the magnitude effect sizes ($R^2$), rather than statistical significance due to power limitations of the current sample. While large enough to detect effects of PGSs and environmental measures accounting for 1% of the variance with 80% power, according to power calculations performed by Duncan & Keller (2011), G×E effects explaining 0.1% of the variance require tens of thousands individuals to be detected (Plomin et al., 2022).

Supplementary Note 2: Description of the TEDS sample.

Our sampling frame consisted of up to 4013 unrelated twins born in England and Wales between 1994 and 1996 who have been enrolled in the Twins Early Development Study (TEDS) (Lockhart et al., 2023). The TEDS twins have been assessed a dozen times from infancy through early adulthood on a wide range of behavioural, psychological, cognitive, physical and environmental measures (Lockhart et al., 2023). Data collection procedures included questionnaires administered by post, by telephone and online, as described in an overview of TEDS (Lockhart et al., 2023). Details can be found in the TEDS data dictionary: https://www.teds.ac.uk/datadictionary/home.htm).

The sample of TEDS twins is representative of the UK population in terms of ethnicity and socioeconomic status (SES) (Error: Reference source not found); for details of representativeness and attrition, see Rimfeld et al. (2019). Individuals with severe medical conditions were excluded from analyses. These conditions include detrimental prenatal and postnatal conditions, as well as other conditions that could seriously impact later development. In addition, twins with uncertain and unknown zygosity were excluded from the analyses. Zygosity was recorded using a parent questionnaire of physical similarity between twins, with 95% accuracy when ascertained by DNA tests (Price et al., 2000).

Supplementary Note 3: Construction of the polygenic scores (PGSs).

PGSs were calculated as the weighted sums of each individual's genotype across all single nucleotides polymorphisms (SNPs):

$$PGS_{ki} = \sum_{j=i}^{m} \hat{\beta}_{kj} g_{kji}$$

Where $PGS_{ki}$ represents the individual i's polygenic score based on summary statistics from $GWA_k$. $\hat{\beta}_{kj}$is an estimate of marker j's effect size for discovery trait k, that is, the effect of having one copy of the reference allele at $SNP_{kj}$ . $g_{kji}$ is individual i's genotype at marker j for discovery trait k, coded as having either 0, 1 or 2 copies of the reference allele at marker kj.

We used PGSs constructed using LD-pred (Vilhjálmsson et al., 2015a)and LD-pred2 (Privé et al., 2020)with infinitesimal prior, which corrects for local linkage disequilibrium (LD; i.e. correlations between SNPs). We used the TEDS and UK Biobank samples as a reference panels for the LD structure for PGSs created using LD-pred and LD-pred2, respectively. We estimated the G, E, G+E and G×E prediction of developmental psychopathology symptoms, employing PGSs calculated using all SNPs, i.e., fraction 1 (Allegrini, Karhunen, et al., 2020).

Supplementary Note 4: Details of elastic net regularization.

We estimated the independent (G and E) and joint (G+E) prediction of the 14 PGSs and environmental measures using a shrinkage model referred to as elastic net regularization to overcome problems of multicollinearity and overfitting (Zou & Hastie, 2005).
Elastic net regularization tries to minimise the following loss function (Allegrini, Karhunen, et al., 2020)

$$||y - X\beta||2 + \lambda(\alpha*|\beta|1 + (1-\alpha)*|\beta|2)$$

where ||y–X'β||2 is the residual sum of squares, |β|2 is the sum of the squared betas (the L2 penalty), |β|1 is the sum of the absolute betas (the L1 penalty) and X is an N*P ('N' observations and 'P' predictors) matrix of polygenic scores and environmental measures (for details, see (Allegrini, Karhunen, et al., 2020)).

For every model tested, we performed the nested repeated cross-validation, using nestedcv for R (S. Bates et al., 2023; R Core Team, 2022). The nested repeated cross-validation splits the data into inner and outer folds. In the inner fold, performed the 10-fold cross-validation repeated 100 times to select the model that minimises the Root Mean Square Error (RMSE), which indicates the smallest cross-validation error (Fushiki, 2011). We then fitted the model on this inner fold and tested the model on the hold-out outer fold, followed by a final cross-validation performed on the entire dataset. The final model was fitted for the whole sample. We used the trained coefficients (i.e., regression weights) to identify the most predictive G and E factors. The joint effect of the PGSs and environmental variables was estimated by fitting all G and E predictors together in elastic net models for each developmental psychopathology phenotype and observing the additional variance explained.

Supplementary Note 5: Testing for gene environment correlation (rGE) using mediation models.

The mediation model estimates the indirect effect of the predictor (X) on the outcome (Y) via a mediator, i.e., an intervening variable (mediator; M; in this project, the single-timepoint or developmental environmental composite) by regressing M on X and regressing Y on both X and M using two separate equations (Baron & Kenny, 1986; Preacher & Kelley, 2011):

1) M_i=d_(M.X) +⟦aX i+e_(M.Xi)
Where Mi is the mediator for individual I; dM.X is the intercept for the mediator (M); aXi is the slope of M regressed on the predictor (X) and eM.Xi is the measurement error for individual i.

2) Y_i= d_(Y.MX)+ ⟦bM⟧_i+ ⟦c'X⟧_i+ e_(Y.MXi)
Where Yi is the outcome for individual I; dY.MX is the intercept for the outcome (Y); bMi is the slope of the outcome (Y) regressed on the mediator (M) controlling for the predictor (X); c'Xi is the slope of the outcome (Y) regressed on the predictor (X) controlling for the mediator (M) and eY.MX is the measurement error for individual i.

The indirect effect of the predictor on the outcome (i.e., the mediation effect) is defined by a^b^, with the sample estimate signified by the circumflex ("^").
When a^^ × b^^= c^^-⟦c^'⟧^, then c^^= a^^ × b^^+ c^(^'). Implementing SEM allows for, a^ and b^ can be derived simultaneously and for testing more complex models with latent class predictor, outcomes, and mediators.

Supplementary Note 6: Distributions and data transformations.

Skewedness of environmental and developmental psychopathology measures was assessed based on histograms and the skew statistic. Variables were transformed based on the skew being lower than -1 or greater than 1. Supplementary Table 11 presents the transformation methods used and comparison of skews prior to and following the transformation. Supplementary Figure 10Supplementary Figure 11 show distributions of environmental and developmental psychopathology scales. Supplementary Figure 12 shows correlations between untransformed and transformed variables.

# Supplementary Tables

Supplementary Table 1. Representativeness of the selected sample.

| Ethnicity and SES | Selected sample | 1st Contact sample | National equivalents[a,b] |
|---|---|---|---|
| % white | 99.9% | 91.7% | 93% |
| % mother A-levels or higher | 39.0% | 35.5% | 35% |
| % father A-levels or higher | 42.3% | 44.8% | 47% |
| % mother employed | 45.3% | 43.1% | 50% |
| % father employed | 85.8% | 91.6% | 91% |
| Note. [a] including cohort of parents with children born in late 1990s and early 2000s; [b] derived from Rimfeld, Malanchini, Spargo, et al. (2019). | | | |

Supplementary Table 9. List of the genome-wide polygenic scores (PGSs).

| Genome-wide association (GWA) study | N (cases/controls) |
|---|---|
| ADHD(Demontis et al., 2023) | 8691/38691 |
| Alcohol dependence (Walters et al., 2018) | 176,024 |
| Anorexia nervosa (Watson et al., 2019) | 16,992/55,525 |
| Anxiety disorders (Purves et al., 2020) | 26,104/58,113 |
| ASD (Grove et al., 2019) | 18,382/27,969 |
| Bipolar disorder (Mullins et al., 2021) | 41,917/ 371,549 |
| Major depressive disorder (Howard et al., 2019) | 170,756/329,443 |
| Externalising behaviour (Karlsson Linnér et al., 2021) | 1,492,085 |
| Neuroticism (Nagel et al., 2018) | 390278 |
| Obsessive-compulsive disorder (Arnold et al., 2018) | 2,688/7,037 |
| Post-traumatic stress disorder (Meier et al., 2019) | 1064538 |
| Schizophrenia (Trubetskoy et al., 2022) | 39,910/60,558 |
| Tourette syndrome (Yu et al., 2019) | 4,819/9,488 |
| Hypomania (Gidziela et al., in preparation) | 156,442 |

Note. *We used PGSs derived from GWA studies of those disorders suggested by Grotzinger et al. (2022), unless newer GWA studies have become available at the time of conducting analyses.

Supplementary Table 10. List of the environmental variables.

| Age of collection | Rater | Items & scales |
|---|---|---|
| Age 9 | Parent | Parent Feelings scale (Deater-Deckard, 2000)<br>• Being a Parent: wish child would leave alone<br>• Being a Parent: does not feel amused by child<br>• Being a Parent: child makes me angry<br>• Being a Parent: does not feel close to child<br>• Being a Parent: feel frustrated by child<br>• Being a Parent: not happy about relationship with child<br>• Being a Parent: feel impatient with child<br><br>Parent Chaos scale (Matheny et al., 1995)<br>• Chaos: no regular bedtime routine<br>• Chaos: cannot hear yourself think<br>• Chaos: a real zoo<br>• Chaos: we do not stay on top of things<br>• Chaos: usually a TV on<br>• Chaos: no calm atmosphere<br><br>Parent Discipline scale (Deater-Deckard et al., 1998)<br>• Discipline: does not explain or reason<br>• Discipline: be firm or calm<br>• Discipline: shout or tell off<br>• Discipline: smack<br><br>Life events<br>• Life Event: Birth of Younger Sibling<br>• Life Event: Divorce/Separation of Parents<br>• Life Event: Death of Grandparent<br>• Life Event: Death of Other Relative/Friend<br>• Life Event: Financial Difficulties<br>• Life Event: Hospitalisation of Elder Twin<br>• Life Event: Hospitalisation of Parent<br>• Life Event: Hospitalisation of Sibling<br>• Life Event: Hospitalisation of Younger Twin<br>• Life Event: Illness/Injury of Relative/Friend<br>• Life Event: Moved House<br>• Life Event: New Child<br>• Life Event: New Parent Figure<br>• Life Event: Other<br>• Life Event: Prolonged Separation from Parent<br>• Count of reported life events |
| Age 9 | Self | Self-reported Feelings scale (Deater-Deckard, 2000)<br>• Being a Parent: parent wishes I would leave alone |

| | | |
|---|---|---|
| | | • Being a Parent: parent does not find me funny<br>• Being a Parent: I make parent angry<br>• Being a Parent: I do not feel close to parent<br>• Being a Parent: I make parent frustrated<br>• Being a Parent: not happy about relationship with parent<br>• Being a Parent: parent gets impatient<br><br>Self-reported Chaos scale (Matheny et al., 1995)<br>• Chaos: no regular bedtime routine<br>• Chaos: cannot hear yourself think<br>• Chaos: a real zoo<br>• Chaos: we do not stay on top of things<br>• Chaos: usually a TV on<br>• Chaos: no calm atmosphere<br><br>Self-reported Discipline scale (Deater-Deckard et al., 1998)<br>• Discipline: parent rarely explains<br>• Discipline: parents are not firm<br>• Discipline: told off or shouted at<br>• Discipline: smacked |
| Age 12 | Parent | Parent Feelings scale (Deater-Deckard, 2000)<br>• Parental Feelings: impatient<br>• Parental Feelings: unhappy<br>• Parental Feelings: not amused<br>• Parental Feelings: leave me alone<br>• Parental Feelings: angry<br>• Parental Feelings: not close<br>• Parental Feelings: frustrated<br><br>Parent Chaos scale (Matheny et al., 1995)<br>• Chaos: no regular bedtime routine<br>• Chaos: cannot hear yourself think<br>• Chaos: we do not stay on top of things<br>• Chaos: usually a TV on<br>• Chaos: no calm atmosphere<br><br>Parent Discipline scale (Deater-Deckard et al., 1998)<br>• Discipline: smack<br>• Discipline: shout<br>• Discipline: rarely explain<br>• Discipline: not firm or calm |
| Age 12 | Self | Self-reported Feelings scale (Deater-Deckard, 2000)<br>• Being a Parent: parent gets impatient<br>• Being a Parent: not happy about relationship with parent<br>• Being a Parent: parent does not find me funny |

| | | |
|---|---|---|
| | | • Being a Parent: parent wishes I would leave alone<br>• Being a Parent: I make parent angry<br>• Being a Parent: I do not feel close to parent<br>• Being a Parent: I make parent frustrated,<br><br>Self-reported Chaos scale (Matheny et al., 1995)<br>• Chaos: no regular bedtime routine<br>• Chaos: cannot hear yourself think<br>• Chaos: a real zoo<br>• Chaos: we do not stay on top of things<br>• Chaos: usually a TV on<br>• Chaos: no calm atmosphere<br><br>Self-reported Discipline scale (Deater-Deckard et al., 1998)<br>• Discipline: smacked<br>• Discipline: told off or shouted at<br>• Discipline: parent rarely explains<br>• Discipline: parents are not firm |
| Age 16 | Parent | • Father highest qualification level<br>• Father SOC level<br>• Mother highest qualification level<br>• Mother SOC level<br>• Household income level |
| Age 16 | Self | Self-reported Chaos scale (Matheny et al., 1995)<br>• Chaos: no regular routine<br>• Chaos: cannot hear yourself think<br>• Chaos: a real zoo<br>• Chaos: we do not stay on top of things<br>• Chaos: usually a TV on<br>• Chaos: no calm atmosphere<br><br>Parental Control ("Child Care and Child Development: Results from the NICHD Study of Early Child Care and Youth Development," 2005)<br>• Parental Control: how late to stay up<br>• Parental Control: which friends<br>• Parental Control: which activities<br>• Parental Control: meet friends<br>• Parental Control: how you dress<br>• Parental Control: what you do with your money<br>• Parental Control: watch on TV<br>• Parental Control: religious training<br><br>Parental Monitoring ("Child Care and Child Development: Results from the NICHD Study of Early Child Care and Youth |

| | | |
|---|---|---|
| | | Development," 2005) Parental Monitoring: who spend time with<br>• Parental Monitoring: how spend free time<br>• Parental Monitoring: how spend money<br>• Parental Monitoring: where after school<br>• Parental Monitoring: where on weekend<br>• Parental Monitoring: problems at school |

Supplementary Table 11. Transformation methods and skew statistics.

| Variable | Rater | Transformation method | Skew before transformation | Skew after transformation |
|---|---|---|---|---|
| Environmental data | | | | |
| Life events | Parent | Square root | 1.31 | 0.16 |
| Developmental psychopathology | | | | |
| SDQ total behaviour problems | Parent | Square root | 1.34 | -0.16 |
| SDQ hyperactivity | Parent | Square root | 1.17 | -0.24 |
| SDQ conduct problems | Parent | Square root | 1.68 | 0.19 |
| SDQ conduct problems | Self | Square root | 1.35 | -0.22 |
| SDQ peer problems | Self | Square root | 1.35 | -0.11 |
| Conners total ADHD | Parent | Square root | 2.04 | 0.34 |
| Conners impulsivity | Parent | Square root | 2.45 | 0.55 |
| Conners inattention | Parent | Square root | 1.75 | 0.29 |
| ICUT callousness | Parent | Square root | 1.68 | 0.05 |
| ICUT callousness | Self | Square root | 1.36 | 0.23 |
| ARBQ anxiety | Parent | Square root | 2.10 | 0.36 |
| CASI anxiety | Self | Square root | 1.17 | -0.02 |
| MFQ depression | Parent | Inverse transformation | 4.00 | -1.02 |
| MFQ depression | Self | Square root | 1.90 | 0.41 |

Supplementary Table 12. Results of the G models, predicting developmental psychopathology using genome-wide polygenic scores (PGSs).

| Developmental psychopathology | R2 | RMSE | alpha | lambda | N |
|---|---|---|---|---|---|
| Parent-rated data | | | | | |
| SDQ total behaviour problems | 0.030 | 0.977 | 0.5 | 0.030 | 4010 |
| SDQ hyperactivity | 0.026 | 0.979 | 0.5 | 0.040 | 4006 |
| SDQ conduct problems | 0.031 | 0.980 | 0.5 | 0.020 | 4011 |
| Conner's total ADHD | 0.031 | 0.988 | 0.5 | 0.020 | 4010 |
| Conner's impulsivity | 0.022 | 0.987 | 0.5 | 0.020 | 4008 |
| Conner's inattention | 0.030 | 0.984 | 0.5 | 0.020 | 4010 |
| ICUT callous-unemotional traits | 0.018 | 0.963 | 0.5 | 0.020 | 4000 |
| ICUT callousness | 0.015 | 0.991 | 0.5 | 0.020 | 4007 |
| ICUT unemotionality | NA | 0.989 | 0.5 | 1.000 | 4012 |
| ICUT uncaring | 0.024 | 0.986 | 0.5 | 0.010 | 4012 |
| MFQ depression | 0.021 | 0.990 | 0.5 | 0.010 | 4013 |
| ARBQ anxiety | 0.019 | 0.994 | 0.5 | 0.020 | 4011 |
| Self-rated data | | | | | |
| SDQ total behaviour problems | 0.031 | 0.983 | 0.5 | 0.040 | 3997 |
| SDQ hyperactivity | 0.027 | 0.984 | 0.5 | 0.030 | 3999 |
| SDQ conduct problems | 0.033 | 0.981 | 0.5 | 0.020 | 3998 |
| SDQ emotional problems | 0.022 | 0.989 | 0.5 | 0.030 | 3999 |
| SDQ peer problems | 0.006 | 0.999 | 0.5 | 0.051 | 3999 |
| SWAN total ADHD | 0.042 | 0.977 | 0.5 | 0.020 | 902 |
| SWAN hyperactivity | 0.014 | 0.989 | 0.5 | 0.121 | 901 |
| SWAN inattention | 0.044 | 0.983 | 0.5 | 0.030 | 901 |
| ICUT callous-unemotional traits | 0.041 | 0.975 | 0.5 | 0.040 | 899 |
| ICUT callousness | 0.030 | 1.008 | 0.5 | 0.051 | 900 |
| ICUT unemotionality | 0.007 | 0.987 | 0.5 | 0.131 | 897 |
| ICUT uncaring | 0.043 | 0.986 | 0.5 | 0.040 | 899 |
| MFQ depression | 0.016 | 1.003 | 0.5 | 0.040 | 4002 |
| CASI anxiety | 0.020 | 0.989 | 0.5 | 0.020 | 4000 |
| HCL hypomania | NA | 0.985 | 0.5 | 1.000 | 1196 |

Note. G models= models using the PGSs to predict symptoms of developmental psychopathology; R2= proportion of variance explained; RMSE= root mean square error; N= sample size.

Supplementary Table 13. Results of the E models, predicting developmental psychopathology using environmental measures.

| Developmental psychopathology | R2 | RMSE | alpha | lambda | N |
|---|---|---|---|---|---|
| Age 9 | | | | | |
| Parent-rated data | | | | | |
| SDQ total behaviour problems | 0.144 | 0.890 | 0.5 | 0.051 | 1672 |
| SDQ hyperactivity | 0.102 | 0.905 | 0.5 | 0.061 | 1669 |
| SDQ conduct problems | 0.116 | 0.920 | 0.5 | 0.051 | 1673 |
| Conner's total ADHD | 0.116 | 0.920 | 0.5 | 0.040 | 1670 |
| Conner's impulsivity | 0.085 | 0.903 | 0.5 | 0.051 | 1668 |
| Conner's inattention | 0.104 | 0.933 | 0.5 | 0.051 | 1670 |
| ICUT callous-unemotional traits | 0.104 | 0.906 | 0.5 | 0.061 | 1670 |
| ICUT callousness | 0.067 | 0.953 | 0.5 | 0.071 | 1671 |
| ICUT unemotionality | 0.049 | 0.953 | 0.5 | 0.061 | 1673 |
| ICUT uncaring | 0.107 | 0.933 | 0.5 | 0.071 | 1673 |
| MFQ depression | 0.060 | 0.961 | 0.5 | 0.051 | 1672 |
| ARBQ anxiety | 0.056 | 0.959 | 0.5 | 0.030 | 1670 |
| Self-rated data | | | | | |
| SDQ total behaviour problems | 0.071 | 0.946 | 0.5 | 0.061 | 1519 |
| SDQ hyperactivity | 0.052 | 0.958 | 0.5 | 0.091 | 1519 |
| SDQ conduct problems | 0.047 | 0.966 | 0.5 | 0.071 | 1518 |
| SDQ emotional problems | 0.022 | 1.006 | 0.5 | 0.051 | 1519 |
| SDQ peer problems | 0.040 | 0.979 | 0.5 | 0.051 | 1519 |
| SWAN total ADHD | 0.040 | 0.961 | 0.5 | 0.081 | 616 |
| SWAN hyperactivity | 0.039 | 0.947 | 0.5 | 0.121 | 615 |
| SWAN inattention | 0.019 | 0.979 | 0.5 | 0.121 | 616 |
| ICUT callous-unemotional traits | 0.077 | 0.971 | 0.5 | 0.131 | 614 |
| ICUT callousness | NA | 0.987 | 0.5 | 0.071 | 615 |
| ICUT unemotionality | 0.022 | 0.972 | 0.5 | 0.111 | 614 |
| ICUT uncaring | 0.061 | 0.981 | 0.5 | 0.121 | 615 |
| MFQ depression | 0.011 | 0.965 | 0.5 | 0.121 | 1520 |
| CASI anxiety | 0.033 | 0.998 | 0.5 | 0.081 | 1520 |
| HCL hypomania | 0.037 | 0.973 | 0.5 | 0.091 | 495 |
| Age 12 | | | | | |
| Parent-rated data | | | | | |
| SDQ total behaviour problems | 0.184 | 0.887 | 0.5 | 0.030 | 3263 |
| SDQ hyperactivity | 0.131 | 0.913 | 0.5 | 0.010 | 3260 |
| SDQ conduct problems | 0.152 | 0.911 | 0.5 | 0.030 | 3264 |
| Conner's total ADHD | 0.156 | 0.905 | 0.5 | 0.010 | 3264 |
| Conner's impulsivity | 0.110 | 0.922 | 0.5 | 0.040 | 3262 |
| Conner's inattention | 0.141 | 0.915 | 0.5 | 0.030 | 3264 |
| ICUT callous-unemotional traits | 0.128 | 0.904 | 0.5 | 0.010 | 3255 |

| | | | | | |
|---|---|---|---|---|---|
| ICUT callousness | 0.094 | 0.941 | 0.5 | 0.010 | 3261 |
| ICUT unemotionality | 0.033 | 0.975 | 0.5 | 0.020 | 3265 |
| ICUT uncaring | 0.133 | 0.932 | 0.5 | 0.000 | 3265 |
| MFQ depression | 0.064 | 0.961 | 0.5 | 0.010 | 3266 |
| ARBQ anxiety | 0.057 | 0.966 | 0.5 | 0.030 | 3264 |
| Self-rated data | | | | | |
| SDQ total behaviour problems | 0.078 | 0.946 | 0.5 | 0.051 | 3184 |
| SDQ hyperactivity | 0.059 | 0.970 | 0.5 | 0.040 | 3186 |
| SDQ conduct problems | 0.075 | 0.958 | 0.5 | 0.030 | 3185 |
| SDQ emotional problems | 0.020 | 0.975 | 0.5 | 0.030 | 3186 |
| SDQ peer problems | 0.038 | 0.986 | 0.5 | 0.030 | 3186 |
| SWAN total ADHD | 0.072 | 0.963 | 0.5 | 0.061 | 722 |
| SWAN hyperactivity | 0.061 | 0.962 | 0.5 | 0.061 | 721 |
| SWAN inattention | 0.067 | 0.975 | 0.5 | 0.030 | 722 |
| ICUT callous-unemotional traits | 0.097 | 0.948 | 0.5 | 0.061 | 720 |
| ICUT callousness | 0.078 | 0.993 | 0.5 | 0.131 | 721 |
| ICUT unemotionality | 0.023 | 0.992 | 0.5 | 0.121 | 721 |
| ICUT uncaring | 0.092 | 0.963 | 0.5 | 0.091 | 721 |
| MFQ depression | 0.018 | 0.982 | 0.5 | 0.040 | 3189 |
| CASI anxiety | 0.041 | 0.979 | 0.5 | 0.030 | 3187 |
| HCL hypomania | 0.027 | 0.971 | 0.5 | 0.051 | 967 |
| Age 16 | | | | | |
| Parent-rated data | | | | | |
| SDQ total behaviour problems | 0.049 | 0.924 | 0.5 | 0.030 | 1059 |
| SDQ hyperactivity | 0.044 | 0.930 | 0.5 | 0.040 | 1058 |
| SDQ conduct problems | 0.034 | 0.934 | 0.5 | 0.051 | 1060 |
| Conner's total ADHD | 0.024 | 0.929 | 0.5 | 0.040 | 1059 |
| Conner's impulsivity | 0.021 | 0.901 | 0.5 | 0.040 | 1057 |
| Conner's inattention | 0.019 | 0.946 | 0.5 | 0.051 | 1059 |
| ICUT callous-unemotional traits | 0.034 | 0.921 | 0.5 | 0.071 | 1060 |
| ICUT callousness | 0.020 | 0.988 | 0.5 | 0.081 | 1060 |
| ICUT unemotionality | 0.008 | 0.973 | 0.5 | 0.091 | 1061 |
| ICUT uncaring | 0.036 | 0.941 | 0.5 | 0.040 | 1061 |
| MFQ depression | 0.020 | 0.959 | 0.5 | 0.000 | 1060 |
| ARBQ anxiety | NA | 0.910 | 0.5 | 1.000 | 1060 |
| Self-rated data | | | | | |
| SDQ total behaviour problems | 0.184 | 0.878 | 0.5 | 0.020 | 1526 |
| SDQ hyperactivity | 0.114 | 0.912 | 0.5 | 0.051 | 1526 |
| SDQ conduct problems | 0.146 | 0.905 | 0.5 | 0.051 | 1526 |
| SDQ emotional problems | 0.100 | 0.972 | 0.5 | 0.030 | 1526 |
| SDQ peer problems | 0.076 | 0.952 | 0.5 | 0.010 | 1526 |
| SWAN total ADHD | 0.106 | 0.895 | 0.5 | 0.071 | 618 |
| SWAN hyperactivity | 0.066 | 0.922 | 0.5 | 0.071 | 618 |

| | | | | | |
|---|---|---|---|---|---|
| SWAN inattention | 0.115 | 0.900 | 0.5 | 0.071 | 618 |
| ICUT callous-unemotional traits | 0.175 | 0.881 | 0.5 | 0.061 | 615 |
| ICUT callousness | 0.106 | 0.940 | 0.5 | 0.081 | 616 |
| ICUT unemotionality | 0.056 | 0.992 | 0.5 | 0.121 | 614 |
| ICUT uncaring | 0.168 | 0.891 | 0.5 | 0.071 | 615 |
| MFQ depression | 0.073 | 0.927 | 0.5 | 0.020 | 1532 |
| CASI anxiety | 0.134 | 0.938 | 0.5 | 0.030 | 1531 |
| HCL hypomania | 0.035 | 0.999 | 0.5 | 0.131 | 484 |

Note. E models= models using environmental data to predict symptoms of developmental psychopathology; R2= proportion of variance explained; RMSE= root mean square error; N= sample size.

Supplementary Table 14. Results of the G+E models, predicting developmental psychopathology using genome-wide polygenic scores and environmental measures.

| Developmental psychopathology | R2 | RMSE | alpha | lambda | N |
|---|---|---|---|---|---|
| Age 9 | | | | | |
| Parent-rated data | | | | | |
| SDQ total behaviour problems | 0.169 | 0.878 | 0.5 | 0.051 | 1672 |
| SDQ hyperactivity | 0.121 | 0.897 | 0.5 | 0.061 | 1669 |
| SDQ conduct problems | 0.142 | 0.907 | 0.5 | 0.040 | 1673 |
| Conner's total ADHD | 0.131 | 0.913 | 0.5 | 0.051 | 1670 |
| Conner's impulsivity | 0.096 | 0.898 | 0.5 | 0.051 | 1668 |
| Conner's inattention | 0.121 | 0.924 | 0.5 | 0.051 | 1670 |
| ICUT callous-unemotional traits | 0.124 | 0.897 | 0.5 | 0.061 | 1670 |
| ICUT callousness | 0.085 | 0.944 | 0.5 | 0.061 | 1671 |
| ICUT unemotionality | 0.049 | 0.953 | 0.5 | 0.071 | 1673 |
| ICUT uncaring | 0.131 | 0.921 | 0.5 | 0.061 | 1673 |
| MFQ depression | 0.075 | 0.954 | 0.5 | 0.051 | 1672 |
| ARBQ anxiety | 0.074 | 0.951 | 0.5 | 0.030 | 1670 |
| Self-rated data | | | | | |
| SDQ total behaviour problems | 0.102 | 0.931 | 0.5 | 0.061 | 1519 |
| SDQ hyperactivity | 0.076 | 0.946 | 0.5 | 0.071 | 1519 |
| SDQ conduct problems | 0.082 | 0.949 | 0.5 | 0.061 | 1518 |
| SDQ emotional problems | 0.043 | 0.996 | 0.5 | 0.061 | 1519 |
| SDQ peer problems | 0.052 | 0.974 | 0.5 | 0.051 | 1519 |
| SWAN total ADHD | 0.073 | 0.946 | 0.5 | 0.061 | 616 |
| SWAN hyperactivity | 0.049 | 0.943 | 0.5 | 0.111 | 615 |
| SWAN inattention | 0.078 | 0.951 | 0.5 | 0.051 | 616 |
| ICUT callous-unemotional traits | 0.106 | 0.958 | 0.5 | 0.121 | 614 |
| ICUT callousness | 0.109 | 0.975 | 0.5 | 0.071 | 615 |
| ICUT unemotionality | 0.034 | 0.969 | 0.5 | 0.121 | 614 |
| ICUT uncaring | 0.106 | 0.959 | 0.5 | 0.091 | 615 |
| MFQ depression | 0.023 | 0.961 | 0.5 | 0.111 | 1520 |
| CASI anxiety | 0.050 | 0.988 | 0.5 | 0.051 | 1520 |
| HCL hypomania | 0.038 | 0.976 | 0.5 | 0.131 | 495 |
| Age 12 | | | | | |
| Parent-rated data | | | | | |
| SDQ total behaviour problems | 0.201 | 0.878 | 0.5 | 0.030 | 3263 |
| SDQ hyperactivity | 0.146 | 0.905 | 0.5 | 0.030 | 3260 |
| SDQ conduct problems | 0.171 | 0.901 | 0.5 | 0.030 | 3264 |
| Conner's total ADHD | 0.175 | 0.896 | 0.5 | 0.030 | 3264 |
| Conner's impulsivity | 0.123 | 0.915 | 0.5 | 0.030 | 3262 |
| Conner's inattention | 0.163 | 0.903 | 0.5 | 0.020 | 3264 |
| ICUT callous-unemotional traits | 0.140 | 0.897 | 0.5 | 0.010 | 3255 |

| | | | | | |
|---|---|---|---|---|---|
| ICUT callousness | 0.102 | 0.937 | 0.5 | 0.020 | 3261 |
| ICUT unemotionality | 0.035 | 0.973 | 0.5 | 0.020 | 3265 |
| ICUT uncaring | 0.149 | 0.924 | 0.5 | 0.010 | 3265 |
| MFQ depression | 0.080 | 0.953 | 0.5 | 0.020 | 3266 |
| ARBQ anxiety | 0.073 | 0.958 | 0.5 | 0.020 | 3264 |
| Self-rated data | | | | | |
| SDQ total behaviour problems | 0.100 | 0.935 | 0.5 | 0.040 | 3184 |
| SDQ hyperactivity | 0.082 | 0.958 | 0.5 | 0.020 | 3186 |
| SDQ conduct problems | 0.096 | 0.947 | 0.5 | 0.030 | 3185 |
| SDQ emotional problems | 0.040 | 0.965 | 0.5 | 0.030 | 3186 |
| SDQ peer problems | 0.042 | 0.984 | 0.5 | 0.040 | 3186 |
| SWAN total ADHD | 0.104 | 0.948 | 0.5 | 0.061 | 722 |
| SWAN hyperactivity | 0.082 | 0.952 | 0.5 | 0.061 | 721 |
| SWAN inattention | 0.104 | 0.959 | 0.5 | 0.051 | 722 |
| ICUT callous-unemotional traits | 0.156 | 0.916 | 0.5 | 0.030 | 720 |
| ICUT callousness | 0.110 | 0.976 | 0.5 | 0.081 | 721 |
| ICUT unemotionality | 0.033 | 0.989 | 0.5 | 0.131 | 721 |
| ICUT uncaring | 0.153 | 0.929 | 0.5 | 0.030 | 721 |
| MFQ depression | 0.036 | 0.973 | 0.5 | 0.030 | 3189 |
| CASI anxiety | 0.059 | 0.970 | 0.5 | 0.030 | 3187 |
| HCL hypomania | NA | 0.983 | 0.5 | 1.000 | 967 |
| Age 12 | | | | | |
| Parent-rated data | | | | | |
| SDQ total behaviour problems | 0.074 | 0.913 | 0.5 | 0.051 | 1059 |
| SDQ hyperactivity | 0.062 | 0.922 | 0.5 | 0.051 | 1058 |
| SDQ conduct problems | 0.062 | 0.921 | 0.5 | 0.051 | 1060 |
| Conner's total ADHD | 0.044 | 0.921 | 0.5 | 0.051 | 1059 |
| Conner's impulsivity | 0.035 | 0.895 | 0.5 | 0.061 | 1057 |
| Conner's inattention | 0.036 | 0.940 | 0.5 | 0.091 | 1059 |
| ICUT callous-unemotional traits | 0.044 | 0.918 | 0.5 | 0.091 | 1060 |
| ICUT callousness | 0.031 | 0.983 | 0.5 | 0.081 | 1060 |
| ICUT unemotionality | NA | 0.976 | 0.5 | 1.000 | 1061 |
| ICUT uncaring | 0.051 | 0.935 | 0.5 | 0.071 | 1061 |
| MFQ depression | 0.038 | 0.953 | 0.5 | 0.071 | 1060 |
| ARBQ anxiety | 0.041 | 0.893 | 0.5 | 0.040 | 1060 |
| Self-rated data | | | | | |
| SDQ total behaviour problems | 0.206 | 0.866 | 0.5 | 0.020 | 1526 |
| SDQ hyperactivity | 0.132 | 0.903 | 0.5 | 0.051 | 1526 |
| SDQ conduct problems | 0.174 | 0.890 | 0.5 | 0.040 | 1526 |
| SDQ emotional problems | 0.120 | 0.961 | 0.5 | 0.030 | 1526 |
| SDQ peer problems | 0.085 | 0.949 | 0.5 | 0.030 | 1526 |
| SWAN total ADHD | 0.131 | 0.884 | 0.5 | 0.071 | 618 |
| SWAN hyperactivity | 0.067 | 0.925 | 0.5 | 0.121 | 618 |

| | | | | | |
|---|---|---|---|---|---|
| SWAN inattention | 0.149 | 0.884 | 0.5 | 0.061 | 618 |
| ICUT callous-unemotional traits | 0.196 | 0.871 | 0.5 | 0.061 | 615 |
| ICUT callousness | 0.124 | 0.932 | 0.5 | 0.081 | 616 |
| ICUT unemotionality | 0.061 | 0.990 | 0.5 | 0.121 | 614 |
| ICUT uncaring | 0.193 | 0.879 | 0.5 | 0.071 | 615 |
| MFQ depression | 0.087 | 0.921 | 0.5 | 0.030 | 1532 |
| CASI anxiety | 0.146 | 0.933 | 0.5 | 0.051 | 1531 |
| HCL hypomania | NA | 1.012 | 0.5 | 1.000 | 484 |

Note. G+E models= models using both the PGSs and environmental data to predict symptoms of developmental psychopathology; R2= proportion of variance explained; RMSE= root mean square error; N= sample size.

Supplementary Table 15. Results of the G+E models, predicting developmental psychopathology using genome-wide polygenic scores and environmental measures in the total sample, including dizygotic co-twins.

| Developmental psychopathology | R2 | RMSE | alpha | lambda | N |
|---|---|---|---|---|---|
| Age 9 | | | | | |
| Parent-rated data | | | | | |
| SDQ total behaviour problems | 0.171 | 0.895 | 0.5 | 0.030 | 2466 |
| SDQ hyperactivity | 0.123 | 0.917 | 0.5 | 0.030 | 2462 |
| SDQ conduct problems | 0.153 | 0.908 | 0.5 | 0.020 | 2467 |
| Conner's total ADHD | 0.139 | 0.922 | 0.5 | 0.030 | 2461 |
| Conner's impulsivity | 0.100 | 0.913 | 0.5 | 0.051 | 2458 |
| Conner's inattention | 0.126 | 0.935 | 0.5 | 0.040 | 2461 |
| ICUT callous-unemotional traits | 0.137 | 0.903 | 0.5 | 0.020 | 2463 |
| ICUT callousness | 0.092 | 0.944 | 0.5 | 0.040 | 2465 |
| ICUT unemotionality | 0.056 | 0.972 | 0.5 | 0.040 | 2467 |
| ICUT uncaring | 0.138 | 0.923 | 0.5 | 0.030 | 2467 |
| MFQ depression | 0.083 | 0.946 | 0.5 | 0.030 | 2464 |
| ARBQ anxiety | 0.070 | 0.948 | 0.5 | 0.020 | 2463 |
| Self-rated data | | | | | |
| SDQ total behaviour problems | 0.091 | 0.946 | 0.5 | 0.040 | 2223 |
| SDQ hyperactivity | 0.070 | 0.958 | 0.5 | 0.051 | 2223 |
| SDQ conduct problems | 0.080 | 0.956 | 0.5 | 0.051 | 2222 |
| SDQ emotional problems | 0.041 | 0.997 | 0.5 | 0.040 | 2223 |
| SDQ peer problems | 0.039 | 0.984 | 0.5 | 0.051 | 2223 |
| SWAN total ADHD | 0.051 | 0.963 | 0.5 | 0.081 | 893 |
| SWAN hyperactivity | 0.042 | 0.963 | 0.5 | 0.091 | 892 |
| SWAN inattention | 0.056 | 0.958 | 0.5 | 0.051 | 893 |
| ICUT callous-unemotional traits | 0.089 | 0.955 | 0.5 | 0.071 | 890 |
| ICUT callousness | 0.091 | 0.953 | 0.5 | 0.040 | 891 |
| ICUT unemotionality | 0.045 | 0.978 | 0.5 | 0.051 | 890 |
| ICUT uncaring | 0.082 | 0.953 | 0.5 | 0.061 | 891 |
| MFQ depression | 0.017 | 0.970 | 0.5 | 0.071 | 2225 |
| CASI anxiety | 0.046 | 0.994 | 0.5 | 0.051 | 2225 |
| HCL hypomania | 0.049 | 0.984 | 0.5 | 0.101 | 735 |
| Age 12 | | | | | |
| Parent-rated data | | | | | |
| SDQ total behaviour problems | 0.197 | 0.886 | 0.5 | 0.020 | 4898 |
| SDQ hyperactivity | 0.140 | 0.913 | 0.5 | 0.020 | 4894 |
| SDQ conduct problems | 0.172 | 0.905 | 0.5 | 0.020 | 4899 |
| Conner's total ADHD | 0.169 | 0.894 | 0.5 | 0.030 | 4897 |
| Conner's impulsivity | 0.121 | 0.918 | 0.5 | 0.020 | 4894 |
| Conner's inattention | 0.153 | 0.908 | 0.5 | 0.020 | 4897 |

| | | | | | |
|---|---|---|---|---|---|
| ICUT callous-unemotional traits | 0.135 | 0.906 | 0.5 | 0.020 | 4886 |
| ICUT callousness | 0.095 | 0.941 | 0.5 | 0.010 | 4894 |
| ICUT unemotionality | 0.036 | 0.982 | 0.5 | 0.030 | 4899 |
| ICUT uncaring | 0.140 | 0.930 | 0.5 | 0.010 | 4899 |
| MFQ depression | 0.078 | 0.949 | 0.5 | 0.010 | 4900 |
| ARBQ anxiety | 0.070 | 0.958 | 0.5 | 0.020 | 4899 |
| Self-rated data | | | | | |
| SDQ total behaviour problems | 0.096 | 0.937 | 0.5 | 0.030 | 4784 |
| SDQ hyperactivity | 0.072 | 0.963 | 0.5 | 0.040 | 4786 |
| SDQ conduct problems | 0.094 | 0.954 | 0.5 | 0.020 | 4785 |
| SDQ emotional problems | 0.034 | 0.967 | 0.5 | 0.020 | 4786 |
| SDQ peer problems | 0.039 | 0.980 | 0.5 | 0.030 | 4786 |
| SWAN total ADHD | 0.087 | 0.947 | 0.5 | 0.040 | 1049 |
| SWAN hyperactivity | 0.063 | 0.958 | 0.5 | 0.061 | 1048 |
| SWAN inattention | 0.080 | 0.957 | 0.5 | 0.051 | 1049 |
| ICUT callous-unemotional traits | 0.112 | 0.926 | 0.5 | 0.040 | 1046 |
| ICUT callousness | 0.092 | 0.951 | 0.5 | 0.040 | 1047 |
| ICUT unemotionality | 0.028 | 0.991 | 0.5 | 0.091 | 1047 |
| ICUT uncaring | 0.101 | 0.938 | 0.5 | 0.061 | 1047 |
| MFQ depression | 0.026 | 0.973 | 0.5 | 0.020 | 4789 |
| CASI anxiety | 0.055 | 0.975 | 0.5 | 0.030 | 4788 |
| HCL hypomania | 0.033 | 0.976 | 0.5 | 0.040 | 1473 |
| Age 16 | | | | | |
| Parent-rated data | | | | | |
| SDQ total behaviour problems | 0.072 | 0.931 | 0.5 | 0.030 | 1580 |
| SDQ hyperactivity | 0.059 | 0.940 | 0.5 | 0.030 | 1578 |
| SDQ conduct problems | 0.057 | 0.933 | 0.5 | 0.030 | 1581 |
| Conner's total ADHD | 0.046 | 0.936 | 0.5 | 0.040 | 1580 |
| Conner's impulsivity | 0.031 | 0.910 | 0.5 | 0.040 | 1577 |
| Conner's inattention | 0.042 | 0.958 | 0.5 | 0.051 | 1580 |
| ICUT callous-unemotional traits | 0.051 | 0.920 | 0.5 | 0.020 | 1582 |
| ICUT callousness | 0.037 | 0.969 | 0.5 | 0.040 | 1582 |
| ICUT unemotionality | NA | 0.994 | 0.5 | 0.091 | 1583 |
| ICUT uncaring | 0.046 | 0.941 | 0.5 | 0.040 | 1583 |
| MFQ depression | 0.040 | 0.959 | 0.5 | 0.061 | 1582 |
| ARBQ anxiety | 0.029 | 0.904 | 0.5 | 0.040 | 1582 |
| Self-rated data | | | | | |
| SDQ total behaviour problems | 0.201 | 0.867 | 0.5 | 0.030 | 2248 |
| SDQ hyperactivity | 0.137 | 0.913 | 0.5 | 0.040 | 2248 |
| SDQ conduct problems | 0.152 | 0.906 | 0.5 | 0.040 | 2248 |
| SDQ emotional problems | 0.108 | 0.967 | 0.5 | 0.020 | 2248 |
| SDQ peer problems | 0.080 | 0.942 | 0.5 | 0.020 | 2248 |
| SWAN total ADHD | 0.088 | 0.916 | 0.5 | 0.121 | 888 |

| | | | | | |
|---|---|---|---|---|---|
| SWAN hyperactivity | 0.058 | 0.942 | 0.5 | 0.101 | 888 |
| SWAN inattention | 0.117 | 0.899 | 0.5 | 0.051 | 888 |
| ICUT callous-unemotional traits | 0.176 | 0.863 | 0.5 | 0.051 | 887 |
| ICUT callousness | 0.121 | 0.907 | 0.5 | 0.051 | 888 |
| ICUT unemotionality | 0.052 | 0.991 | 0.5 | 0.111 | 886 |
| ICUT uncaring | 0.160 | 0.871 | 0.5 | 0.071 | 887 |
| MFQ depression | 0.068 | 0.936 | 0.5 | 0.030 | 2255 |
| CASI anxiety | 0.137 | 0.938 | 0.5 | 0.030 | 2254 |
| HCL hypomania | 0.068 | 0.978 | 0.5 | 0.061 | 724 |

Note. G+E models= models using both the PGSs and environmental data to predict symptoms of developmental psychopathology; R2= proportion of variance explained; RMSE= root mean square error; N= sample size.

Supplementary Table 16. Results of the cross-rater G+E models, predicting parent-rated developmental psychopathology using genome-wide polygenic scores and self-rated environmental measures and vice versa.

| Developmental psychopathology | R2 | RMSE | alpha | lambda | N |
|---|---|---|---|---|---|
| Age 9 | | | | | |
| Parent-rated data | | | | | |
| SDQ total behaviour problems | 0.116 | 0.897 | 0.5 | 0.061 | 1534 |
| SDQ hyperactivity | 0.104 | 0.897 | 0.5 | 0.020 | 1530 |
| SDQ conduct problems | 0.094 | 0.927 | 0.5 | 0.040 | 1535 |
| Conner's total ADHD | 0.104 | 0.917 | 0.5 | 0.020 | 1532 |
| Conner's impulsivity | 0.072 | 0.902 | 0.5 | 0.030 | 1530 |
| Conner's inattention | 0.092 | 0.927 | 0.5 | 0.040 | 1532 |
| ICUT callous-unemotional traits | 0.098 | 0.902 | 0.5 | 0.030 | 1531 |
| ICUT callousness | 0.066 | 0.949 | 0.5 | 0.040 | 1533 |
| ICUT unemotionality | 0.042 | 0.957 | 0.5 | 0.040 | 1534 |
| ICUT uncaring | 0.096 | 0.939 | 0.5 | 0.081 | 1534 |
| MFQ depression | 0.034 | 0.963 | 0.5 | 0.061 | 1533 |
| ARBQ anxiety | 0.043 | 0.957 | 0.5 | 0.030 | 1531 |
| Self-rated data | | | | | |
| SDQ total behaviour problems | 0.108 | 0.922 | 0.5 | 0.051 | 1656 |
| SDQ hyperactivity | 0.068 | 0.947 | 0.5 | 0.071 | 1656 |
| SDQ conduct problems | 0.089 | 0.942 | 0.5 | 0.051 | 1655 |
| SDQ emotional problems | 0.062 | 0.987 | 0.5 | 0.051 | 1656 |
| SDQ peer problems | 0.042 | 0.973 | 0.5 | 0.061 | 1656 |
| SWAN total ADHD | 0.061 | 0.959 | 0.5 | 0.121 | 669 |
| SWAN hyperactivity | 0.033 | 0.959 | 0.5 | 0.162 | 668 |
| SWAN inattention | 0.026 | 0.985 | 0.5 | 0.202 | 669 |
| ICUT callous-unemotional traits | 0.079 | 0.959 | 0.5 | 0.121 | 668 |
| ICUT callousness | 0.078 | 0.990 | 0.5 | 0.111 | 669 |
| ICUT unemotionality | NA | 0.981 | 0.5 | 1.000 | 668 |
| ICUT uncaring | 0.114 | 0.950 | 0.5 | 0.091 | 669 |
| MFQ depression | 0.028 | 0.970 | 0.5 | 0.071 | 1656 |
| CASI anxiety | 0.056 | 0.992 | 0.5 | 0.061 | 1655 |
| HCL hypomania | NA | 0.984 | 0.5 | 1.000 | 529 |
| Age 12 | | | | | |
| Parent-rated data | | | | | |
| SDQ total behaviour problems | 0.124 | 0.915 | 0.5 | 0.020 | 3195 |
| SDQ hyperactivity | 0.096 | 0.932 | 0.5 | 0.030 | 3192 |
| SDQ conduct problems | 0.099 | 0.937 | 0.5 | 0.020 | 3196 |
| Conner's total ADHD | 0.103 | 0.934 | 0.5 | 0.020 | 3196 |
| Conner's impulsivity | 0.070 | 0.944 | 0.5 | 0.020 | 3194 |
| Conner's inattention | 0.095 | 0.939 | 0.5 | 0.020 | 3196 |

| | | | | | |
|---|---|---|---|---|---|
| ICUT callous-unemotional traits | 0.081 | 0.931 | 0.5 | 0.030 | 3188 |
| ICUT callousness | 0.058 | 0.965 | 0.5 | 0.030 | 3194 |
| ICUT unemotionality | 0.023 | 0.978 | 0.5 | 0.051 | 3197 |
| ICUT uncaring | 0.091 | 0.956 | 0.5 | 0.040 | 3197 |
| MFQ depression | 0.041 | 0.969 | 0.5 | 0.020 | 3198 |
| ARBQ anxiety | 0.044 | 0.973 | 0.5 | 0.030 | 3197 |
| Self-rated data | | | | | |
| SDQ total behaviour problems | 0.086 | 0.946 | 0.5 | 0.030 | 3253 |
| SDQ hyperactivity | 0.063 | 0.965 | 0.5 | 0.040 | 3255 |
| SDQ conduct problems | 0.081 | 0.956 | 0.5 | 0.040 | 3254 |
| SDQ emotional problems | 0.039 | 0.973 | 0.5 | 0.040 | 3255 |
| SDQ peer problems | 0.019 | 0.996 | 0.5 | 0.061 | 3255 |
| SWAN total ADHD | 0.104 | 0.952 | 0.5 | 0.040 | 739 |
| SWAN hyperactivity | 0.055 | 0.971 | 0.5 | 0.081 | 738 |
| SWAN inattention | 0.122 | 0.953 | 0.5 | 0.051 | 739 |
| ICUT callous-unemotional traits | 0.094 | 0.947 | 0.5 | 0.051 | 737 |
| ICUT callousness | 0.080 | 0.999 | 0.5 | 0.111 | 738 |
| ICUT unemotionality | 0.028 | 0.983 | 0.5 | 0.091 | 738 |
| ICUT uncaring | 0.088 | 0.960 | 0.5 | 0.081 | 738 |
| MFQ depression | 0.025 | 0.986 | 0.5 | 0.040 | 3258 |
| CASI anxiety | 0.049 | 0.976 | 0.5 | 0.030 | 3256 |
| HCL hypomania | NA | 0.985 | 0.5 | 1.000 | 990 |
| Age 16 | | | | | |
| Parent-rated data | | | | | |
| SDQ total behaviour problems | 0.114 | 0.875 | 0.5 | 0.051 | 1525 |
| SDQ hyperactivity | 0.095 | 0.897 | 0.5 | 0.040 | 1522 |
| SDQ conduct problems | 0.099 | 0.896 | 0.5 | 0.051 | 1526 |
| Conner's total ADHD | 0.101 | 0.899 | 0.5 | 0.040 | 1525 |
| Conner's impulsivity | 0.077 | 0.883 | 0.5 | 0.020 | 1523 |
| Conner's inattention | 0.097 | 0.906 | 0.5 | 0.040 | 1525 |
| ICUT callous-unemotional traits | 0.114 | 0.873 | 0.5 | 0.040 | 1523 |
| ICUT callousness | 0.061 | 0.945 | 0.5 | 0.040 | 1523 |
| ICUT unemotionality | NA | 0.959 | 0.5 | 0.081 | 1525 |
| ICUT uncaring | 0.105 | 0.897 | 0.5 | 0.061 | 1525 |
| MFQ depression | 0.068 | 0.938 | 0.5 | 0.040 | 1525 |
| ARBQ anxiety | 0.049 | 0.918 | 0.5 | 0.051 | 1524 |
| Self-rated data | | | | | |
| SDQ total behaviour problems | 0.090 | 0.905 | 0.5 | 0.030 | 1054 |
| SDQ hyperactivity | 0.056 | 0.958 | 0.5 | 0.020 | 1054 |
| SDQ conduct problems | 0.082 | 0.961 | 0.5 | 0.071 | 1054 |
| SDQ emotional problems | 0.065 | 0.974 | 0.5 | 0.030 | 1054 |
| SDQ peer problems | 0.025 | 0.954 | 0.5 | 0.071 | 1054 |
| SWAN total ADHD | 0.065 | 0.934 | 0.5 | 0.081 | 442 |

| | | | | | |
|---|---|---|---|---|---|
| SWAN hyperactivity | 0.039 | 0.942 | 0.5 | 0.141 | 442 |
| SWAN inattention | 0.050 | 0.968 | 0.5 | 0.101 | 442 |
| ICUT callous-unemotional traits | NA | 0.967 | 0.5 | 1.000 | 440 |
| ICUT callousness | 0.046 | 1.013 | 0.5 | 0.111 | 440 |
| ICUT unemotionality | NA | 1.046 | 0.5 | 1.000 | 438 |
| ICUT uncaring | 0.036 | 0.959 | 0.5 | 0.152 | 439 |
| MFQ depression | 0.033 | 0.964 | 0.5 | 0.071 | 1059 |
| CASI anxiety | 0.054 | 0.958 | 0.5 | 0.030 | 1060 |
| HCL hypomania | 0.040 | 0.991 | 0.5 | 0.192 | 319 |

Note. G+E models= models using both the PGSs and environmental data to predict symptoms of developmental psychopathology; R2= proportion of variance explained; RMSE= root mean square error; N= sample size.

Supplementary Table 17. Results of the G+E models, predicting developmental psychopathology using genome-wide polygenic scores and environmental measures in male only sample.

| Developmental psychopathology | R2 | RMSE | alpha | lambda | N |
|---|---|---|---|---|---|
| Age 9 | | | | | |
| Parent-rated data | | | | | |
| SDQ total behaviour problems | 0.233 | 0.813 | 0.5 | 0.051 | 712 |
| SDQ hyperactivity | 0.194 | 0.851 | 0.5 | 0.051 | 710 |
| SDQ conduct problems | 0.160 | 0.883 | 0.5 | 0.091 | 713 |
| Conner's total ADHD | 0.184 | 0.922 | 0.5 | 0.081 | 713 |
| Conner's impulsivity | 0.117 | 0.912 | 0.5 | 0.091 | 711 |
| Conner's inattention | 0.172 | 0.959 | 0.5 | 0.091 | 713 |
| ICUT callous-unemotional traits | 0.175 | 0.905 | 0.5 | 0.061 | 713 |
| ICUT callousness | 0.118 | 0.888 | 0.5 | 0.091 | 712 |
| ICUT unemotionality | 0.062 | 0.972 | 0.5 | 0.141 | 714 |
| ICUT uncaring | 0.159 | 0.923 | 0.5 | 0.091 | 714 |
| MFQ depression | 0.080 | 0.911 | 0.5 | 0.081 | 713 |
| ARBQ anxiety | 0.141 | 0.860 | 0.5 | 0.051 | 712 |
| Self-rated data | | | | | |
| SDQ total behaviour problems | 0.110 | 0.915 | 0.5 | 0.091 | 635 |
| SDQ hyperactivity | 0.078 | 0.972 | 0.5 | 0.131 | 635 |
| SDQ conduct problems | 0.075 | 0.937 | 0.5 | 0.111 | 634 |
| SDQ emotional problems | 0.038 | 0.884 | 0.5 | 0.131 | 635 |
| SDQ peer problems | 0.075 | 0.963 | 0.5 | 0.071 | 635 |
| SWAN total ADHD | 0.105 | 0.927 | 0.5 | 0.172 | 240 |
| SWAN hyperactivity | 0.087 | 0.879 | 0.5 | 0.182 | 240 |
| SWAN inattention | 0.109 | 0.972 | 0.5 | 0.162 | 240 |
| ICUT callous-unemotional traits | 0.129 | 0.986 | 0.5 | 0.182 | 240 |
| ICUT callousness | 0.045 | 1.000 | 0.5 | 0.293 | 240 |
| ICUT unemotionality | NA | 0.939 | 0.5 | 1.000 | 240 |
| ICUT uncaring | 0.163 | 0.956 | 0.5 | 0.162 | 240 |
| MFQ depression | 0.043 | 0.951 | 0.5 | 0.121 | 635 |
| CASI anxiety | 0.058 | 0.913 | 0.5 | 0.111 | 635 |
| HCL hypomania | 0.071 | 1.000 | 0.5 | 0.263 | 190 |
| Age 12 | | | | | |
| Parent-rated data | | | | | |
| SDQ total behaviour problems | 0.213 | 0.857 | 0.5 | 0.030 | 1440 |
| SDQ hyperactivity | 0.156 | 0.900 | 0.5 | 0.030 | 1438 |
| SDQ conduct problems | 0.168 | 0.891 | 0.5 | 0.040 | 1441 |
| Conner's total ADHD | 0.198 | 0.919 | 0.5 | 0.040 | 1443 |
| Conner's impulsivity | 0.131 | 0.938 | 0.5 | 0.071 | 1441 |
| Conner's inattention | 0.186 | 0.939 | 0.5 | 0.030 | 1443 |

| | | | | | |
|---|---|---|---|---|---|
| ICUT callous-unemotional traits | 0.137 | 0.937 | 0.5 | 0.051 | 1436 |
| ICUT callousness | 0.103 | 0.918 | 0.5 | 0.051 | 1438 |
| ICUT unemotionality | 0.037 | 0.999 | 0.5 | 0.081 | 1443 |
| ICUT uncaring | 0.134 | 0.953 | 0.5 | 0.081 | 1443 |
| MFQ depression | 0.080 | 0.924 | 0.5 | 0.061 | 1442 |
| ARBQ anxiety | 0.100 | 0.889 | 0.5 | 0.051 | 1441 |
| Self-rated data | | | | | |
| SDQ total behaviour problems | 0.093 | 0.912 | 0.5 | 0.091 | 1398 |
| SDQ hyperactivity | 0.077 | 0.955 | 0.5 | 0.051 | 1398 |
| SDQ conduct problems | 0.096 | 0.931 | 0.5 | 0.071 | 1397 |
| SDQ emotional problems | 0.031 | 0.847 | 0.5 | 0.081 | 1398 |
| SDQ peer problems | 0.039 | 0.984 | 0.5 | 0.081 | 1398 |
| SWAN total ADHD | 0.256 | 0.831 | 0.5 | 0.040 | 279 |
| SWAN hyperactivity | 0.099 | 0.889 | 0.5 | 0.202 | 279 |
| SWAN inattention | 0.218 | 0.906 | 0.5 | 0.091 | 279 |
| ICUT callous-unemotional traits | 0.096 | 1.004 | 0.5 | 0.253 | 279 |
| ICUT callousness | 0.064 | 1.011 | 0.5 | 0.253 | 279 |
| ICUT unemotionality | NA | 0.991 | 0.5 | 1.000 | 279 |
| ICUT uncaring | 0.214 | 0.947 | 0.5 | 0.111 | 279 |
| MFQ depression | 0.026 | 0.969 | 0.5 | 0.071 | 1400 |
| CASI anxiety | 0.058 | 0.895 | 0.5 | 0.051 | 1398 |
| HCL hypomania | NA | 1.007 | 0.5 | 1.000 | 409 |
| Age 16 | | | | | |
| Parent-rated data | | | | | |
| SDQ total behaviour problems | 0.063 | 0.924 | 0.5 | 0.121 | 420 |
| SDQ hyperactivity | 0.056 | 0.925 | 0.5 | 0.121 | 419 |
| SDQ conduct problems | 0.068 | 0.922 | 0.5 | 0.131 | 421 |
| Conner's total ADHD | 0.029 | 0.957 | 0.5 | 0.182 | 420 |
| Conner's impulsivity | 0.045 | 0.914 | 0.5 | 0.121 | 418 |
| Conner's inattention | 0.027 | 0.992 | 0.5 | 0.172 | 420 |
| ICUT callous-unemotional traits | 0.037 | 0.965 | 0.5 | 0.152 | 420 |
| ICUT callousness | NA | 0.969 | 0.5 | 1.000 | 420 |
| ICUT unemotionality | NA | 1.014 | 0.5 | 0.121 | 421 |
| ICUT uncaring | 0.038 | 0.953 | 0.5 | 0.152 | 421 |
| MFQ depression | 0.057 | 0.919 | 0.5 | 0.081 | 420 |
| ARBQ anxiety | 0.030 | 0.855 | 0.5 | 0.172 | 420 |
| Self-rated data | | | | | |
| SDQ total behaviour problems | 0.185 | 0.834 | 0.5 | 0.061 | 609 |
| SDQ hyperactivity | 0.106 | 0.924 | 0.5 | 0.081 | 609 |
| SDQ conduct problems | 0.120 | 0.892 | 0.5 | 0.081 | 609 |
| SDQ emotional problems | 0.138 | 0.818 | 0.5 | 0.091 | 609 |
| SDQ peer problems | 0.103 | 0.935 | 0.5 | 0.071 | 609 |
| SWAN total ADHD | 0.160 | 0.854 | 0.5 | 0.182 | 228 |

| | | | | | |
|---|---|---|---|---|---|
| SWAN hyperactivity | 0.200 | 0.822 | 0.5 | 0.101 | 228 |
| SWAN inattention | 0.110 | 0.917 | 0.5 | 0.273 | 228 |
| ICUT callous-unemotional traits | 0.152 | 0.929 | 0.5 | 0.222 | 228 |
| ICUT callousness | 0.120 | 0.926 | 0.5 | 0.202 | 228 |
| ICUT unemotionality | 0.092 | 0.931 | 0.5 | 0.192 | 227 |
| ICUT uncaring | 0.199 | 0.905 | 0.5 | 0.131 | 227 |
| MFQ depression | 0.082 | 0.911 | 0.5 | 0.081 | 613 |
| CASI anxiety | 0.126 | 0.869 | 0.5 | 0.091 | 612 |
| HCL hypomania | NA | 1.071 | 0.5 | 1.000 | 180 |

Note. G+E models= models using both the PGSs and environmental data to predict symptoms of developmental psychopathology; R2= proportion of variance explained; RMSE= root mean square error; N= sample size.

Supplementary Table 18. Results of the G+E models, predicting developmental psychopathology using genome-wide polygenic scores and environmental measures in female only sample.

| Developmental psychopathology | R2 | RMSE | alpha | lambda | N |
|---|---|---|---|---|---|
| Age 9 | | | | | |
| Parent-rated data | | | | | |
| SDQ total behaviour problems | 0.154 | 0.912 | 0.5 | 0.091 | 960 |
| SDQ hyperactivity | 0.106 | 0.911 | 0.5 | 0.091 | 959 |
| SDQ conduct problems | 0.140 | 0.924 | 0.5 | 0.071 | 960 |
| Conner's total ADHD | 0.136 | 0.885 | 0.5 | 0.051 | 957 |
| Conner's impulsivity | 0.097 | 0.883 | 0.5 | 0.071 | 957 |
| Conner's inattention | 0.129 | 0.875 | 0.5 | 0.061 | 957 |
| ICUT callous-unemotional traits | 0.134 | 0.865 | 0.5 | 0.051 | 957 |
| ICUT callousness | 0.089 | 0.974 | 0.5 | 0.081 | 959 |
| ICUT unemotionality | 0.051 | 0.938 | 0.5 | 0.081 | 959 |
| ICUT uncaring | 0.131 | 0.912 | 0.5 | 0.091 | 959 |
| MFQ depression | 0.100 | 0.975 | 0.5 | 0.081 | 959 |
| ARBQ anxiety | 0.038 | 1.018 | 0.5 | 0.131 | 958 |
| Self-rated data | | | | | |
| SDQ total behaviour problems | 0.109 | 0.939 | 0.5 | 0.091 | 884 |
| SDQ hyperactivity | 0.090 | 0.923 | 0.5 | 0.071 | 884 |
| SDQ conduct problems | 0.103 | 0.953 | 0.5 | 0.091 | 884 |
| SDQ emotional problems | 0.053 | 1.069 | 0.5 | 0.101 | 884 |
| SDQ peer problems | 0.064 | 0.971 | 0.5 | 0.071 | 884 |
| SWAN total ADHD | 0.046 | 0.973 | 0.5 | 0.162 | 376 |
| SWAN hyperactivity | NA | 0.993 | 0.5 | 1.000 | 375 |
| SWAN inattention | NA | 0.966 | 0.5 | 1.000 | 376 |
| ICUT callous-unemotional traits | 0.137 | 0.922 | 0.5 | 0.121 | 374 |
| ICUT callousness | 0.137 | 0.973 | 0.5 | 0.091 | 375 |
| ICUT unemotionality | 0.060 | 0.982 | 0.5 | 0.111 | 374 |
| ICUT uncaring | 0.129 | 0.942 | 0.5 | 0.162 | 375 |
| MFQ depression | 0.035 | 0.956 | 0.5 | 0.081 | 885 |
| CASI anxiety | 0.060 | 1.035 | 0.5 | 0.081 | 885 |
| HCL hypomania | NA | 0.967 | 0.5 | 1.000 | 305 |
| Age 12 | | | | | |
| Parent-rated data | | | | | |
| SDQ total behaviour problems | 0.200 | 0.890 | 0.5 | 0.051 | 1823 |
| SDQ hyperactivity | 0.151 | 0.903 | 0.5 | 0.030 | 1822 |
| SDQ conduct problems | 0.180 | 0.906 | 0.5 | 0.040 | 1823 |
| Conner's total ADHD | 0.166 | 0.871 | 0.5 | 0.030 | 1821 |
| Conner's impulsivity | 0.117 | 0.898 | 0.5 | 0.040 | 1821 |
| Conner's inattention | 0.150 | 0.870 | 0.5 | 0.040 | 1821 |

| | | | | | |
|---|---|---|---|---|---|
| ICUT callous-unemotional traits | 0.137 | 0.869 | 0.5 | 0.051 | 1819 |
| ICUT callousness | 0.098 | 0.955 | 0.5 | 0.071 | 1823 |
| ICUT unemotionality | 0.033 | 0.956 | 0.5 | 0.061 | 1822 |
| ICUT uncaring | 0.158 | 0.905 | 0.5 | 0.040 | 1822 |
| MFQ depression | 0.089 | 0.973 | 0.5 | 0.030 | 1824 |
| ARBQ anxiety | 0.063 | 1.007 | 0.5 | 0.040 | 1823 |
| Self-rated data | | | | | |
| SDQ total behaviour problems | 0.108 | 0.954 | 0.5 | 0.051 | 1786 |
| SDQ hyperactivity | 0.088 | 0.961 | 0.5 | 0.061 | 1788 |
| SDQ conduct problems | 0.102 | 0.959 | 0.5 | 0.061 | 1788 |
| SDQ emotional problems | 0.049 | 1.049 | 0.5 | 0.051 | 1788 |
| SDQ peer problems | 0.056 | 0.980 | 0.5 | 0.040 | 1788 |
| SWAN total ADHD | 0.110 | 0.970 | 0.5 | 0.071 | 443 |
| SWAN hyperactivity | 0.107 | 0.979 | 0.5 | 0.061 | 442 |
| SWAN inattention | 0.091 | 0.967 | 0.5 | 0.081 | 443 |
| ICUT callous-unemotional traits | 0.172 | 0.884 | 0.5 | 0.081 | 441 |
| ICUT callousness | 0.160 | 0.946 | 0.5 | 0.061 | 442 |
| ICUT unemotionality | 0.053 | 0.988 | 0.5 | 0.141 | 442 |
| ICUT uncaring | 0.141 | 0.907 | 0.5 | 0.071 | 442 |
| MFQ depression | 0.050 | 0.975 | 0.5 | 0.040 | 1789 |
| CASI anxiety | 0.067 | 1.023 | 0.5 | 0.051 | 1789 |
| HCL hypomania | 0.025 | 0.957 | 0.5 | 0.162 | 558 |
| Age 16 | | | | | |
| Parent-rated data | | | | | |
| SDQ total behaviour problems | 0.086 | 0.906 | 0.5 | 0.071 | 639 |
| SDQ hyperactivity | 0.075 | 0.918 | 0.5 | 0.051 | 639 |
| SDQ conduct problems | 0.072 | 0.918 | 0.5 | 0.071 | 639 |
| Conner's total ADHD | 0.061 | 0.897 | 0.5 | 0.061 | 639 |
| Conner's impulsivity | 0.040 | 0.881 | 0.5 | 0.071 | 639 |
| Conner's inattention | 0.060 | 0.897 | 0.5 | 0.061 | 639 |
| ICUT callous-unemotional traits | 0.068 | 0.878 | 0.5 | 0.061 | 640 |
| ICUT callousness | 0.043 | 0.997 | 0.5 | 0.121 | 640 |
| ICUT unemotionality | NA | 0.941 | 0.5 | 1.000 | 640 |
| ICUT uncaring | 0.069 | 0.921 | 0.5 | 0.091 | 640 |
| MFQ depression | 0.068 | 0.952 | 0.5 | 0.071 | 640 |
| ARBQ anxiety | 0.048 | 0.919 | 0.5 | 0.040 | 640 |
| Self-rated data | | | | | |
| SDQ total behaviour problems | 0.238 | 0.877 | 0.5 | 0.020 | 917 |
| SDQ hyperactivity | 0.165 | 0.885 | 0.5 | 0.081 | 917 |
| SDQ conduct problems | 0.225 | 0.880 | 0.5 | 0.061 | 917 |
| SDQ emotional problems | 0.136 | 1.037 | 0.5 | 0.040 | 917 |
| SDQ peer problems | 0.112 | 0.938 | 0.5 | 0.010 | 917 |
| SWAN total ADHD | 0.133 | 0.906 | 0.5 | 0.141 | 390 |

| | | | | | |
|---|---|---|---|---|---|
| SWAN hyperactivity | 0.104 | 0.938 | 0.5 | 0.131 | 390 |
| SWAN inattention | 0.139 | 0.891 | 0.5 | 0.111 | 390 |
| ICUT callous-unemotional traits | 0.233 | 0.843 | 0.5 | 0.111 | 387 |
| ICUT callousness | 0.126 | 0.949 | 0.5 | 0.141 | 388 |
| ICUT unemotionality | 0.067 | 1.021 | 0.5 | 0.192 | 387 |
| ICUT uncaring | 0.264 | 0.827 | 0.5 | 0.081 | 388 |
| MFQ depression | 0.106 | 0.923 | 0.5 | 0.040 | 919 |
| CASI anxiety | 0.174 | 0.964 | 0.5 | 0.040 | 919 |
| HCL hypomania | 0.071 | 0.951 | 0.5 | 0.141 | 304 |

Note. G+E models= models using both the PGSs and environmental data to predict symptoms of developmental psychopathology; R2= proportion of variance explained; RMSE= root mean square error; N= sample size.

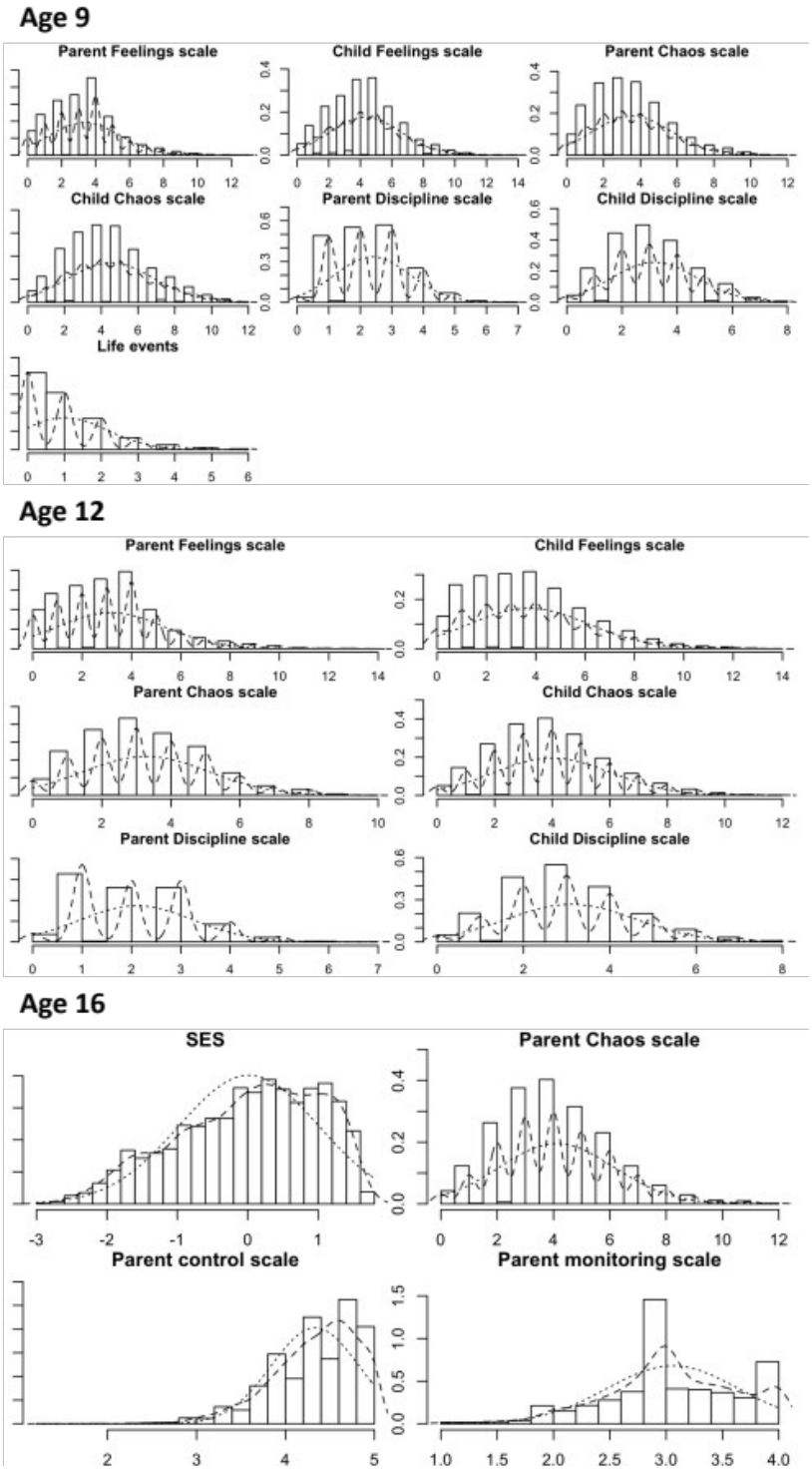
Supplementary Table 19. Results of the mediation models testing for gene environment correlation in developmental psychopathology.

| Predictor | Outcome | Mediator | Estimate | SE | Z-value | P-value |
|---|---|---|---|---|---|---|
| PGSs as predictors | | | | | | |
| ADHD | Self-rated SDQ total behaviour problems | Age 12 Child-reported Chaos scale | 0.016 | 0.004 | 4.313 | <0.001 |
| Neuroticism | Self-rated SDQ total behaviour problems | Age 12 Child-reported Chaos scale | 0.012 | 0.004 | 3.375 | 0.001 |
| Anxiety | Self-rated SDQ total behaviour problems | Age 12 Being a Parent: I make parent angry | 0.008 | 0.004 | 1.983 | 0.047 |
| ADHD | Self-rated SDQ total behaviour problems | Age 12 Child-reported Feelings scale | 0.019 | 0.004 | 4.432 | <0.001 |
| Anxiety | Self-rated SDQ total behaviour problems | Age 12 Chaos: a real zoo | 0.002 | 0.003 | 0.655 | 0.512 |
| Neuroticism | Self-rated SDQ total behaviour problems | Age 12 Chaos: we do not stay on top of things | 0.001 | 0.002 | 0.583 | 0.56 |
| Schizophrenia | Self-rated SDQ total behaviour problems | Age 12 Being a Parent: I make parent angry | -0.003 | 0.004 | -0.759 | 0.448 |
| Environments as predictors | | | | | | |
| Age 12 Child-reported Chaos scale | Self-rated SDQ total behaviour problems | ADHD | 0.008 | 0.002 | 3.721 | <0.001 |
| Age 12 Child-reported Chaos scale | Self-rated SDQ total behaviour problems | Neuroticism | 0.006 | 0.002 | 3.065 | 0.002 |
| Age 12 Being a Parent: I make parent angry | Self-rated SDQ total behaviour problems | Anxiety | 0.001 | 0.001 | 1.11 | 0.267 |
| Age 12 Child- | Self-rated SDQ total | ADHD | 0.008 | 0.002 | 3.719 | <0.001 |

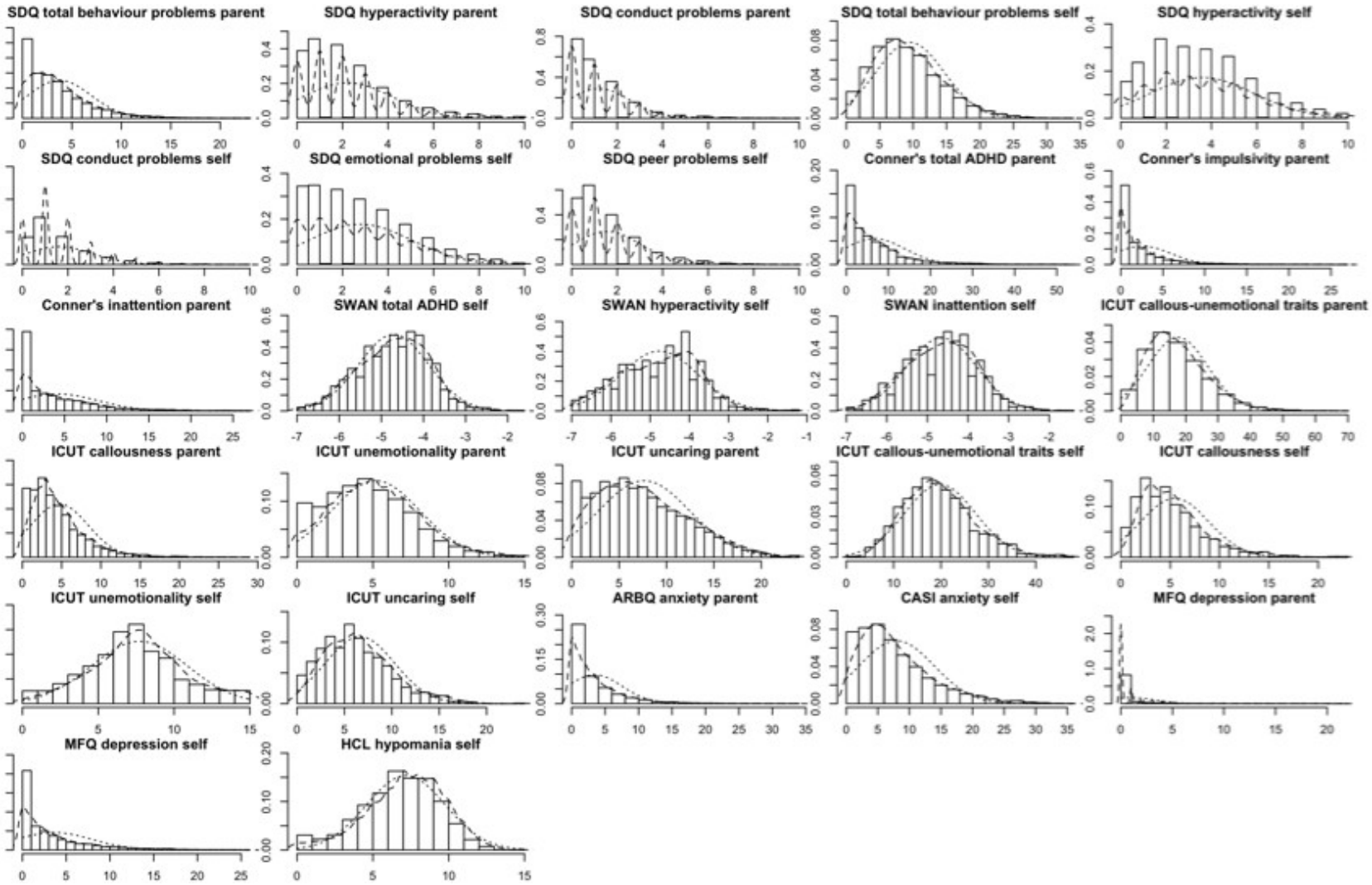
| | | | | | | |
|---|---|---|---|---|---|---|
| reported Feelings scale | behaviour problems | | | | | |
| Age 12 Chaos: a real zoo | Self-rated SDQ total behaviour problems | Anxiety | <0.001 | 0.001 | 0.618 | 0.536 |
| Age 12 Chaos: we do not stay on top of things | Self-rated SDQ total behaviour problems | Neuroticism | 0.001 | 0.002 | 0.583 | 0.56 |
| Age 12 Being a Parent: I make parent angry | Self-rated SDQ total behaviour problems | Schizophrenia | -0.001 | 0.001 | -0.731 | 0.465 |

Note. SE= standard error.

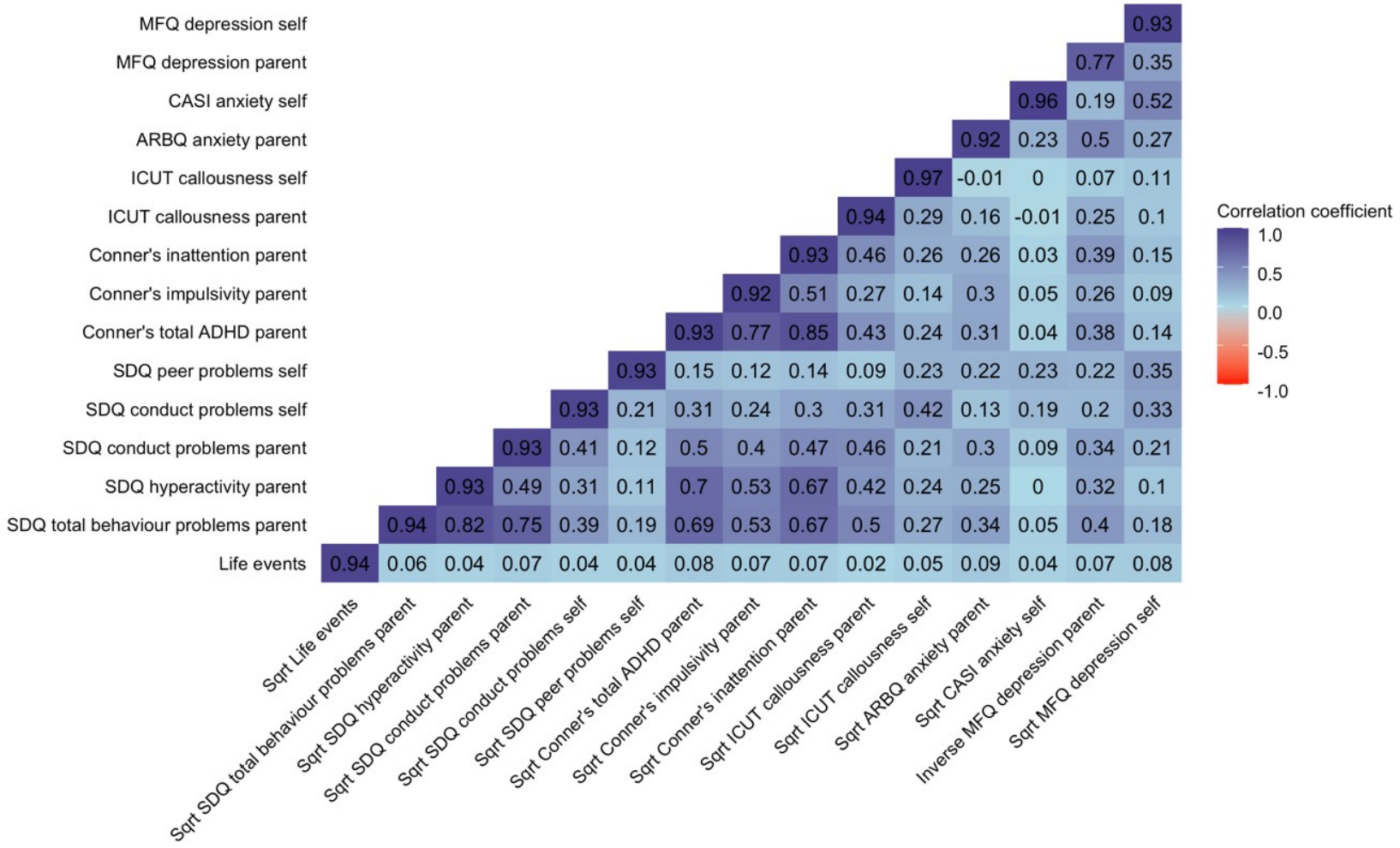
Supplementary Figures



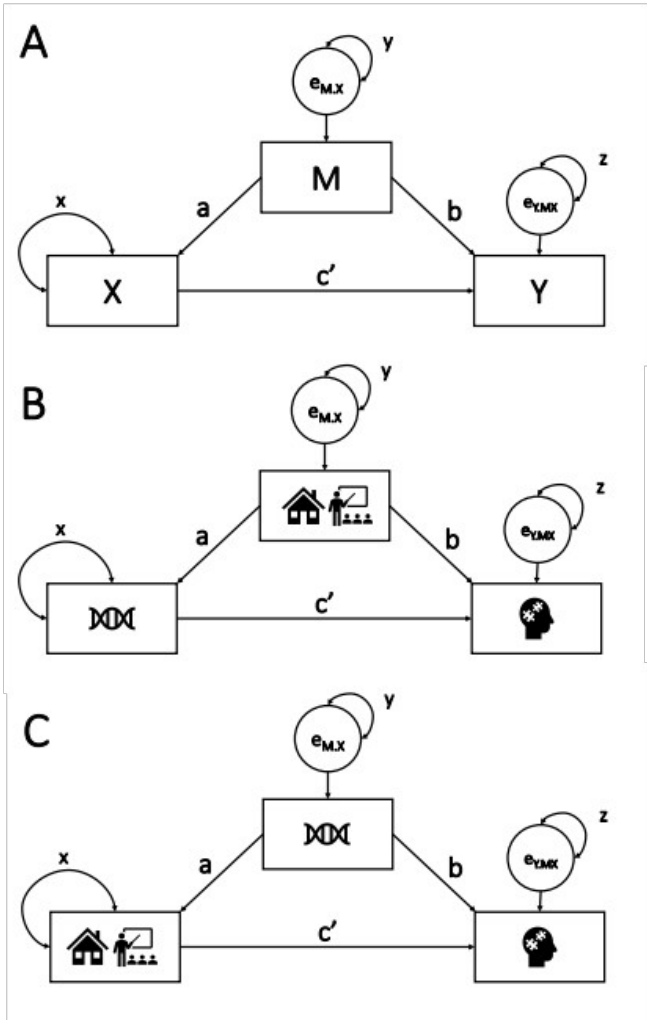

Supplementary Figure 10. Distributions of environmental data.




Supplementary Figure 11. Distributions of developmental psychopathology data.

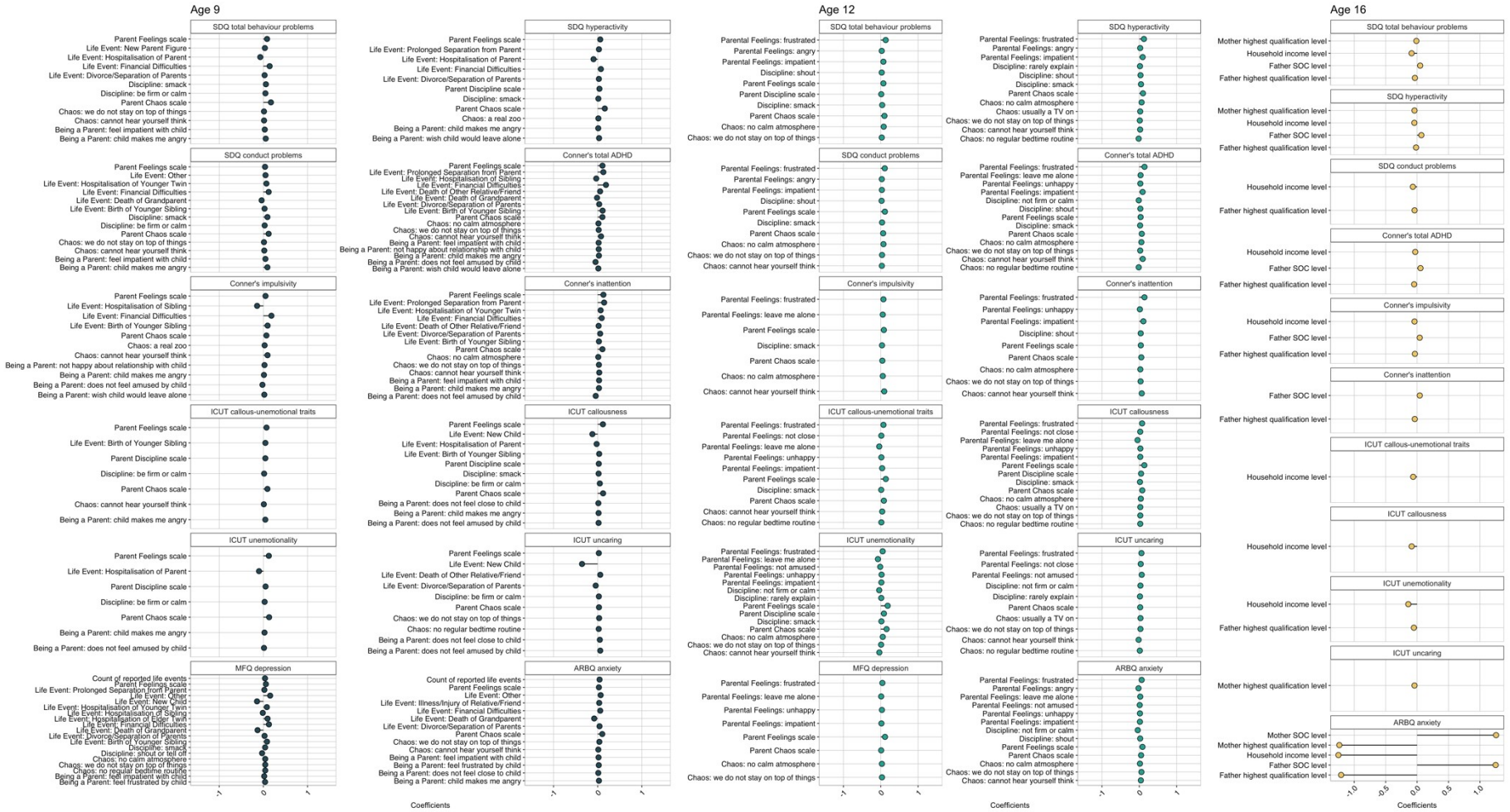



Supplementary Figure 12. Correlations between untransformed and transformed variables.



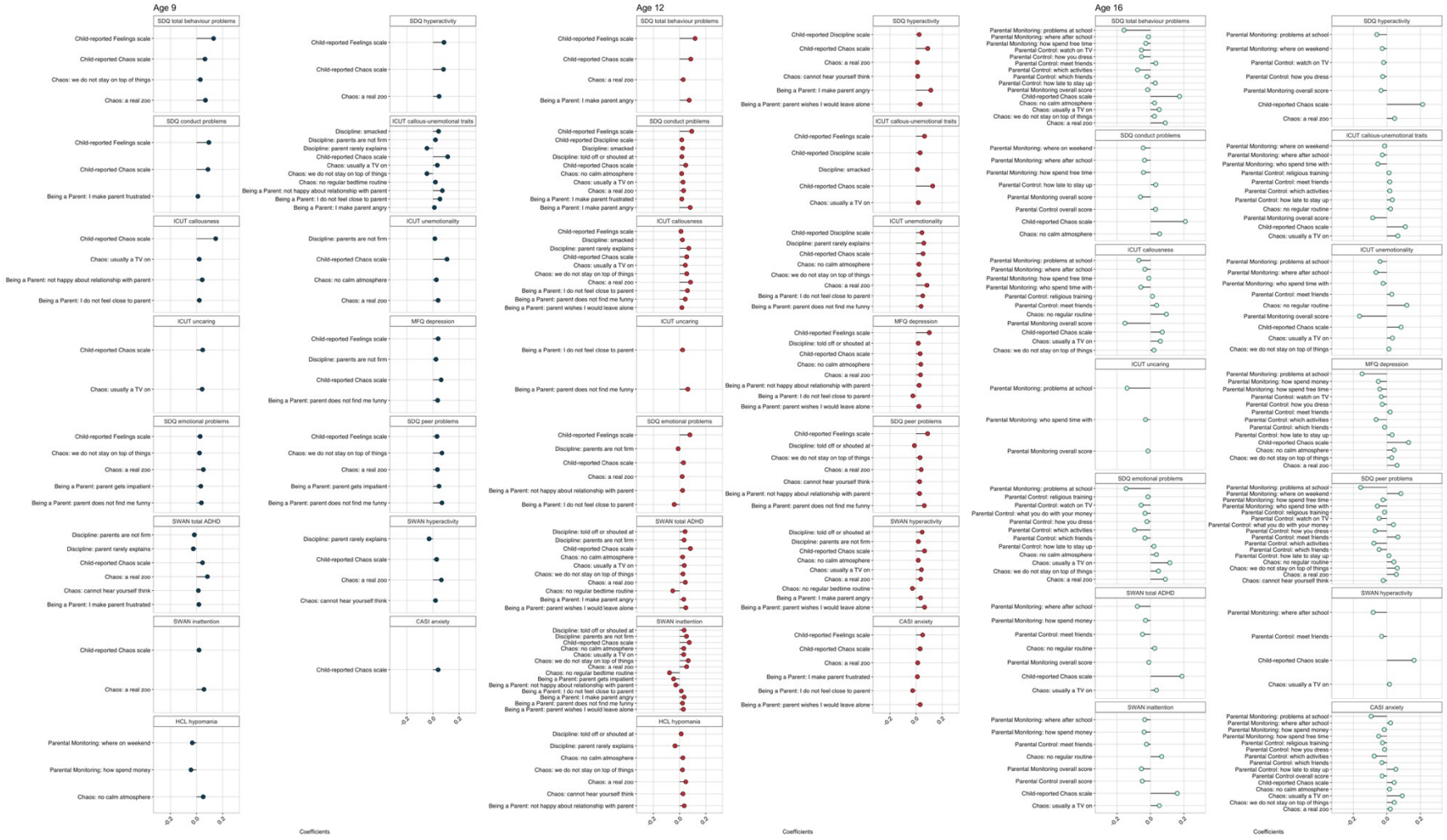

Supplementary Figure 13. Mediation and gene environment correlation (rGE) models. Panel A presents the mediation model of X on Y, mediated by M. Panel B presents the rGE model of G on behaviour problems, mediated by E. Panel C presents the rGE model of E on behaviour problems, mediated by G. Circles indicate residuals. Parameters a, b and c represent regression weights. Parameters x, y and z represent variance parameters.

Note. Model illustrated in panel C is abstract due to the fact that G cannot by causally influenced by E.



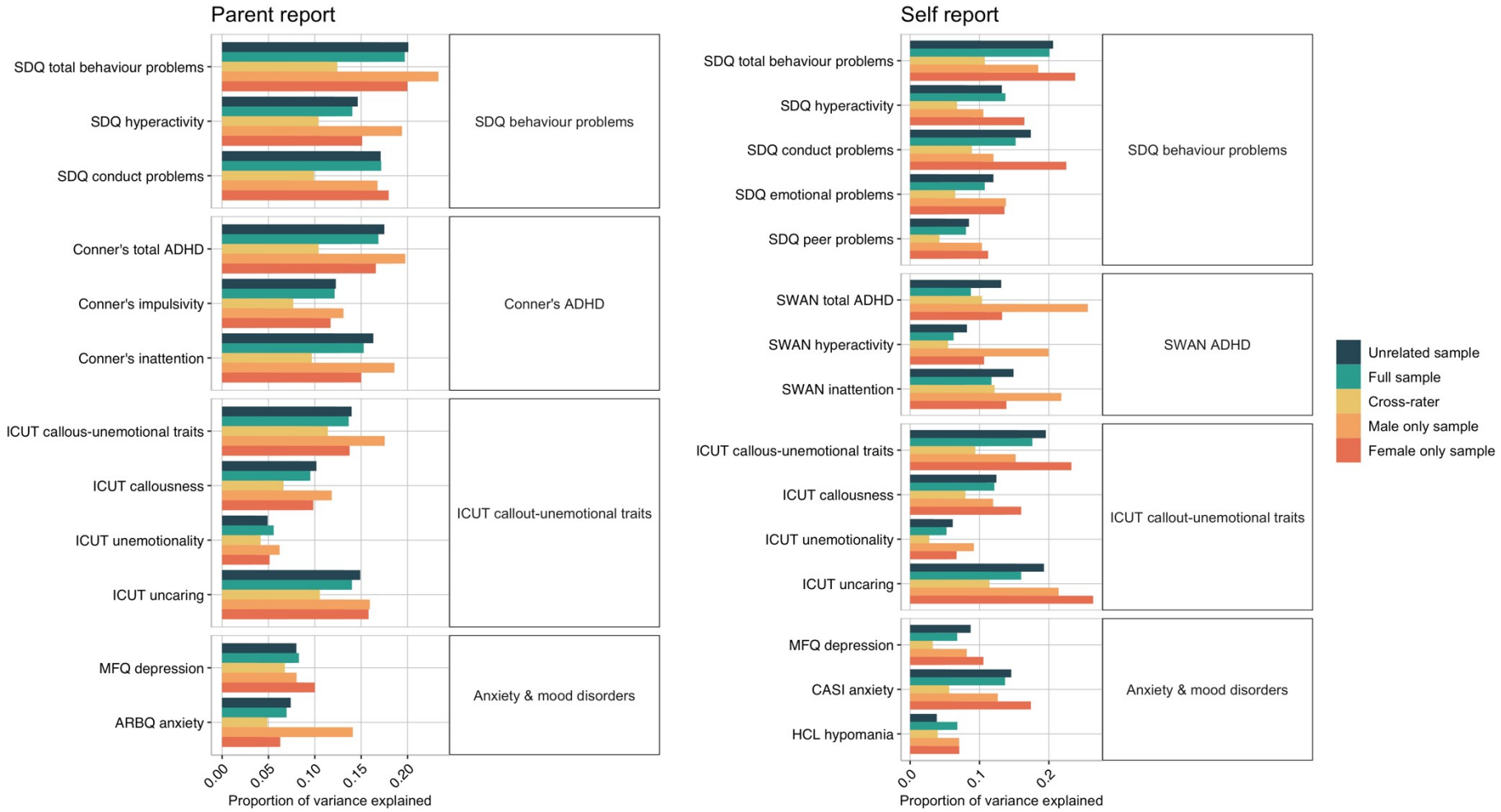

Supplementary Figure 14. Elastic net coefficients of the association between parent-rated environments measures at ages 9, 12 and 16 and developmental psychopathology measures.

Note. For clarity of visualisation, only those environments with coefficients lower than -0.01 or greater than 0.01 are included in the figure.

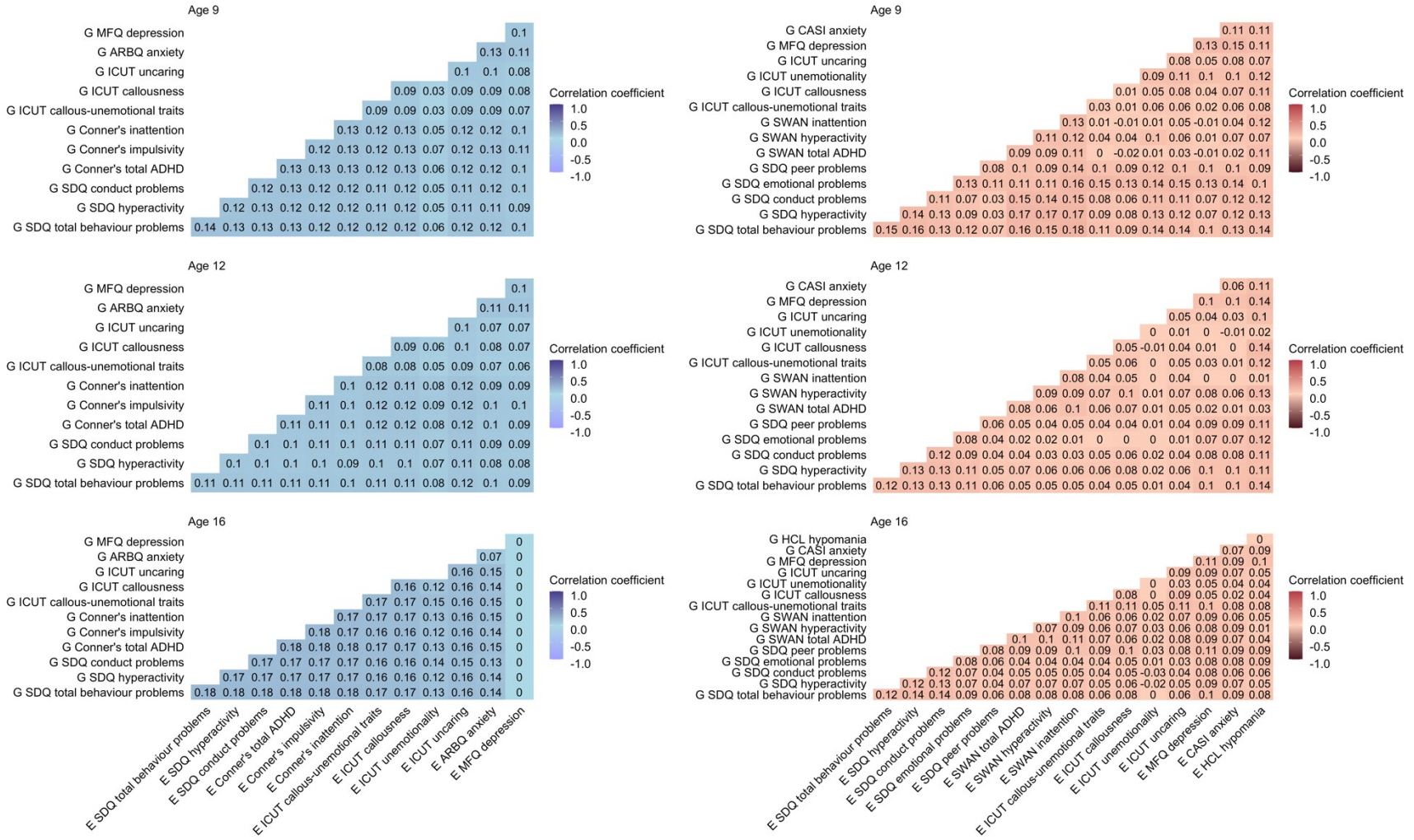



Supplementary Figure 15. Elastic net coefficients of the association between self-rated environments measures at ages 9, 12 and 16 and developmental psychopathology measures.

Note. For clarity of visualisation, only those environments with coefficients lower than -0.01 or greater than 0.01 are included in the figure.




Supplementary Figure 16. Comparison of the proportion of variance explained by sensitivity models.




Supplementary Figure 31. Correlations between predicted values from G and E models for parent and self-rated symptoms of developmental psychopathology.