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Regular Article

Genetic and phenotypic evidence of the predictive validity of preschool parent reports of hyperactivity/impulsivity and inattention

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Abstract

To determine the validity of parent reports (PRs) of ADHD in preschoolers, we assessed hyperactivity/impulsivity (HI) and inattention (IN) in 1114 twins with PRs at 1.5, 2.5, 4, 5, 14, 15, and 17 years, and teacher-reports at 6, 7, 9, 10, and 12. We examined if preschool PRs (1) predict high HI/IN trajectories, and (2) capture genetic contributions to HI/IN into adolescence. Group-based trajectory analyses identified three 6–17 years trajectories for both HI and IN, including small groups with high HI ($N = 88$, 10.4%, 77% boys) and IN ($N = 158$, 17.3%, 75% boys). Controlling for sex, each unit of HI PRs starting at 1.5 years and at 4 years for IN, increased more than 2-fold the risk of belonging to the high trajectory, with incremental contributions (Odds Ratios = 2.5–4.5) at subsequent ages. Quantitative genetic analyses showed that genetic contributions underlying preschool PRs accounted for up to a quarter and a third of the heritability of later HI and IN, respectively. Genes underlying 1.5-year HI and 4-year IN contributed to 6 of 8 later HI and IN time-points and largely explained the corresponding phenotypic correlations. Results provide phenotypic and genetic evidence that preschool parent reports of HI and IN are valid means to predict developmental risk of ADHD.

Keywords: ADHD; genetic modeling; group-based trajectory analysis; hyperactivity/impulsivity and inattention; preschool parent reports

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Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is the most common neurobehavioral disorder in childhood and one of the most heritable, with estimates generally in the 50–80% range across the lifespan (see Grimm et al., 2020 for a recent meta-analysis). It is marked by developmentally inappropriate levels of two behavioral dimensions (Narad et al., 2015) hyperactivity/impulsivity (HI) and inattention (IN), that interfere with functioning or development (Subcommittee on Attention-Deficit/Hyperactivity Disorder, Steering Committee on Quality Improvement and Management, 2011). A lifelong disorder with roots in early childhood, it affects 5%–8% of children (Danielson et al., 2018; Willoughby et al., 2012) and 9%–14% of adolescents (Danielson et al., 2018; Merikangas et al., 2010), with a male to female ratio in the general population of 2 : 1 by middle school (American Psychiatric Association, 2013; Danielson et al., 2018). Although symptom levels vary during development and stability of ADHD dimensions is moderate in population studies, up to 90% of children diagnosed in childhood retain significant impairments in early adulthood (Sibley et al., 2022).

ADHD is generally diagnosed in primary school (Visser et al., 2014), but clinicians are posing them earlier (Danielson et al., 2018, Halperin & Marks, 2019), and applying pharmacological treatments as early as age 3 (Cortese et al., 2022; Young et al., 2021). A survey by the American Center for Disease Control showed the prevalence of ADHD in 2–5-year-olds hovered around 2.1% in 2016, but there is recent evidence that the preschool prevalence is similar to school-age (Tobarra-Sanchez et al., 2022). Yet, some scholars caution that preschool is too early for a reliable assessment (Overgaard et al., 2022). Thus, there is no consensus as to how early ADHD can be detected (Halperin & Marks, 2019).

Assessment concerns in preschoolers

In preschoolers, the challenge is to distinguish HI and IN levels that may be disruptive-but-normative from pathological levels that reflect both the genetic loading of ADHD (Tobarra-Sanchez et al., 2022) and the risk of a persistent trajectory (Halperin & Marks, 2019; Overgaard et al., 2022; Vergunst et al., 2019). The choice of information is a controversial issue in that respect (Schneider et al., 2020). Systematic observation is time consuming (Chen et al., 2022; Schneider et al., 2020), and although multiple sources of

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information can be integrated (Chen et al., 2022), it is often unfeasible. For practical reasons, structured interviews with parents and parent reports (PRs) are the norm to assess HI/IN in preschoolers, whether to inform diagnosis or conduct research. The rationale is that, although they may be biased (Chen et al., 2017; Moens et al., 2018), parents have more opportunities than other source to observe their preschooler over long periods and in multiple settings (Schneider et al., 2020). By primary school, teachers are deemed a more valid source namely because they have access to a comparison group and the learning environment makes ADHD symptoms more salient (Narad et al., 2015). For these reasons, the validity of PRs of preschool HI and IN need to be assessed.

On way to address the issue is to test the predictive validity of preschool PRs across developmental periods and informants. Predictive validity refers to how well a measure predicts future outcomes. As a bidimensional disorder, ADHD lies at the extreme end of the continuous distributions of HI and IN, or IN alone for ADHD, predominantly inattentive presentation. In a lifelong disorder (Sibley et al., 2022), with a strong genetic underpinning (Grimm et al., 2020), we expect valid preschool assessments of HI/IN to (1) predict developmental trajectories over time, and (2) capture the genetic liability of HI/IN through time.

Phenotypic stability of HI/IN from preschool onward

We found four studies reporting longitudinal correlations of HI and IN using PRs in preschoolers. Rietveld et al. (2003) reported correlations ranging from .44 to .65 between mother ratings of ADHD composites at ages 1.5, 3, and 5 years in a twin sample. Leblanc et al. (2008) reported correlations ranging from .29 to .55 and .39 to 50 in HI symptoms based on father- and mother-reports, respectively, between ages 1.5, 2.5, 4, and 5 years in a population-based sample of 1,112 twins (Leblanc et al., 2008). Using a composite measure of ADHD, Price et al. (2005) found correlations ranging from .46 to .60 across 3 yearly assessments in 2-, 3-, and 4-year-olds in a cohort of over 6000 twin pairs (Price et al., 2005). Kuntsi et al. (2005) extended the study of the same sample up to age 8 and found increasing correlations with age from preschool to primary school ($r = .26$ from ages 2 to 8; $r = .37$ from ages 3 to 8; and $r = .46$ from ages 4 to 8). Although PRs show some stability through time, no study spanned beyond early primary school, and they all relied on a single informant (father or mother), which can inflate correlations.

Other longitudinal studies in preschool and from preschool onward looked at stability by mapping developmental trajectories. They used single informant PRs in preschool, teacher-reports in primary school and self-reports in adolescence. The studies did not report cross-time correlations, but they consistently identified a group of children showing high symptom levels from onset. From 1.5 to 5 years, Salla et al. (2016) identified chronic HI and IN levels in 13.4% and 2.5% of preschoolers, respectively, in a population-based longitudinal birth cohort. Covering the same age-range, Leblanc et al. (2008) identified a subgroup with 7.1% of preschoolers with chronic HI levels. One study spanning preschool into primary school in a birth cohort from the general population (Galera et al., 2011; 1.5–8 years), found that 16.1% and 13% of children followed high trajectories of HI and IN, respectively. Finally, one study spanning a birth cohort from the general population from preschool into adolescence (Vergunst et al., 2018; 1.5–17 years) combined two high trajectories of HI and IN comprising 21.4% and 20.2% of the sample, respectively. In sum, regardless of informant change (or not), trajectory studies starting at 1.5 years provide some evidence that preschool PRs detect the onset of high chronic levels of HI/IN. However, the studies spanning beyond preschool did not test if PRs in preschool predict future trajectories.

Genetic stability of HI/IN from preschool onward

A handful of studies examined the role of genetic factors in the phenotypic stability of HI/IN dimensions in preschoolers, all using maternal PRs and ADHD composites. In a population-based sample investigating parent-reported ADHD symptoms, Eilertsen et al. (2019) found that genetic correlations range from .77 between ages 1.5 and 3 years and .89 between ages 3 and 5 years. Price et al., (2001, 2005) found that genetic factors explained 91% of the covariance between ADHD composites at ages 2, 3 and 4 years in a twin cohort exploring genetic and environmental continuity and change of parent-reported ADHD symptoms. With the same sample followed over 4 time-points from ages 2 to 8 years, Kuntsi et al. (2005) found that genetic factors at ages 2, 3, and 4 contributed, respectively, to 32%, 45%, and 51% of the heritability of ADHD at age 8. Thus, across the preschool and early primary school years, genetic factors overlap and largely explain stability.

One possible caveat is that estimates in these studies could be inflated by the use of a single parent informant. In genetic studies using a combination of parent, teacher and/or self-reports spanning primary school to late adolescence (Chang et al., 2013; Faraone et al., 2015; Greven et al., 2011; Larsson et al., 2014; Larsson et al., 2004; Pingault et al., 2015), the genetic overlap across age was larger within the same informant than across informants. Nonetheless, regardless of informant, the results showed that the stability of HI/IN in primary school and adolescence stems from a cascade of broad genetic factors (additive or dominant) present at onset, with systematic age-specific genetic and unique environment contributions (Chang et al., 2013; Greven et al., 2011; Larsson et al., 2011; Pingault et al., 2015).

The present study

In sum, PRs are the norm to assess preschoolers. They show increasing phenotypic stability during preschool and a similar genetic architecture to what is observed in primary school and adolescence with other informants. Yet, their validity remains controversial. Given the changing normative nature of HI and IN across development, we need empirical evidence that preschool PRs of HI and IN are valid means of capturing the early development of ADHD and its underlying genetic liability. A genetically informed longitudinal design that starts with PRs in preschool and with multiple assessments by various informants through late adolescence is well-suited for this purpose. First, at the phenotypic level, it can examine if preschool PRs predict later HI/IN from different informants as well as chronic developmental courses of HI and IN. Second, at the genetic level, it can assess if genetic factors underlying preschool PRs of HI/IN overlap with genetic influences detected at later ages. In a population-based birth cohort of twins with multi-informant assessments of HI and IN at 12 time-points from ages 1.5 to 17 years, we examined: (1) if PRs at ages 1.5, 2.5, 4, and 5 years predict subsequent high HI/IN trajectories from primary school into late adolescence (Objective 1) and, (2) if genetic contributions to preschool PRs of HI/IN span into adolescence across informants (Objective 2).

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Method

Sample

Data are issued from the Quebec Newborn Twin Study (QNTS; Boivin et al., 2013). Parents of all twins born in the Greater Montreal area between April 1995 and December 1998 (989 families) were identified through birth records and invited by letter or phone to participate; 662 families agreed to participate and met inclusion criteria (parent fluency in either French or English, infants born without major medical conditions and available birth records). Quasi-annual assessments on a range of behavioral, cognitive, social, biological, genetic, and family characteristics were carried out starting at 6 months and are ongoing (Boivin et al., 2019). Ethical approvals, parent, teacher and participant consent were obtained before each data collection. Non-identifying information was used in all analyses. The QNTS sample's sociodemographic characteristics are comparable to those of an epidemiological sample of singletons born during the same period in the same province.

We used the Goldsmith (1991) questionnaire on physical similarity to determine zygosity. DNA tests on a subsample of same-sex twin pairs ($n = 123$) showed a 96% accuracy rate (Forget-Dubois et al., 2003). In 2007, zygosity was reassessed in inconclusive cases through a brief telephone interview (adapted from Spitz et al., 1996). The initial sample included 254 monozygotic (MZ) pairs (125 male and 129 female), 210 same-sex dizygotic (DZ) pairs (105 male and 105 female), and 203 opposite-sex DZ pairs (Boivin et al., 2013).

For this study, we used data collected when the twins were 1.5 ($M = 1.55$, $SD = 0.05$), 2.5 ($M = 2.58$, $SD = 0.07$), 4 ($M = 4.11$, $SD = 0.15$), 5 ($M = 5.28$, $SD = 0.27$), 6 ($M = 6.04$, $SD = 0.27$), 7 ($M = 7.06$, $SD = 0.27$), 9 ($M = 9.07$, $SD = 0.29$), 10 ($M = 10.00$, $SD = 0.28$), 12 ($M = 12.09$, $SD = 0.28$), 14 ($M = 14.075$, $SD = 0.29$), 15 ($M = 15.09$, $SD = 0.26$), and 17 ($M = 17.07$, $SD = 0.30$) years of age. Selected participants had to have complete HI/IN data for at least one time-point. The final sample included 1114 participants at age 1.5 years, 1045 at 2.5, 912 at 4, 937 at 5, 788 at 6, 838 at 7, 754 at 9, 779 at 10, 629 at 12, 831 at 14, 792 at 15, and 820 at 17. Attrition rate from ages 1.5 to 17 years was 27.5%, an average of 1.77% per year. Ns vary across assessments for a variety of reasons (families/participants lost to the study, families not participating at specific data collections, individual teacher's agreement to participate or missing items). Though Little's MCAR test shows data were not missing completely at random (MCAR) over the course of the study ($\chi^2 = 6026.49$, $df = 4919$, $p < .001$), data were MCAR during the preschool ($\chi^2 = 112.52$, $df = 97$, $p = .13$) and primary school years ($\chi^2 = 79.76$, $df = 73$, $p = .28$) and MCAR between the first and last time-points (1.5–17 years: $\chi^2 = 6.55$, $df = 8$, $p = .59$). Nonetheless, we implemented maximum likelihood strategies in trajectory analyses, binary logistic models and genetic models to avoid bias due to missing values.

Measures

HI and IN symptoms included, respectively, four and three items from the Social Behavior Questionnaire (SBQ) (see Collet et al., 2022). Items for HI were (1) can't sit still, (2) is restless or hyperactive, (3) impulsive, acts without thinking, and (4) difficulty waiting his/her turn in games/activities; items for IN were (1) cannot concentrate, cannot pay attention for a long time, (2) is inattentive, and (3) is easily distracted. At each age, items were rated on a three-point scale (0 = never, 1 = sometimes, 2 = often), and averaged to yield HI and IN scores between 0 and 2. The SBQ has good psychometric properties (Collet et al., 2022). Ordinal alphas in this sample ranged between .74 and .94 for HI, and between .74 and .97 for IN.

Fathers and mothers rated HI and IN symptoms for both twins through face-to-face computerized interviews or questionnaires (depending on where the data collection took place – home/laboratory visit or by mail – and the parent's choice when available) from ages 1.5 to 5 years (94%–98% of mothers and 53%–72% of fathers, regardless of zygosity) and from ages 14 to 17 years (95%–96% of mothers and 60%–62% of fathers). Correlations between father and mother for the same child at the same age ranged from .44 to .47 in preschool and .45 to .49 in adolescence for HI ratings, and from .28 to .39 in preschool and .61 to .64 in adolescence for IN ratings. Mother- and father- ratings were averaged at each age allowing one missing value to keep multiple raters when available. Different teachers each year (home room teachers only) assessed symptoms on the same scales using questionnaires from ages 6 to 12 years. Most twin pairs were not assessed by the same teacher (60.8%–76.4%) across primary school. Teachers were not solicited in adolescence because students change teachers for different subjects and it would have been difficult to identify a specific teacher very knowledgeable of the participants' HI and IN behaviors.

Table 1 presents correlations across ages between 1.5 and 17 years for HI (below diagonal) and IN (above diagonal), highlighting correlations across preschool and later measures (bottom left for HI and top right for IN). Overall, correlations between preschool PRs and later measures were at best modest for HI (rs = .09–.37) and IN (rs = .05–36) but increased from ages 1.5 to 5 years, similarly for HI and IN (Fisher z test results comparing correlations are available on the Supplementary Information document – Table M1).

Statistical analyses

Trajectory analyses

We used group-based trajectory analyses with the PROC TRAJ procedure (Daniel S. Nagin & Tremblay, 2005) on SAS version 9.4 (SAS Institute Inc, 2014) to identify trajectory patterns for HI and IN from ages 6 to 17 including teacher ratings from ages 6 to 12 and parent ratings from ages 14 to 17 years. Participants with a minimum of 2 out of 8 measures were included ($n = 957$; 49.8% boys, 43.8% MZ twins). The analyses generated solutions for 2–6-trajectory groups based on minimizing within- and maximizing between-trajectory differences. For each solution, slopes were tested. Analyses used a maximum likelihood estimator and data were modeled using a censored normal distribution. Model selection was based on seven criteria: (1) the Bayesian Information Criterion (BIC > .90) and the Akaike Information Criterion (AIC – lowest value) for fit adequacy and parsimony, (2) group intercept and slope significance, (3) average probability of group membership > .80, (4) no group membership < 5%, (5) odds of correct classification ≥ 5 for all groups, (6) difference between estimated group probabilities π_j (i.e., the population size of trajectory group j estimated by the model) and the proportion P_j assigned to the group (i.e., the actual proportion of individuals assigned to group j) using the maximum probability rule, and (7) coherence with theory.

Binomial logistic regressions

We used binomial regression models implemented in Mplus version 8.1 (Muthén & Muthén, 2017) with a maximum likelihood

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Table 1. Homotypic correlations for hyperactivity/impulsivity (below diagonal) and inattention (above diagonal). Correlations between preschool and later measures are highlighted. Adjacent time-point correlations appear in bold

Inattention													
Hyperactivity/Impulsivity	Age	1.5	2.5	4	5	6	7	9	10	12	14	15	17
	1.5		**.41**	.27	.20	.09	.09	.08	.05	.08	.08	.06	.07
	2.5	**.60**		**.34**	.34	.11	.13	.15	.12	.09	.17	.12	.18
	4	.44	**.51**		**.49**	.18	.23	.20	.17	.15	.26	.25	.27
	5	.40	.54	**.63**		**.28**	.27	.26	.28	.22	.34	.31	.36
	6	.14	.21	.31	**.31**		**.52**	.40	.41	.40	.37	.28	.25
	7	.17	.23	.30	.35	**.60**		**.56**	.49	.44	.43	.34	.33
	9	.22	.26	.27	.29	.52	**.60**		**.57**	.51	.47	.36	.35
	10	.09	.16	.18	.24	.42	.53	**.59**		**.53**	.41	.34	.35
	12	.16	.25	.23	.26	.39	.44	.49	**.57**		**.49**	.41	.34
	14	.23	.31	.35	.37	.34	.36	.44	.39	**.34**		**.63**	.53
	15	.18	.27	.30	.33	.27	.32	.39	.34	.38	**.59**		**.65**
	17	.14	.18	.30	.28	.20	.28	.37	.33	.30	.53	**.65**	

estimator to predict membership *versus* non-membership in the high 6–17 years trajectories of HI and IN. Sex was entered first in all models. Measures at 1.5, 2.5, 4, and 5 years were entered in successive models (2–5) to estimate their added contributions through time.

Genetic modeling

We used the Cholesky decomposition model implemented in Mplus version 8.1 (Muthén & Muthén, 2017) to decompose the variances and covariances of HI and IN across 12 time-points. This choice of model was based on one study (Kuntsi et al., 2005) showing the Cholesky model fit longitudinal ADHD symptoms data better than five alternate models (i.e., the independent pathway model, the common pathway model, the simplex model and the state-trait model). Participants with missing data were included using full information maximum likelihood to handle missing values. We used the usual fit indices (Akaike Information Criteria, Comparison Fit Index and Root Mean Square Error of Approximation) to assess and compare nested model fit and 95% confidence intervals to assess the significance of estimates.

Genetic modeling decomposes phenotypic variances and covariances into their genetic (additive A and/or dominant D), shared environment (C) and unique environment (E; including measurement error) components. The rationale is based on the fact that, by descent, monozygotic twins (MZ) share 100% of their segregating genes while dizygotic twins (DZ) share on average 50% and that both types of twin pairs grow in the same family. The extent to which MZ twins are more similar than DZ twins reflects contributions from genes. Similarity within families, regardless of zygosity, reflects shared environment contributions. Unique environment reflects differences within MZ twin pairs. The model postulates equal environments for MZ and DZ, whereby environmentally caused similarity does not differ for MZ and DZ twins. The model further assumes the additivity of variance and covariance components. The Cholesky decomposition estimates the contributions of A (and/or D), C, and E components specific to each time-point and from all previous data points (Loehlin et al., 2005).

Results

Descriptive statistics

Table 2 presents means and SDs for the total sample, by sex and by zygosity for HI (top panel) and IN (bottom panel).

HI means peaked at age 4, whereas IN peaked at age 7. Overall, *t*-tests and Levene tests (see Supplementary Information document – Table S1) identified (1) higher levels of HI in preschool PRs (.73–.92) than in primary school teacher-reports (.34–.56) and adolescence PRs (.31–.44); (2) higher levels of IN in primary school teacher-reports (.66–.85) than preschool (.50–.70) and adolescence (.45–.62) PRs (except at age 4 years); (3) sex mean and variance differences, with higher levels in boys than girls of both HI and IN at all time-points, except IN at 1.5 years, and greater variances on all measures in boys from age 6 years onward; (4) lower levels of HI and IN in MZs at 6, 7, 17 years and 7 and 17 years than in DZ, and (5) lower variances in HI and IN in MZs than DZ at 1.5, 2.5, 4, 7, 15, and 17 years, and at 5 and 17, respectively. Nonetheless, constraining sex and zygosity means and variances to equality in genetic models did not deteriorate model fit (data available on request) indicating no consistent scalar or contrast effect. We did not pursue further testing of age-specific contrast or scalar effects.

Objective 1

Trajectories analyses were implemented separately for HI and IN, testing 2–6-trajectory solutions between ages 6 and 17 years (see Supplementary Information document – Table S2).

For both HI and IN, based on predefined criteria, the 3-trajectory solution with significant multinomial quadratic terms was retained (Fig. 1). The 3-trajectory solutions for HI and IN are consistent with theory and identify a high decreasing subgroup with membership proportions (10.4% for HI and 17.3% for IN).

Table 3 presents binomial logistic regression results of models predicting membership *versus* non-membership in the high

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Table 2. Means (SD) for the total sample, by sex, zygosity, and age for hyperactivity/impulsivity (top) and inattention (bottom) by age

Hyperactivity/Impulsivity								
Age	Sample	Males	Females	MZM	MZF	DZM	DZF	DZO
1.5	.75 (.47)	.80 (.48)	.70 (.45)	.81 (.45)	.72 (.40)	.76 (.48)	.71 (.50)	.75 (.49)
2.5	.73 (.47)	.80 (.48)	.66 (.46)	.79 (.45)	.69 (.44)	.75 (.50)	.71 (.49)	.74 (.49)
4	.92 (.42)	.98 (.41)	.86 (.41)	.98 (.38)	.87 (.40)	.89 (.42)	.86 (.42)	.96 (.45)
5	.86 (.42)	.93 (.41)	.80 (.42)	.94 (.41)	.83 (.39)	.86 (.38)	.84 (.46)	.85 (.43)
6	.56 (.60)	.71 (.65)	.41 (.50)	.65 (.62)	.36 (.47)	.77 (.69)	.46 (.56)	.58 (.59)
7	.49 (.55)	.63 (.60)	.35 (.47)	.57 (.58)	.30 (.43)	.64 (.62)	.39 (.47)	.56 (.58)
9	.48 (.53)	.63 (.63)	.29 (.46)	.63 (.66)	.25 (.43)	.60 (.60)	.38 (.52)	.47 (.59)
10	.40 (.53)	.56 (.58)	.25 (.43)	.56 (.61)	.24 (.43)	.56 (.59)	.31 (.48)	.37 (.46)
12	.34 (.48)	.48 (.53)	.22 (.41)	.45 (.54)	.21 (.39)	.46 (.50)	.27 (.48)	.36 (.49)
14	.44 (.41)	.53 (.42)	.34 (.37)	.49 (.42)	.37 (.36)	.51 (.42)	.37 (.40)	.43 (.39)
15	.33 (.35)	.37 (.37)	.29 (.34)	.33 (.36)	.30 (.31)	.36 (.37)	.35 (.39)	.32 (.36)
17	.31 (.35)	.35 (.38)	.28 (.32)	.30 (.37)	.27 (.27)	.36 (.37)	.32 (.38)	.33 (.38)
Inattention								
Age	Sample	Males	Females	MZM	MZF	DZM	DZF	DZO
1.5	.50 (.45)	.53 (.46)	.48 (.44)	.52 (.48)	.52 (.45)	.47 (.45)	.48 (.46)	.52 (.43)
2.5	.52 (.46)	.58 (.47)	.47 (.45)	.57 (.48)	.49 (.45)	.54 (.45)	.50 (.46)	.53 (.47)
4	.78 (.40)	.83 (.45)	.74 (.41)	.81 (.42)	.81 (.42)	.78 (.50)	.70 (.42)	.79 (.42)
5	.70 (.43)	.78 (.43)	.63 (.43)	.79 (.42)	.66 (.40)	.71 (.46)	.64 (.48)	.70 (.43)
6	.78 (.66)	.93 (.69)	.63 (.61)	.91 (.71)	.58 (.58)	.99 (.70)	.75 (.67)	.75 (.63)
7	.85 (.69)	.99 (.70)	.70 (.64)	.98 (.72)	.58 (.60)	.98 (.69)	.81 (.66)	.88 (.68)
9	.83 (.70)	.99 (.73)	.67 (.64)	.98 (.76)	.53 (.60)	.99 (.68)	.82 (.65)	.78 (.72)
10	.79 (.70)	.96 (.72)	.63 (.64)	.99 (.71)	.48 (.56)	.90 (.75)	.78 (.71)	.73 (.69)
12	.66 (.68)	.82 (.70)	.52 (.63)	.82 (.72)	.53 (.60)	.78 (.68)	.59 (.71)	.66 (.69)
14	.62 (.56)	.78 (.53)	.48 (.55)	.77 (.55)	.48 (.56)	.71 (.50)	.50 (.58)	.65 (.57)
15	.46 (.49)	.56 (.51)	.37 (.46)	.57 (.54)	.36 (.49)	.49 (.49)	.43 (.44)	.47 (.49)
17	.45 (.49)	.54 (.51)	.37 (.46)	.48 (.49)	.27 (.36)	.49 (.49)	.49 (.57)	.51 (.53)

decreasing trajectories of HI (top) and IN (bottom) from preschool PRs.

Odds ratios (ORs) for sex varied between 3.10 and 3.77 in all models indicating that being a boy increased about 3–4-fold the risk of belonging to high trajectories of both HI and IN. When entered, HI at ages 1.5, 2.5, 4, and 5 years all predicted membership, above and beyond sex and previous HI. Every level unit of the newly introduced HI measure increased the risk of belonging to the high trajectory 2–4.5-fold (ORs = 2.09, 4.59). In the final model, only sex and HI at age 5 years uniquely predicted membership. Similarly, when entered, IN at ages 4 and 5 years predicted membership above and beyond sex and previous IN. Every level unit of the newly introduced IN increased the risk of belonging to the high trajectory 2.5–4-fold (ORs = 2.53, 4.09). In the final model, only sex and IN at age 5 years uniquely predicted membership.

Objective 2

Table 4 presents intraclass correlations (ICCs) for MZ and DZ twins for HI (right) and IN (left). As MZ ICCs exceeded double the DZ ICCs for all HI measures, and eight out of 12 IN measures, ADE (additive genetic, dominant genetic and unique environment model), ACE (additive genetic, shared environment and unique environment model) and nested models AE (additive genetic and unique environment model) were tested. MZ and DZ variances and means were constrained to equality without deteriorating model fit. For both HI and IN, the best fitting model was an AE model (Table 5).

Table 6 provides standardized estimates of A (left) and E (right) for all time-points for HI (top) and IN (bottom) and the contributions of preschool time-points to all later time-points (with 95% confidence intervals).

HI heritability was relatively stable from ages 1.5 to 17 years (.51– .79) with no consistent differences across ages and informants. Together, preschool measures accounted for 24%, 23%, 13%, 11%, 16%, 23%, 22%, and 16.5%, respectively, of the total heritability of HI at ages 6 to 17 years (i.e., the sum of the A contribution to each preschool measure divided by the total heritability). Notably, genetic factors at age 1.5 years accounted for 4%–13% of the heritability of all eight primary school and

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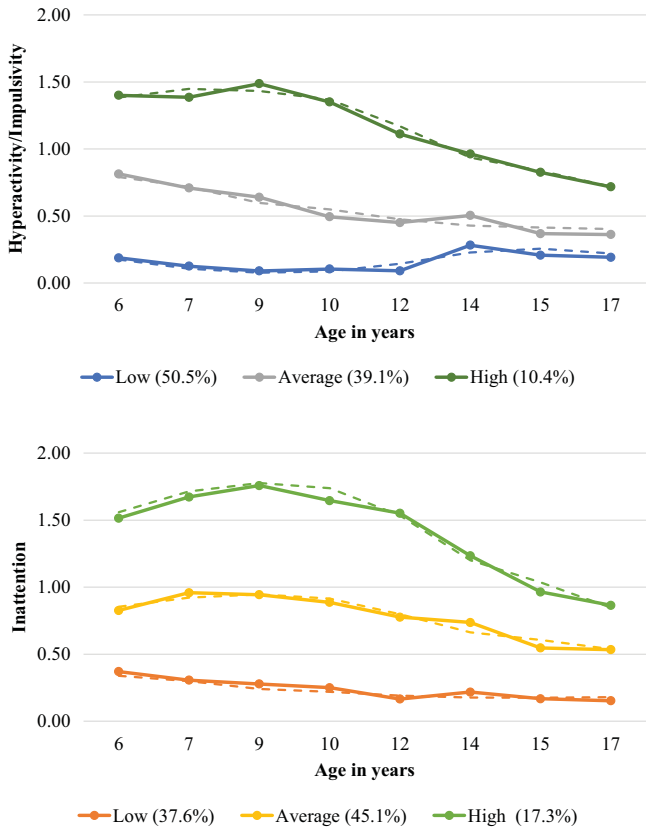

Figure 1. Trajectories of hyperactivity/impulsivity (top panel) and inattention (bottom panel) from 6 to 17 years. Dotted lines illustrate estimated values; bold lines illustrate observed values.

adolescence measures except for two at ages 10 and 17. Genes at age 1.5 years explained 92%, 100%, 85%, 94%, 81%, and 68% of the albeit modest correlations with measures at ages 6, 7, 9, 12, 14, and 15 respectively. Persisting genetic contributions from teacher-reports at age 6 through primary school accounted for 28%–59% of the heritability of later measures (see Supplementary Information document – Table S3). Contributions of E overlapped in preschool measures but were largely age-specific thereafter.

IN heritability was also relatively stable from ages 1.5 to 17 years (.41–.62), albeit more moderate than HI heritability overall, and with no consistent differences across ages and informants. Together, preschool measures accounted for 11%, 19%, 21%, 24%, 18%, 20%, 36%, and 26% of the heritability of IN at ages 6, 7, 9, 10, 12, 14, 15, and 17, respectively. Similar to HI, we observed persisting genetic contributions from preschool IN except at age 4. Significant contributions accounted for 11% – 25% of the heritability of all eight primary school and adolescence measures except for two at ages 6 and 14. Genes at age 4 years explained 92%, 96%, 100%, 85%, 80%, and 79% of the phenotypic correlations with measures at 7, 9, 10, 12, 15, and 17, respectively. Persisting genetic contributions through primary school, accounting for 21%–48% of the heritability of later measures, were also observed from teacher-reports at age 6. Genetic factors from previous ages completely accounted for the heritability of IN from ages 14 to 17 (see Supplementary Information document – Table S3). Finally, contributions of E were mostly age specific.

Parameter estimates for the full Cholesky decomposition are provided in Supplementary Information document – Table S3. They show that, after age 6, additional genetic and unique environment contributions for both HI and IN are mostly age specific.

Discussion

This population-based study provides empirical evidence that preschool parent reports of hyperactivity/impulsivity and inattention capture both phenotypic and genetic liabilities that span over 15 years, and across multiple informants. As such, it offers new insights into the predictive validity of preschool PRs of HI and IN. At the phenotypic level, the findings show that, starting at age 1.5 years for HI and 4 years for IN, preschool parent reports predict trajectories depicting high levels of HI and IN from ages 6 to 17 years. Moreover, the prediction is incremental: subsequent preschool assessments increase the relative risk. At the genetic level, the most striking result is that the ages of onset of the phenotypic predictions coincide with new genetic influences that are largely responsible for the stability of ADHD dimensions from preschool to adolescence. Together, genes expressed before age 6 account for up to a quarter of the heritability of HI and a third of the heritability of IN up to age 17 years.

Predicting developmental trajectories

The first objective was to determine if preschool PRs predict subsequent high HI/IN trajectories into late adolescence. No study had previously examined the longitudinal stability of preschool HI and IN over this age range. We identified three-trajectory patterns with one high decreasing trajectory for both HI and IN. Similar three-trajectory patterns were observed in most trajectory/profile studies including preschoolers (Galera et al., 2011; Leblanc et al., 2008; Salla et al., 2016) and older children and adolescents (Pingault et al., 2011; Sasser et al., 2016). Vergunst et al., (2018) is the only previous study to cover preschool through adolescence. These authors also found small groups of preschoolers following chronic trajectories of HI and IN but did not test if preschool levels predicted these outcomes. Our study provides evidence that high trajectories of HI/IN from primary school to adolescence, largely informed by different raters at different ages, can be predicted by monitoring preschool development. Monitoring is the key word: while individual preschool time-points, starting at age 1.5 years for HI and 4 years for IN, predict the high trajectory outcomes, regression models show that each subsequent time-point adds to the prediction. These results are also consistent with studies showing that HI in toddlers, and possibly earlier, is more predictive as a dimension of ADHD than IN (Joseph et al., 2023). Overall, the phenotypic results suggest that timely monitoring is needed to assess risk more reliably than single screening assessments and that parents of preschoolers provide valuable information in that respect.

Early onset genetic factors and their role in phenotypic stability

The second objective of this study was to test if genetic contributions to preschool PRs of HI/IN span into adolescence and across informants. The rationale is that, as valid predictors of later HI/IN, preschool PRs should capture the underlying genetic liability of *what is stable* in ADHD dimensions. The high heritability of both HI and IN from preschool onward is well documented (Grimm et al., 2020). Estimates of heritability in this

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Table 3. Binary logistic regression models predicting high decreasing trajectories of HI (top) and IN (bottom) from 1.5, 2.5, 4, and 5-year parent reports of HI and IN

Hyperactivity/Impulsivity								
Model	Predictor	Loglikelihood	LRT	*p*	*B*	SE	*p*	OR [95%CI]
1		− 2277.66 (10)						
	Sex				1.33	.26	< .001	3.77 [2.25, 6.32]
2		− 2272.10 (11)	9.32	.002				
	Sex				1.25	.27	< .001	3.48 [2.07, 5.85]
	1.5 yr HI				0.74	.24	.002	2.09 [1.31, 3.36]
3		− 2263.56 (12)	18.880	< .001				
	Sex				1.12	.27	< .001	3.21 [1.90, 5.44]
	1.5 yr HI				0	.29	.99	1.00 [0.57, 1.78]
	2.5 yr HI				1.36	.31	< .001	3.88 [2.11, 7.16]
4		− 2260.10 (13)	6.92	.009				
	Sex				1.13	.27	< .001	3.10 [1.83, 5.27]
	1.5 yr HI				− 0.13	.30	.66	0.88 [0.50, 1.58]
	2.5 yr HI				1.07	.33	.001	2.91 [1.53, 5.55]
	4 yr HI				0.92	.36	.01	2.50 [1.24, 5.02]
5		− 2253.39 (14)	13.43	< .001				
	Sex				1.16	.27	< .001	3.19 [1.87, 5.45]
	1.5 yr HI				− 0.23	.31	.45	0.79 [0.43, 1.45]
	2.5 yr HI				0.82	.34	.02	2.27 [1.16, 4.42]
	4 yr HI				0.35	.39	.36	1.42 [0.67, 3.03]
	5 yr HI				1.50	.41	< .001	4.49 [2.03, 9.97]
Inattention								
Model	Predictor	Loglikelihood	LRT	*p*	*B*	SE	*p*	OR [95%CI]
1		− 2439.91 (10)						
	Sex				1.32	.20	< .001	3.73 [2.53, 5.50]
2		− 2439.92 (11)	0.01	.93				
	Sex				1.32	.20	< .001	3.74 [2.53, 5.52]
	1.5 yr IN				− 0.02	.20	.92	0.98 [0.66, 1.46]
3		− 2437.85 (12)	4.12	.062				
	Sex				1.29	.20	< .001	3.64 [2.47, 5.38]
	1.5 yr IN				− 0.22	.23	.34	0.08 [0.51, 1.26]
	2.5 yr IN				0.45	.22	.06	1.58 [1.02, 2.44]
4		− 2430.41 (13)	14.88	< .001				
	Sex				1.26	.20	< .001	3.54 [2.39, 5.25]
	1.5 yr IN				− 0.31	.23	.18	0.733 [0.46, 1.16]
	2.5 yr IN				0.22	.23	.35	1.246 [0.79, 1.97]
	4 yr IN				0.93	.24	< .001	2.52 [1.57, 4.07]
5		− 2417.026 (14)	26.77	< .001				
	Sex				1.18	.21	< .001	3.26 [2.18, 4.86]
	1.5 yr IN				− 0.33	.24	.17	0.79 [0.45, 1.15]
	2.5 yr IN				0.04	.24	.86	1.04 [0.65, 1.67]
	4 yr IN				0.42	.27	.12	1.52 [0.90, 2.57]
	5 yr IN				1.41	.28	< .001	4.09 [2.37, 7.06]

Note. Constant is included in all models but not shown; LRT = Likelihood Ratio Test.

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Table 4. MZ and DZ intraclass correlations (ICC) for hyperactivity/impulsivity (left) and inattention (right) by age

	Hyperactivity/Impulsivity				Inattention			
	MZ		DZ		MZ		DZ	
Age	ICC	N pairs	ICC	N pairs	ICC	N pairs	ICC	N pairs
1.5	.60	226	.06	334	.44	221	.24	332
2.5	.55	217	.01	310	.58	213	.23	307
4	.58	189	.14	263	.44	189	.18	263
5	.64	196	.04	267	.41	196	.12	267
6	.66	160	.33	224	.55	160	.25	224
7	.61	174	.25	235	.61	174	.39	236
9	.73	152	.18	209	.61	152	.19	209
10	.60	157	.21	215	.53	157	.16	215
12	.53	109	.20	172	.55	109	.32	172
14	.67	162	.10	236	.52	162	.01	236
15	.61	152	.16	227	.47	152	.05	227
17	.72	161	.22	235	.56	161	.27	236

Table 5. Comparisons of Cholesky model fits for HI and IN. The best fitting models appear in bold

Models	DF	AIC	BIC	CFI	RMSEA
HI ADE	246	8989.30	10,093.27	.95	.04
HI ACE	246	9080.30	10,184.27	.93	.05
HI AE	**168**	**8936.92**	**9690.84**	**.95**	**.04**
IN ADE	246	13,264.18	14,367.78	.93	.04
IN ACE	246	13,258.08	14,362.57	.93	.04
IN AE	**168**	**13,138.99**	**13,892.67**	**.94**	**.04**

Note. ADE = Additive genetic, dominant genetic and unique environment model; ACE = Additive genetic, shared environment and unique environment model; AE = Additive genetic and unique environment model; DF = Degrees of freedom; AIC = Akaike information criterion; BIC = Bayesian information criterion; CFI = Comparison fit index; RMSEA = Root mean square error of approximation.

study are well within the expected range overall, slightly higher for HI than IN, with no systematic change across ages.

The most remarkable results pertain to the presence of early onset genetic factors, as early as age 1.5 years for HI and 4 years for IN, which show enduring contributions through adolescence. Genes underlying individual differences in HI at age 1.5 years, as reported by parents, account for a modest portion of the heritability of later HI but are almost entirely responsible for the stability of this dimension of ADHD from preschool to adolescence. This occurs later for IN, at age 4 years, even before the attentional demands of formal schooling. The daily routine of a 4-year-old may be less likely to make IN salient, yet our results show that parents are sensitive to heritable individual differences underlying the later stability of IN. Moreover, when genetic factors present between ages 1.5 and 5 are considered, together they explain a substantial proportion of the heritability of later HI and IN.

Previous studies had shown that ADHD symptoms were highly heritable at ages 1.5–2 years and that these genetic factors were shared with symptoms up to ages 4–5 (Eilertsen et al., 2019; Price et al., 2001, 2005) and age 8 (Kuntsi et al., 2005). However, no behavior genetic study had shown that genetic influences identified in preschool explained part of the heritability of HI and IN into late adolescence. Nevertheless, these results are consistent with a recent systematic review (Bonvicini et al., 2018) and a recent meta-analysis of genome-wide studies of ADHD (Rovira et al., 2020) showing that many ADHD candidate genes and SNPs overlap in children and adults.

Genetic factors than also span longitudinally were found at age 6 years, at school entry. These could underlie symptom changes as cognitive demands and behavioral regulation increase, but also the change from parent to teacher-reports. Hypotheses regarding the sources of change are more limited in this context. Nonetheless, the substantial genetic contributions of preschool PRs into primary school and adolescence, and again at age 6 with teacher-reports, could be reflected by the decrease in dopamine (DA) transporter density during life (Jucaite et al., 2010). DA transporter and receptor genes are the most important components in the etiology of ADHD (Wu et al., 2012). As both hypo- and hyperdopaminergic states will impair the prefrontal cortex (PFC) functions (Arnsten, 1998), and the PFC is primary in mediating executive functions whose impairments are correlated with ADHD symptoms (Willcutt et al., 2005), it is plausible that the age-dependent decrease in DA transporters and receptors may impair the PFC functions, which in turn may affect the ADHD symptoms throughout adolescence and adulthood. Alternatively, common genetic variations underlying risk for other traits (e.g., developmental dyslexia, language development, general cognitive ability) may also contribute to HI and IN symptoms (Couto et al., 2009; Mascheretti et al., 2017; Wigg et al., 2008). Another possibility is the presence of gene-by-environment interactions whereby the cognitive and social demands at specific periods (e.g., increasing demands for self-regulation in toddlers, increasing cognitive demands in late preschool and exposure to schooling in early primary school) foster the expression of genetic liabilities in a diathesis-stress fashion (Kovas & Plomin, 2007).

Overall, the present results suggest that the genetic factors involved in individual differences of ADHD dimensions are in place before school entry, that PRs are able to detect them, and that the same genetic factors continue to play a role in later HI and IN heritability. This pattern is consistent with previous studies in primary school and adolescence (Pingault et al., 2015) and suggests the onset is probably earlier.

Environmental contributions to the longitudinal architecture of HI and IN

Unique environment factors contributed substantially to individual differences in IN (.37–.60) and to a lesser extent in HI (.22–.50), more so than in previous studies. There are two predominant patterns of environmental influences on ADHD: transient effects contributing to single measurement occasions and stable effects that persist over time (Livingstone et al., 2016). As in previous studies, we found mostly transient unique environment factors (Chang et al., 2013; Faraone et al., 2015; Greven et al., 2011; Kuntsi et al., 2005; Larsson et al., 2004, 2014; Pingault et al., 2015).

Unique environment factors are rarely of a persistent nature in psychopathology. Traditional interpretations of environmental risks in psychopathology target family-level risks (Froehlich et al., 2011; Law et al., 2014; Sfelinioti & Livaditis, 2017; Thapar et al., 2012; Vergunst et al., 2019; Wolford et al., 2017). However, if these

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Table 6. standardized parameter estimates from Cholesky model for HI and IN of additive genetic (A) and nonshared environment (E) for preschool measures to subsequent measures. Significant parameters based on 95% confidence intervals are presented in bold

	A parameter for Hyperactivity/Impulsivity					E parameter for Hyperactivity/Impulsivity				
Age	1.5	2.5	4	5	Total	1.5	2.5	4	5	Total
1.5	**.56 [.47, .65]**				.56	**.44 [.36, .53]**				.44
2.5	**.31 [.22, .40]**	**.21 [.13, .28]**			.52	**.06 [.02, .10]**	**.42 [.35, .50]**			.48
4	**.22 [.13, .30]**	.03 [.00, .08]	**.32 [.23, .39]**		.57	.02 [.00, .04]	**.06 [.02, .09]**	**.36 [.30, .43]**		.44
5	**.19 [.10, .27]**	**.10 [.20, .17]**	**.15 [.08, .22]**	**.19 [.12, .27]**	.62	.02 [.00, .04]	**.05 [.02, .08]**	**.03 [.01, .05]**	**.28 [.23, .34]**	.38
6	**.03 [.01, .07]**	.01 [– .02, .04]	**.07 [.01, .14]**	**.06 [.01, .12]**	.70	.00 [.00, .01]	.02 [.00, .04]	.00 [– .01, .01]	.01 [.00, .01]	.30
7	**.05 [.01, .09]**	0 [– .01, .02]	.03 [– .01, .07]	**.07 [.01, .14]**	.65	.00 [.00, .00]	**.04 [.01, .07]**	.01 [.00, .03]	.00 [– .01, .01]	.35
9	**.06 [.02, .11]**	0 [– .01, .01]	.02 [– .01, .05]	.01 [– .02, .04]	.70	.00 [.00, .01]	.02 [.00, .05]	.01 [– .01, .02]	.01 [– .01, .02]	.30
10	.02 [.00, .05]	0 [– .01, .02]	.03 [– .01, .07]	.01 [– .02, .04]	.57	.00 [.00, .00]	.01 [– .01, .03]	.00 [.00, .00]	.02 [– .01, .04]	.43
12	**.04 [.01, .08]**	0 [– .01, .01]	.04 [– .02, .09]	.00 [– .01, .01]	.51	.00 [.00, .00]	**.05 [.01, .09]**	.00 [.00, .00]	.02 [– .01, .04]	.50
14	**.08 [.02, .15]**	.03 [– .02, .09]	.00 [.00, .00]	.04 [– .02, .10]	.66	.01 [– .01, .02]	.02 [.00, .04]	**.05 [.02, .08]**	.01 [– .01, .03]	.35
15	**.03 [.01, .08]**	.04 [– .02, .09]	.03 [– .01, .08]	.05 [– .02, .11]	.67	.01 [– .01, .03]	.03 [.00, .05]	.01 [.00, .03]	.00 [.00, .00]	.33
17	.03 [–.01, .07]	.03 [– .03, .08]	.03 [– .02, .07]	.04 [– .03, .11]	.79	.00 [– .01, .01]	.00 [– .01, .01]	.01 [.00, .03]	.00 [.00, .00]	.22
	A parameter for Inattention					E parameter for Inattention				
Age	1.5	2.5	4	5	Total	1.5	2.5	4	5	Total
1.5	**.45 [.38, .52]**				.45	**.55 [.48, .63]**				.55
2.5	**.21 [.13, .28]**	**.37 [.30, .45]**			.58	.02 [.00, .04]	**.40 [.34, .47]**			.42
4	**.12 [.05, .19]**	**.03 [– .01, .07]**	**.33 [.25, .42]**		.48	.00 [.00–, 04]	.01 [– .01, .03]	**.51 [.43, .59]**		.52
5	**.07 [.02, .12]**	.02 [– .01, .06]	**.13 [.05, .21]**	**.19 [.10, .27]**	.41	.00 [.00, .01]	.03 [.00, .05]	**.05 [.01, .09]**	**.52 [.44, .60]**	.60
6	.00 [– .01, .01]	.01 [– .01, .02]	.02 [– .02, .05]	.03 [– .02, –.07]	.53	.00 [– .01, .01]	.00 [– .01, .01]	.01 [– .01, .03]	.03 [.00, .05]	.48
7	.00 [– .01, .01]	.02 [– .01, .05]	**.10 [.03, .17]**	.00 [– .01, .02]	.64	.01 [.00, .02]	.00 [.00, .01]	.00 [.00, .01]	.02 [.00, .04]	.36
9	.00 [– .01, .01]	.01 [– .01, .03]	**.09 [.02, .16]**	.04 [– .02, .11]	.61	.00 [– .01, .01]	.02 [.00, .04]	.00 [.00, .00]	.00 [– .01, .01]	.39
10	.01 [– .01, .03]	.02 [– .01, .06]	**.08 [.01, .15]**	.01 [– .02, .04]	.50	.00 [.00, .01]	.00 [.00, .00]	.00 [.00, .00]	**.03 [.01, .07]**	.49
12	.01 [– .01, .03]	.01 [– .01, .02]	**.07 [.01, .14]**	.02 [– .03, .06]	.62	.00 [.00, .00]	.00 [.00, .00]	.00 [– .01, .01]	.01 [– .01, .03]	.40
14	.00 [– .01, .01]	.03 [– .02, .07]	.02 [– .02, .05]	.04 [– .03, .10]	.44	.00 [– .01, .01]	.01 [– .01, .02]	.03 [.00, .06]	.03 [.00, .06]	.56
15	.00 [.00, .01]	.01 [– .02, .04]	**.11 [.03, .20]**	.04 [– .03, .11]	.44	.00 [– .01, .01]	.01 [– .01, .03]	.01 [– .01, .02]	.01 [– .01, .03]	.57
17	.00 [– .01, .01]	.01 [– .02, .04]	**.09 [.01, .17]**	.06 [– .03, .14]	.62	.00 [– .01, .01]	.02 [.00, .05]	.00 [– .01, .01]	.02 [.00, .05]	.37

were affecting children from the same family similarly, we should find shared environment factors in the etiology of ADHD symptoms, yet very few studies do so (Wood et al., 2010). An explanation for the inconsistencies across genetic and phenotypic studies regarding what constitutes unique environment may be that presumably shared environmental risks affect children within families differently (Barkley, 2016; Capusan et al., 2016; Jimenez et al., 2017; Lehn et al., 2007; Pettersson et al., 2015).

Biological processes occurring during foetal development such as post-twinning de novo copy number variants (Ehli et al., 2012) or methylation processes (Walton et al., 2017) not shared by co-twins could create differences that emerge at an age when normative HI should start decreasing in most children. Tikhodeyev and Shcherbakova (2019) argued that the stochasticity of molecular processes at critical stages of development can cause MZ dissimilarities and that most of the unique environment factors affecting a variety of phenotypes are internal in nature rather than external. These could influence the individual structure and functional capacity of brain networks involved in behavior and cognition (Faraone et al., 2015), particularly of the frontal executive brain (Barkley, 2016).

Issues with parent reports?

PRs of HI and IN are the most frequent sources of information in preschoolers. Although most recognize the ecological validity of PRs at face value (Schneider et al., 2020), many question the ability of parents to provide unbiased assessments and to recognize what deviates from the normative development of behavior/attention regulation. Participants in this study were assessed almost yearly and by up to seven different raters at different time-points. Fathers and mothers provided concurrent assessments in preschool and in adolescence; teachers provided successive assessments during primary school. Our results replicate earlier findings of modest agreement across raters (Schneider et al., 2020) but also shed new light on what can and cannot be attributed to parent biases.

First, although agreement was higher within PRs and across teachers, there was increasing agreement *between* teachers and parents by adolescence suggesting that lower agreement at earlier ages may reflect developmental changes in ADHD dimensions. Indeed, agreement across parent- and teacher-reports did not differ at the transition from primary school to adolescence. Second, low DZ correlations often attributed to parent contrast effects show similar patterns in teacher-reports where twins mostly have different teachers. Third, levels of HI are highest in preschool PRs but lowest in adolescence PRs. Often, high HI levels in PRs were deemed inflated, reflecting parents' difficulties in dealing with hyperactive children (Chen et al., 2017; Moens et al., 2018). Similarly, PRs were deemed less reliable in capturing IN in preschoolers. On the contrary, teachers are deemed a more valid source in young children because they often tend to consider child behavior as normative (Narad et al., 2015). However, mean levels of IN did not differ across parents and teachers from ages 4 to 12 but declined in adolescence PRs. The aggregation of concurrent mother- and father-reports likely reduced both contrast effects and inflated means (Sollie et al., 2013). Although we cannot exclude the effects of *rater changes*, these results suggest that successive parent- and teacher-reports could likely reflect *developmental changes*.

Limits

These results need to be considered within the limits of the study. First, the sample had low power to detect dominant genetic factors, although intraclass correlation patterns appeared to suggest them. Second, there was no way to assess cross-informant agreement at the same age because we lacked overlapping parent- and teacher-reports. However, we were able to document that preschool PRs of HI/IN predict later HI/IN and capture their etiological continuity, regardless of informant. Third, although we were able to assess the predictive validity of preschool PRs of HI/IN across primary school and adolescence, significant impairments are retained also into early adulthood. Future studies are therefore needed in order to assess phenotypic and etiological continuity from early ages through adulthood. Fourth, the SBQ used only seven items to assess HI/IN and some aspects of the IN dimension specific to preschooler may be lacking. However, a good construct validity was previously reported (Collet et al., 2022) and our results showed the current scales predict developmental trajectories. Fifth, the present study measures HI and IN dimensions in a population-based sample of twins; the obtained results cannot be therefore generalized to clinical samples.

Conclusion

Behavior genetic studies often neglect the theoretical or clinical questions their intricate models address. This study highlights the usefulness of complementary clinically driven phenotypic and genetic analyses. The American Academy of Pediatrics invites practitioners to consider ADHD as a diagnosis as early as age 4, to either provide environmental support, parent training and/or pharmacological treatments that shield preschoolers from other deleterious effects of ADHD. Our results, from both a phenotypic and a genetic perspective, provide empirical evidence that PRs are valid means to monitor highly hyperactive/impulsive and/or inattentive toddlers when close follow-ups are implemented to detect the persistence of symptoms. The consistent predictions of age 6–17 years high trajectories of ADHD dimensions from successive preschool PRs empirically support this conclusion as do the genetic influences persisting into adolescence. Thus, not only do preschool parents reports of HI/IN incrementally predict chronic trajectories into late adolescence at the phenotypic level, but they also capture the genetic liability largely responsible for the stability of ADHD dimensions from preschool onward. Both medical and educational professionals should therefore be encouraged to get information about children for early identification and treatment of at-risk kids. This may potentially change the trajectory of psychiatric morbidity later in life and improve functional outcomes.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S095457942400035X.

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Competing interests. None.

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