Archival Report

Biological Psychiatry

Phenotypic and Genetic Associations Between Preschool Fine Motor Skills and Later Neurodevelopment, Psychopathology, and Educational Achievement

Aislinn Bowler, Tomoki Arichi, Pasco Fearon, Emma Meaburn, Jannath Begum-Ali, Greg Pascoe, Mark H. Johnson, Emily J.H. Jones, and Angelica Ronald

ABSTRACT

BACKGROUND: Fine motor skills are heritable and comprise important milestones in development, and some evidence suggests that impairments in fine motor skills are associated with neurodevelopmental conditions, psychiatric disorders, and poor educational outcomes.

METHODS: In a preregistered study of 9625 preschool children from TEDS (Twins Early Development Study), fine motor assessments (drawing, block building, folding, and questionnaires) were conducted at 2, 3, and 4 years of age. A cross-age fine motor score was derived using principal component analysis. Multivariate regression analysis was used to examine the relationships between the fine motor score and neurodevelopmental traits, psychopathology, and educational outcomes at 3 later ages (7–8, 12, and 16 years) and cross-age psychopathology composite scores. Polygenic scores (PGSs) were created for attention-deficit/hyperactivity disorder (ADHD), autism, schizophrenia, anxiety, major depressive disorder, obsessive-compulsive disorder, and years of education. We ran single-PGS models and a multi-PGS model.

RESULTS: Fine motor skills were negatively associated with neurodevelopmental traits and psychopathology across childhood and adolescence and positively associated with educational achievement in adolescence ($\beta = 0.25$, $p < .001$). Superior fine motor skills were associated with a higher years-of-education PGS ($\beta = 0.07$, $p < .001$), a lower ADHD PGS ($\beta = -0.04$, $p = .011$), and a higher anxiety PGS ($\beta = 0.03$, $p = .040$). Similarly, the multi-PGS model retained the PGSs for years of education ($\beta = 0.07$), ADHD ($\beta = -0.03$), and anxiety ($\beta = 0.01$). A non-preregistered analysis in an independent preschool sample replicated the ADHD PGS association, but not the years of education or anxiety PGS associations.

CONCLUSIONS: Fine motor skills are linked genetically and phenotypically to later neurodevelopment, psychopathology, and educational outcomes. Future work should investigate the mechanisms that underlie the role of fine motor development in later outcomes.

https://doi.org/10.1016/j.biopsych.2023.11.017

Proficient motor skills require both the acquisition of physical capabilities, such as muscle tone, and substantial neurodevelopment, both of which develop steeply over the first years after the birth of a child (1). The large number of connections between motor areas and cognitive regions in the brain (2), the emerging evidence of impaired fine motor skills in individuals with neurodevelopmental or psychiatric traits and diagnoses (3–7), and the shared genetic etiology across neurodevelopmental and psychiatric disorders (8–11) suggest that motor skills may sit on the same pathway as multiple neurodevelopmental, psychiatric, and educational outcomes later in development. Observing fine motor skills early in life could contribute to the ability to preempt these later outcomes at a time in development when neuroplasticity is elevated (12).

Motor skills are highly heritable. In a meta-analysis of infant twin studies, psychomotor functions (which included phenotypes such as activity level, fine motor skills, and sitting without support) were the most heritable psychologically relevant domain in infancy [pooled $h^2 = 0.59$ (13)]. In addition, investigations into specific skills have revealed significant heritability of drawing skill (requiring proficient fine motor skills for success) at 4 years ($h^2 = 0.29$), which was as high as the heritability for intelligence (14). These studies support the notion that fine motor skills are heritable and indicate the opportunity for investigations into joint genetic underpinnings of fine motor skills and traits that are seen later in development.

Atypical motor development during the first years after birth could be an early marker for the later development of neurodevelopmental or psychiatric disorders. However, this

ISSN: 0006-3223

Biological Psychiatry May 1, 2024; 95:849–858 www.sobp.org/journal

question has not been extensively studied with respect to fine motor skills. In one study, questionnaire-assessed fine motor skills at age 6 years were associated with psychopathology at 11 years, including peer problems, emotional symptoms, and conduct problems (15). According to a systematic review, there is consistent evidence that impaired fine motor skills may be significantly associated with the neurodevelopmental condition attention-deficit/hyperactivity disorder (ADHD) (4). However, a more recent systematic review concluded that it remained unclear whether early fine motor impairments are associated with later ADHD (16). Furthermore, associations between early fine motor skills and autism spectrum disorder (henceforward, 'autism') are seen in the first 2 years after birth. Atypical longitudinal trajectories of early fine motor skills are also associated with autism (17), in addition to alterations in trajectories that combine early fine motor, gross motor, and language skills (6,7). Moreover, a meta-analysis investigating motor skills in first-degree relatives found evidence for impaired early fine motor skills in individuals with a family history of schizophrenia (3). Taken together, these findings indicate that it is unclear whether there is an association between impaired early motor skills and later neurodevelopmental conditions and psychopathology. However, some genetic influences are shared across neurodevelopmental and psychiatric conditions (8–11). Therefore, exploring whether there is an association between early fine motor impairments and not only specific neurodevelopmental and psychopathological phenotypes but also an overall composite score spanning these traits is warranted.

There is consistent evidence for an association between fine motor development and later cognitive outcomes. One study found an association between a "design copy" fine motor task at 3 and 4 years old and achievement scales (letter-word identification, passage comprehension, and sound awareness) at 5 years old (18). A longitudinal study across multiple American cohorts also found associations between fine motor skills (e.g., block building and drawing) at 5 years and later academic achievement at up to 10 years (19). Other studies have shown associations between childhood fine motor skills and IQ at 7 to 13 years (20), fluid intelligence and visual processing at 4 to 16 years (21), and academic performance at 6 to 12 years (15). However, a study by Piek *et al.* found that fine motor trajectories between 4 months and 4 years were not associated with later cognitive outcomes at 6 to 11 years (22). Further investigation is required to understand whether early fine motor skills are also associated with educational outcomes.

The association between motor skills and neurodevelopmental and psychiatric disorders could result from shared genetic underpinnings. Polygenic scores (PGSs) are a recent methodology that enables exploration of shared genetic effects. PGSs are calculated by summing the genetic risk from common single nucleotide polymorphisms derived from genome-wide association studies weighted by their effect sizes. A prospective population cohort study has shown that genetic liability for autism is associated with very early neuromotor measures (9–20 weeks) (23), providing preliminary evidence for shared genetic influences between early infancy motor development and autism. In the gross motor domain, age of first unsupported walking was associated with PGSs for neurodevelopmental disorders: specifically, a PGS for ADHD was associated with earlier walking, and a PGS for autism was associated with later walking (24); the PGS for autism (but not those for ADHD or schizophrenia) was also associated with overall (fine and gross) motor skills at age 3 years, but not at 6 or 18 months (25). We are aware of only 1 previous study that investigated neurodevelopmental or psychiatric disorder PGSs and early fine motor skills specifically, which found that fine motor skills at 18 months were not associated with the PGS for autism, schizophrenia, or ADHD (26). This study used parent-reported fine motor milestone achievements, which relies on parent recall. Alternatively, these skills can be assessed by asking children to complete fine motor tasks as they develop them.

Prospective studies enriched for infants with a family history of autism and ADHD have investigated the longitudinal development of early fine motor skills (6,7,17,27,28). However, an investigation has yet to take place into the associations between fine motor skills in early childhood and neurodevelopmental and psychiatric traits at multiple time points across childhood and adolescence. Understanding whether fine motor skills are associated with traits across childhood and adolescence or at specific ages is important. Given that autism, ADHD, and behavioral problems are most commonly diagnosed in early to midchildhood, the associations with fine motor skills may be stronger earlier in childhood. In contrast, depression is diagnosed more commonly in adolescence, and thus associations with early fine motor skills may be stronger during adolescence than middle childhood.

Given the existing literature, our study aimed to assess phenotypic and genetic associations between early fine motor skills and later neurodevelopmental, psychiatric, and cognitive traits. A measure of fine motor skills was derived from a combination of questionnaire items and parent-administered tasks with 2-, 3-, and 4-year-old children. The derived fine motor measure was then used to investigate phenotypic associations between early fine motor skills and later neurodevelopmental, psychiatric, and cognitive traits from childhood to adolescence. We collated these traits into 3 ages, midchildhood (7–8 years), late childhood (12 years), and adolescence (16 years) and derived psychopathology composite score scores (across age) to investigate how associations differ across development. In addition, in single- and multi-polygenic score analyses, we investigated the associations between PGSs and fine motor skills. We included PGSs for traits where evidence, as alluded to above, suggests that there might be associations, including autism, ADHD, schizophrenia, and educational outcomes, and those whose associations are as yet unclear, including obsessive–compulsive disorder, major depressive disorder, and anxiety.

In the longitudinal phenotypic analysis, our preregistered hypotheses were: 1) Fine motor skills in early childhood will be associated with autistic traits, ADHD, anxiety-depression, depression, behavior problems, psychopathology composite scores, and psychotic experiences; 2) Fine motor skills in early childhood will be more strongly associated with autistic traits, ADHD, and behavioral problems in midchildhood than in late childhood and adolescence; 3) Fine motor skills in early childhood will be more strongly associated with anxiety and depression traits in adolescence than in late childhood and

Table 1. Sample Demographics

	Preschool Measures/Overall, N = 9625							
	Age 2, n = 3945	Age 3, n = 5811	Age 4, n = 7798	Midchildhood, n = 7329	Late Childhood, n = 6365	Adolescence, n = 6503	Phenotypic Composite, n = 7779	PGS Data, n = 4514
Sex								
Male		4742 (49.3%)		3753 (51.2%)	3303 (51.9%)	3380 (52.5%)	3809 (49.0%)	2178 (48.2%)
Female		4883 (50.7%)		3576 (48.8%)	3062 (48.1%)	3061 (47.5%)	3970 (51.0%)	2336 (51.8%)
Age of Assessment, Years								
Self		–		–	11.32 (0.71)	16.35 (0.68)	–	–
GCSE		–		–	–	16.35 (0.68)	–	–
Parent	2.07 (0.14)	3.03 (0.14)	4.04 (0.13)	Age 7: 7.06 (0.25); age 8: 7.90 (0.53)	11.31 (0.69)	16.30 (0.29)	–	–
Teacher		–		7.20 (0.28)	11.56 (0.66)	–	–	–
Zygosity								
MZ		3295 (34.2%)		2593 (35.4%)	2287 (35.9%)	2323 (35.7%)	2743 (35.3%)	1164 (25.8%)
DZ		6330 (65.8%)		4736 (64.6%)	4078 (64.1%)	4180 (64.3%)	5036 (64.7%)	3350 (74.2%)

Values are presented as n (%) or mean (SD).

DZ, dizygotic; GCSE, General Certificate of Secondary Education; MZ, monozygotic; PGS, polygenic score.

midchildhood; and 4) Higher fine motor skills in early childhood will be associated with higher educational outcomes (General Certificate of Secondary Education results).

In the PGS analysis, our preregistered predictions were: 5) Higher fine motor skills will be associated with lower autism, ADHD, schizophrenia, and psychopathology composite score PGSs and a higher years-of-education PGS. Associations with obsessive-compulsive disorder, anxiety, and major depressive disorder PGSs will be smaller; and 6) The amount of variance explained in fine motor skills in the multiple PGS model will be greater than in any single-PGS analysis.

METHODS AND MATERIALS

Preregistration

This study's methods and hypotheses were preregistered on the Open Science Framework (https://osf.io/ej3r6) (29). Analyses that were not preregistered are indicated.

Sample

The participants are from TEDS (Twins Early Development Study), a longitudinal study of >10,000 twin pairs from England and Wales (Table 1). Children who were born between 1994 and 1996 were recruited to the sample, which was representative of the U.K. population on socioeconomic status (SES), ethnicity, and parental occupation (30). Standard exclusions used for TEDS were applied (see Supplement). All analyses were limited to unrelated individuals (1 twin was randomly selected from each pair) and to those who completed preschool fine motor skills assessments at at least one age point (at 2, 3, or 4 years, N = 9625).

Ethical approval for TEDS was provided by the King's College London ethics committee. Written parental and/or self-consent was obtained from all participants.

Measures

Polygenic Scores. Genotyping information can be found in the Supplemental Methods. In TEDS, PGSs were created for n = 4514 for ADHD (31), autism (32), schizophrenia (33), obsessive–compulsive disorder (34), major depressive disorder (35), anxiety (36), and years of education (37). PGS calculation was conducted using LDpred software with a method detailed previously (38). PGSs at p-value thresholds of .01, .3, and 1 were created, as is standard practice (39). All PGSs were regressed on 10 principal components of genetic ancestry, genotyping chip, sex, and gestational age and then z-standardized.

Preschool Motor Skill Assessments. The items were selected from a hybrid assessment consisting of fine motor tasks (administered by parents) and parent questionnaire items about nonverbal cognition from the Parent Report of Children's Abilities, used at ages 2, 3, and 4 years. This measure has been shown to have good validity at age 2 years against a gold-standard scale of infant development (40). Specifically, parents were given booklets that included instructions on how to direct their children to complete the tasks, which were either completed directly in the booklet (e.g., drawing) or observed and reported on by the parent (e.g., block building). The motor-relevant tasks were drawing, block building, folding, and questionnaire items relating to motor activities observed in the home (Table S1A, B).

Later Childhood Measures. The later childhood measures (Table S1C) were collected at 3 ages (midchildhood: ages 7 to 8; late childhood: age 12; and adolescence: age 16). They included multiple raters (parent, self, or teacher). For most traits that were measured across ages, the same questionnaires were used; however, questionnaires for autistic traits and anxiety/anxiety-depression, varied across age (see Table S1C). All phenotypic variables were z-standardized. Sample sizes differed longitudinally due to missing data (midchildhood, n = 4265; late childhood, n = 3664; adolescence, n = 3926). For the psychopathology composite score analysis, we used imputation to devise the score for participants who had at least 1 phenotypic measure (n = 7779).

Statistical Analysis

Fine Motor Composite Score. Fine motor data from all ages (2, 3, and 4 years) were used to derive a fine motor composite score. A principal component analysis with 1 principal component was conducted with the *principal* function from the *psych* R package (41). The final score was regressed on sex and gestational age and *z*-standardized. Additional details about the analysis can be found in the Supplemental Methods. There were no significant differences between monozygotic and dyzygotic twins in fine motor scores ($t_{6389.7} = -1.52$, $p = .128$).

Psychopathology Composite Score. A psychopathology composite score for 3 raters (self, parent, and teacher) was generated by including all psychiatric and neurodevelopmental traits between 7 and 16 years and taking the factor scores from the first principal component in a principal component analysis (Table S2). See the Supplemental Methods for more details.

Longitudinal Phenotypic Analysis. A multivariate regression analysis of fine motor skills predicting multiple phenotypic traits was performed for each age of assessment (midchildhood, late childhood, adolescence, and the cross-age psychopathology composite score) using the Lavaan R package (42). All regression analyses included measures from all available raters (self, parent, and teacher). Each *p* value was false discovery rate–corrected for the multiple comparisons within each model (midchildhood, $n = 5$; late childhood, $n = 8$; adolescence, $n = 15$; and psychopathology composite score, $n = 3$). All analyses controlled for gestational age, age of assessment, and sex, apart from the psychopathology composite score analysis, which did not control for age due to multiple assessments.

Regression of Fine Motor Score on PGSs. Individual regression analyses were run for each PGS. A non-preregistered permutation-based method was used to generate an empirical *p* value for the best-performing *p*-threshold for each PGS (see Supplement). The preregistered regression analysis with false discovery rate–correction can be found in Table S5.

The multiple regression model used each PGS at the *p*-value thresholds (pTs) that were selected in the permutation-based analysis. All variables were forced into the model. An elastic net regularized regression method was used to account for multicollinearity and improve prediction (43). The model was run using the *glmnet* R package (44). See the Supplement for further details about methods.

PGS Replication Analysis in an Independent Sample. A non-preregistered replication analysis was completed in the BASIS-STAARS (the British Autism Study of Infant Siblings and the Studying Autism and ADHD in the Early Years) sample, which is enriched with families with ADHD and autism ($n = 202$). Fine motor skills were measured at 24 and 36 months with a standardized assessment, the Mullen Scales of Early Learning (45). The published fine motor t score was used. As before, PGSs were analyzed at 3 similar *p*-value thresholds (.01, .5, 1). The PGSs that were found to be significantly associated with fine motor skills in the multi-PGS model in the original (i.e., TEDS) sample were tested in the replication sample. Two regression models were performed, one for each age measurement, 24 and 36 months. A permutation-based correction was used, as was done previously. See the Supplemental Methods for further details.

Sensitivity Analyses. We reran the phenotypic analysis, including SES as a covariate for models (non-preregistered). Furthermore, we reran all phenotypic and genetic analyses with the following changes: excluding all parent-rated questionnaire items from the fine motor composite score (non-preregistered) and excluding individuals classed as "extremely preterm" and "very preterm" (gestational age <32 weeks at birth, see Supplemental Methods).

RESULTS

Longitudinal Phenotypic Results

Figure 1 and Table 2 show the full results from the longitudinal phenotypic multivariate analysis. The midchildhood model revealed significant associations between higher fine motor scores and lower scores for all included phenotypic traits, for example, autistic traits (Childhood Autism Spectrum Test parent-rated, $\beta = -0.10$, 95% CI: -0.12 to -0.07, $p < .001$) and ADHD traits (Conners' Parent Rating Scale, $\beta = -0.15$, 95% CI: -0.17 to -0.12, $p < .001$).

The late childhood model revealed significant associations between higher fine motor scores and lower scores for multiple phenotypic traits, for example autistic traits (Childhood Autism Spectrum Test parent-rated, $\beta = -0.10$, 95% CI: -0.13 to -0.06, $p < .001$), ADHD traits (Conners' Parent Rating Scale, $\beta = -0.13$, 95% CI: -0.17 to -0.10, $p < .001$), and depression traits (Moods and Feelings Questionnaire parent-rated, $\beta = -0.08$, 95% CI: -0.12 to -0.05, $p < .001$; and self-rated, $\beta = -0.09$, 95% CI: -0.19 to -0.05, $p < .001$).

The adolescence regression model revealed significant associations between higher fine motor scores and scores for multiple phenotypic traits, for example lower autistic traits (Abbreviated Autism Spectrum Quotient, parent-rated, $\beta = -0.12$, 95% CI: -0.15 to -0.08, $p < .001$), ADHD (Conners' Parent Rating Scale, $\beta = -0.11$, 95% CI: -0.14 to -0.08, $p < .001$), and depression traits (Moods and Feelings Questionnaire parent-rated, $\beta = -0.07$, 95% CI: -0.10 to -0.04, $p < .001$) and higher educational achievement ($\beta = 0.25$, 95% CI: 0.22 to 0.28, $p < .001$).

The psychopathology composite score regression model revealed significant associations between higher fine motor skills and lower parent-rated ($\beta = -0.18$, 95% CI: 0.20 to 0.16, $p < .001$), self-rated ($\beta = -0.15$, 95% CI: -0.18 to -0.13, $p < .001$), and teacher-rated ($\beta = -0.12$, 95% CI: -0.14 to -0.09, $p < .001$) psychopathology composite scores.

PGS Results

Results revealed a significant association between higher years-of-education PGS and higher fine motor scores (pT = 1, $\beta = 0.07$, 95% CI: 0.04 to 0.10, empirical $p < .001$, $R^2 = 0.005$), a significant association between lower ADHD PGS and higher fine motor scores (pT = 0.01, $\beta = -0.04$, 95% CI: -0.07 to -0.01, empirical $p = .011$, $R^2 = 0.002$), and a significant

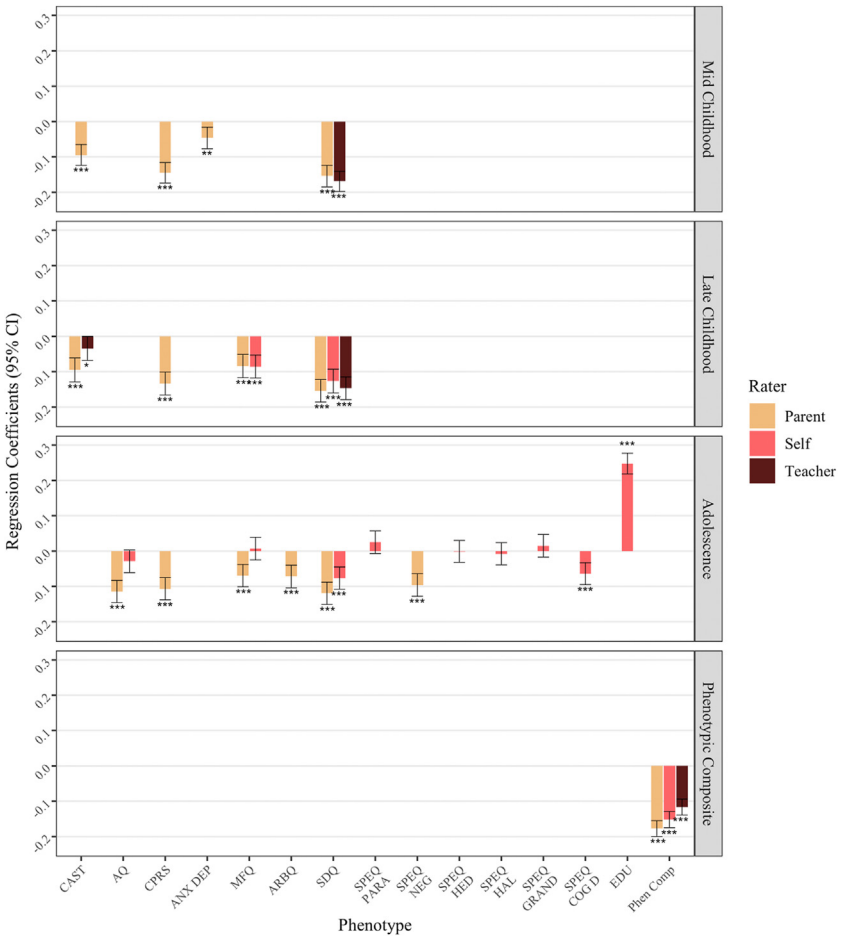

Figure 1. Model results for the longitudinal phenotypic multivariate regression models regressing outcomes on early fine motor skills. Covariates: gestational age, age of measurement, sex. Midchildhood: 7 to 8 years; late childhood: 12 years; adolescence: 16 years. Psychopathology composite is a composite score of all neurodevelopmental and psychiatric traits across childhood and adolescence. False discovery rate–corrected *p* values: **p* < .05, ***p* < .01, ****p* < .001. ANX DEP, anxiety and depression traits; AQ, Abbreviated Autism Spectrum Quotient; ARBQ, Anxiety-Related Behaviours Questionnaire; CAST, Childhood Autism Spectrum Test; CogD, cognitive disorganization; CPRS, Conners' Parent Rating Scale; EDU, educational achievement; GRAND, grandiosity; HAL, hallucinations; HED, hedonia; MFQ, Mood and Feelings Questionnaire; NEG, negative symptoms; PARA, paranoia; SDQ, Strengths and Difficulties Questionnaire—total behavioral problems; SPEQ, Specific Psychotic Experiences Questionnaire.

association between higher anxiety PGS and higher fine motor scores (pT = 0.3, β = 0.03, 95% CI: 0.00 to 0.06, empirical *p* = .040, R^2 = 0.001) (see Figure 2 and Table S6A). The preregistered analysis results with false discovery rate–correction can be found in the Supplement; conclusions are similar (Table S5). Consistent with the regression results, higher quantiles on the years-of-education PGS and the anxiety PGS were associated with higher fine motor scores (Figure S1A, C, respectively), and higher quantiles in the ADHD PGS were associated with lower fine motor scores (Figure S1B).

The multi-PGS regularized regression model retained 3 PGS variables (Figure 3, Table 3). There was a positive association for the years-of-education PGS (β = 0.07), a negative association for the ADHD PGS (β = −0.03), and a positive association for the anxiety PGS (β = 0.01) with fine motor skills. The model R^2 was 0.0048, which was 1.75% higher than the best-performing single-score model (years of education, R^2 = 0.0047).

Tests for replication of the significant PGS findings from TEDS in an independent sample, BASIS-STAARS, revealed a significant association between lower ADHD PGS and higher fine motor scores at 36 months (pT = 0.01, β = −0.15, 95% CI: −0.29 to −0.01, empirical *p* = .043, R^2 = 0.023) (Table S6C), consistent with the TEDS results. No significant association was found at 24 months. The years-of-education PGS (empirical *p* values = .421, .129) and the anxiety PGS (empirical *p* values = .285, .240) associations did not replicate at either age in the BASIS-STAARS sample.

Non-preregistered mediation models were run between all PGSs and all phenotypic measures with fine motor skills as the mediator (suggested by a reviewer, see the Supplemental Methods). The analysis revealed significant part-mediating effects of fine motor skills on the association between an anxiety PGS and late childhood parent-rated ADHD traits (pT = 0.3, average causal mediation effect [ACME] = −0.005, *p* = .046, proportion mediated = 1.62%), late childhood parent-rated depression traits (best pT = 1, ACME = −0.003, *p* = .046, proportion mediated = 5.25%), late childhood self-rated behavioral problems (pT = 1, ACME = −0.004, *p* = .046, proportion mediated = 7.33%), the years-of-education PGS and lower neurodevelopmental and psychiatric traits (multiple associations, largest effect; midchildhood Strengths and Difficulties Questionnaire behavioral problems, teacher-rated, pT = 1, ACME = −0.015, *p* < .001, proportion mediated = 17.53%), and the years-of-education PGS and educational achievement

Table 2. Model Results for the Longitudinal Phenotypic Multivariate Regression Models Regressing Outcomes on Early Fine Motor Skills

	Age When Dependent Variable Measured, β (95% CI)			
Dependent Variable	Midchildhood	Late Childhood	Adolescence	Phenotypic Composite
CAST Parent	−0.095[a] (−0.124, −0.065)	–	–	–
CPRS Parent	−0.145[a] (−0.174, −0.116)	–	–	–
ANX DEP Parent	−0.046[b] (−0.077, −0.016)	–	–	–
SDQ Parent	−0.154[a] (−0.185, −0.124)	–	–	–
SDQ Teacher	−0.169[a] (−0.198, −0.141)	–	–	–
CAST Parent	–	−0.095[a] (−0.129, −0.061)	–	–
CASTTeacher	–	-0.034[c] (−0.068, 0.000)	–	–
CPRS Parent	–	−0.134[a] (−0.166, −0.101)	–	–
MFQ Parent	–	−0.084[a] (−0.117, −0.051)	–	–
MFQ Self	–	−0.086[a] (−0.118, −0.053)	–	–
SDQ Parent	–	−0.154[a] (−0.186, −0.122)	–	–
SDQ Self	–	−0.126[a] (−0.160, −0.093)	–	–
SDQ Teacher	–	−0.147[a] (−0.179, −0.115)	–	–
AQ Parent	–	–	−0.115[a] (−0.146, −0.083)	–
AQ Self	–	–	−0.029 (−0.061, 0.003)	–
CPRS Parent	–	–	−0.107[a] (−0.138, −0.075)	–
MFQ Parent	–	–	−0.069[a] (−0.101, −0.038)	–
MFQ Self	–	–	0.007 (−0.025, 0.039)	–
ARBQ Parent	–	–	−0.072[a] (−0.104, −0.040)	–
SDQ Parent	–	–	−0.119[a] (−0.151, −0.088)	–
SDQ Self	–	–	−0.077[a] (−0.108, −0.045)	–
SPEQPARA Self	–	–	0.025 (−0.007, 0.057)	–
SPEQNEG Parent	–	–	−0.096[a] (−0.128, −0.064)	–
SPEQHED Self	–	–	−0.001 (−0.032, 0.030)	–
SPEQHAL Self	–	–	−0.008 (−0.039, 0.024)	–
SPEQGRAND Self	–	–	0.015 (−0.017, 0.047)	–
SPEQCogD Self	–	–	−0.064[a] (−0.095, −0.033)	–
EDU Self	–	–	0.248[a] (0.218, 0.277)	–
Phen Comp Parent	–	–	–	−0.177[a] (−0.200, −0.155)
Phen Comp Self	–	–	–	−0.152[a] (−0.175, −0.129)
Phen Comp Teacher	–	–	–	−0.116[a] (−0.139, −0.094)

Covariates: gestational age, age of measurement, sex. Midchildhood: 7–8 years; late childhood: 12 years; adolescence: 16 years. Phen comp is a psychopathology composite score calculated from all available neurodevelopmental and psychiatric traits across childhood and adolescence.

ANX DEP, anxiety and depression traits; AQ, Abbreviated Autism Spectrum Quotient; ARBQ, Anxiety-Related Behaviours Questionnaire; CAST, Childhood Autism Spectrum Test; CogD, cognitive disorganization; CPRS, Conners' Parent Rating Scale; EDU, educational achievement; GRAND, grandiosity; HAL, hallucinations; HED, hedonia; MFQ, Mood and Feelings Questionnaire; NEG, negative symptoms; PARA, paranoia; SDQ, Strengths and Difficulties Questionnaire—total behavioral problems; SPEQ, Specific Psychotic Experiences Questionnaire.

[a] $p < .001$.

[b] $p < .01$.

[c] $p < .05$.

(best pT = 1, ACME = 0.017, $p < .001$, proportion mediated = 5.10%) (see Figure S2 and Supplemental Data 1).

Sensitivity Analyses

The majority of our findings in the TEDS sample reported above remained consistent in terms of significance in sensitivity analyses that excluded premature children (n = 36 of 38 findings) (Tables S8, S9), sensitivity analyses that excluded parent questionnaire items from the fine motor score (n = 37 of 38 findings) (Tables S6B, S10), and sensitivity analyses that controlled for SES (n = 29 phenotypic associations of 31) (Table S11, Supplemental Results).

DISCUSSION

This study investigated phenotypic and genetic associations between preschool fine motor skills and later neurodevelopment, psychopathology, and educational achievement. Lower fine motor skills were associated with more autistic traits, ADHD, anxiety and/or depression, behavioral

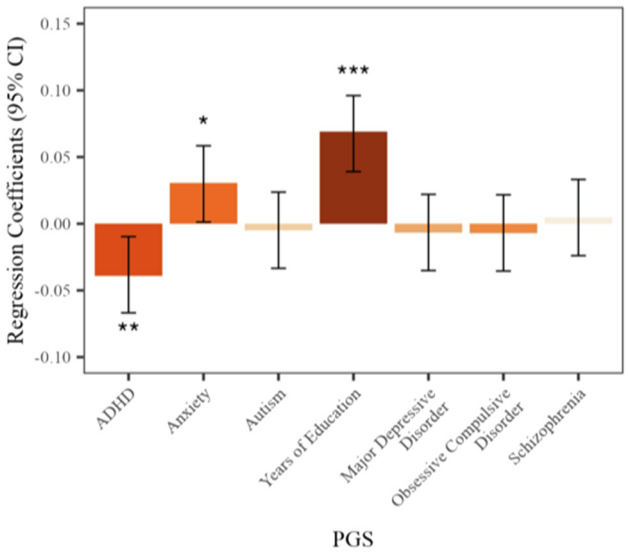

Figure 2. Associations of polygenic scores (PGSs) and fine motor skills with permutation correction. Covariates: genotyping chip, 10 genetic ancestry principal components, gestational age, and sex. Empirical *p* values: $^{*}p < .05$, $^{***}p < .001$. ADHD, attention-deficit/hyperactivity disorder.

problems, negative symptoms, and cognitive disorganization and with higher psychopathology composite scores and better educational outcomes. These results support emerging evidence of an association between early fine motor skills and later neurodevelopmental and psychiatric traits and educational outcomes (46,47). The association between the genetic propensity for ADHD and lower fine motor skills supported preregistered hypotheses and was reinforced by a nonpreregistered replication result in an independent sample.

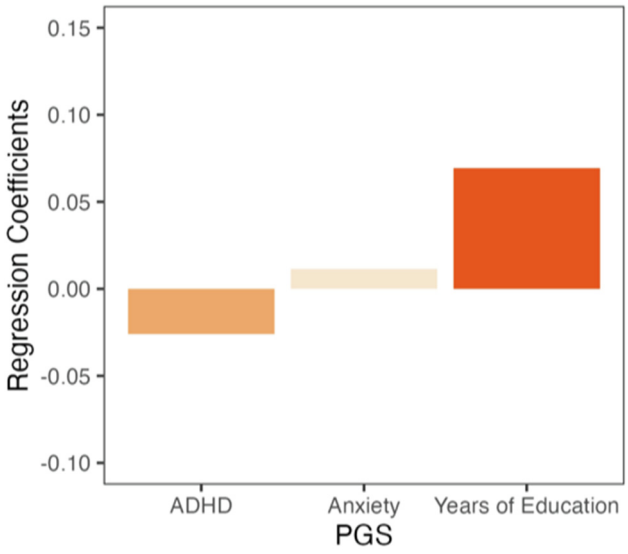

Figure 3. Multipolygenic score model showing associations between polygenic scores (PGSs) and fine motor skills score. Covariates: genotyping chip, 10 genetic ancestry principal components, gestational age, and sex. Regression coefficient calculated from a holdout set of 20% of the data. ADHD, attention-deficit/hyperactivity disorder.

Table 3. Multipolygenic Score Model Showing Associations Between PGSs and Fine Motor Skills Score

	β	
PGS	Train	Test
ADHD	−0.016	−0.026
Anxiety	0.029	0.011
Years of Education	0.049	0.069

Results for train and test sets for each predictor retained the model; an unbiased estimate of variance explained from the holdout set of 20% of the data was $R^2 = 0.005$.

ADHD, attention-deficit/hyperactivity disorder; PGS, polygenic score.

The genetic and phenotypic associations between fine motor skills and educational performance accounted for the highest effect sizes in our study. Our results concur with previously reported associations between fine motor skills and cognitive performance (15,18,20,21,48–51). The mediation analysis also revealed that fine motor skills mediated the association between the years-of-education PGS and educational achievement. However, the association between fine motor skills and years-of-education PGS was not replicated, and effect sizes are modest. Additional work is needed to test whether these findings can be replicated in larger samples.

As predicted, lower fine motor skills were associated with more anxiety traits. Conversely, a higher genetic predisposition to anxiety was associated with higher fine motor skills, although we note that this PGS association had the smallest effect size. Furthermore, fine motor skills significantly mediated the association between the anxiety PGS and multiple childhood neurodevelopmental and psychiatric traits. Considering the lack of replication in the independent sample, the inconsistency in the direction of associations with the phenotypic results, and the mediation findings, our findings of associations with anxiety require further exploration.

Findings for autism/autistic traits were not consistent across phenotypic and genetic analyses. We found a phenotypic association between lower fine motor skills and autistic traits across multiple ages (6,7,17). However, the lack of an association between the autism PGS and fine motor skills is consistent with previous findings of no genetic associations of the autism PGS with gross motor skills (26). Furthermore, autism and autistic traits are not the same phenotypes, although they are genetically related (52). Further investigation once larger genome-wide association studies with sufficient statistical power have been achieved in the future would be of interest.

Possible mechanisms and pathways underlying the associations between fine motor skills and later outcomes may include atypical early sensorimotor alterations, which could lead to impairments in motor skills and then impact neurodevelopmental outcomes (53), or executive functioning (54). Furthermore, impairments and delays in motor skills may impact the acquisition of social experience, thereby leading to further developmental disruption (51,55,56). There may also be shared/common genetic pathways. Future work could investigate pleiotropic genetic effects and potential mechanisms that underlie the associations that we report herein.

Contrary to our stated hypotheses, confidence intervals indicated that there were no measurement age differences in

associations between fine motor skills and ADHD, anxiety, and/or depression traits. In support of our hypotheses, some of the behavioral problems' and autistic traits' associations with fine motor skills in mid- and/or late childhood were stronger in magnitude than in adolescence according to the confidence intervals, suggesting that the magnitude of the associations of these traits with fine motor skills may diminish over time.

Confidence intervals indicated a larger magnitude of association with fine motor skills for parent-rated than for self-rated autistic and depression traits in adolescence. Furthermore, the association between fine motor skills and the parent-rated psychopathology composite score was higher in magnitude than the association with the teacher-rated psychopathology composite score. These findings are consistent with rater differences in capturing psychopathology (57–60).

Non-preregistered sensitivity phenotypic analyses with SES as a covariate were added in response to reviewer comments and revealed that the majority of the phenotypic associations remained the same regarding statistical significance. Most of the findings also remained the same regarding significance when infants who were born at <32 weeks were excluded.

The current study has several strengths. Firstly, we employed a large prospective design in a representative community sample and included multiple raters. We also derived a novel preschool fine motor skills score. Furthermore, we partially replicated the genetic results in a sample that used an alternative fine motor measure, which suggests that the association between the ADHD PGS and lower fine motor skills is not specific to the sample, the twins, or the measure employed.

The current study also has some limitations. Firstly, we recognize that, although comparable to those in other studies, the effect sizes for the associations between the PGSs for anxiety, ADHD, and educational achievement with preschool fine motor skills were all small (all under 1%). This limits the clinical significance of the findings for individuals. Associations with a PGS are partly dependent on the reliability of the PGS, and currently there is no standard statistical approach for adjusting for variations in the reliability of PGSs. Secondly, we are assuming that our results from twins are generalizable to singletons. This is supported by evidence showing that twins are similar to singletons in cognitive ability, externalizing behaviors, and motor milestones (61–63). In addition, while the phenotypic longitudinal data could have been analyzed using growth models, this would not have achieved our goal, which was to test phenotypic associations at separate stages in childhood and adolescence. We also note that not all traits were measured by the same questionnaire longitudinally. Moreover, it was not possible to control for SES in the PGS models due to SES acting as a collider (64,65). Lastly, information about gross motor skills was not collected in TEDS, so we could not make comparisons across motor domains.

Conclusions

Skills such as drawing and block building in the first years after birth are associated with neurodevelopmental, psychiatric, and educational traits between 3 to 12 years later and appear to be genetically associated with ADHD and years of education. Additional work is necessary to understand whether this is due in part to shared common genetic pathways or early developmental alterations. Our results suggest that fine motor skills may have a role in pathways that lead to major life outcomes.

ACKNOWLEDGMENTS AND DISCLOSURES

TEDS is supported by UK Medical Research Council (Grant No. MR/V012878/1 and previously by Grant No. MR/M021475/1), with additional support from US National Institutes of Health (Grant No. AG046938). AB received support from a Medical Research Council studentship (MR/R015759/1 [to AR]). TA received support from the Medical Research Council Centre for Neurodevelopmental Disorders, King's College London (MR/N026063/1) and a Clinician Scientist Transition Support Award (MR/V036874/1). AR received support from Simons Foundation (724306). The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results. Any views expressed are those of the author(s) and not necessarily those of the funders.

We gratefully acknowledge the participants and their families for their contributions to the TEDS and BASIS-STAARS studies and the contribution of Tony Charman and the BASIS-STAARS research team to the BASIS-STAARS study.

For BASIS-STAARS, the genetic data collection and generation and the manuscript preparation were funded by European Union's Horizon 2020 research and innovation program under Marie Skłodowska-Curie (Grant No. 642996), Economic and Social Research Council Grant No. ES/R009368/1 (to EJHJ), and by Simons Foundation Autism Research Initiative Pilot Award Grant No. 511504 (to EJHJ and EM). The experimental and behavioral data collection for BASIS-STAARS was funded by Medical Research Council Programme Grant Nos. G0701484 and MR/K021389/1, the BASIS funding consortium led by Autistica (http://www.basisnetwork.org). The behavioral data collection used in this publication has received partial funding from the Innovative Medicines Initiative Joint Undertaking under Grant No. 115300 for the EU-AIMS project, which receives resources from the European Union's Seventh Framework Programme (FP7/2007-2013), and the European Federation of Pharmaceutical Industries and Associations companies and by the Innovative Medicines Initiative 2 Joint Undertaking under Grant No. 777394 for the project Autism Innovative Medicine Studies (AIMS)-2-TRIALS, which receives support from the European Union's Horizon 2020 research and innovation program and the European Federation of Pharmaceutical Industries and Associations companies' in-kind contributions and from Autism Speaks (#1292), Autistica, and the Simons Foundation for Autism Research Initiative.

AB has previously presented data from this study at the Behavior Genetics Association Annual Meetings, online, June 2021; June 2023 and at the London Genetics Network Annual Meeting, December 2022.

A previous version of this article was published as a preprint on PsyArXiv: https://osf.io/preprints/psyarxiv/y87wq.

AR is a Joint Editor of the *Journal of Child Psychology and Psychiatry*, for which she receives an honorarium. PF is Deputy Editor-in-Chief of the *Journal of Child Psychology and Psychiatry*, for which he receives an honorarium. MHJ receives royalties from Oxford University Press, Wiley-Blackwell, and MIT Press. All other authors report no biomedical financial interests or potential conflicts of interest.

ARTICLE INFORMATION

From the Centre for Brain and Cognitive Development, Birkbeck, University of London, London, United Kingdom (AB, EM, JB-A, MHJ, EJHJ, AR); Centre for the Developing Brain, School of Imaging Sciences and Biomedical Engineering, King's College London, London, United Kingdom (TA); Pediatric Neurosciences, Evelina London Children's Hospital, Guy's and St. Thomas' NHS Foundation Trust, London, United Kingdom (TA); Centre for Family Research, Department of Psychology, University of Cambridge, Cambridge, United Kingdom (PF); Research Department of Clinical, Educational and Health Psychology, University College London, London, United Kingdom (PF); Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, United Kingdom (GP); Department of Psychology, University of Cambridge, Cambridge, United Kingdom (MHJ);

and School of Psychology, University of Surrey, Guildford, United Kingdom (AR).

Address correspondence to Aislinn Bowler, M.Sc., at abowle02@mail.bbk.ac.uk.

Received May 18, 2023; revised Nov 21, 2023; accepted Nov 22, 2023.

Supplementary material cited in this article is available online at https://doi.org/10.1016/j.biopsych.2023.11.017.

REFERENCES

1. Knickmeyer RC, Gouttard S, Kang C, Evans D, Wilber K, Smith JK, *et al.* (2008): A structural MRI study of human brain development from birth to 2 years. J Neurosci 28:12176–12182.
2. Diamond A (2000): Close interrelation of motor development and cognitive development and of the cerebellum and prefrontal cortex. Child Dev 71:44–56.
3. Burton BK, Hjorthøj C, Jepsen JR, Thorup A, Nordentoft M, Plessen KJ (2016): Research Review: Do motor deficits during development represent an endophenotype for schizophrenia? A meta-analysis. J Child Psychol Psychiatry 57:446–456.
4. Kaiser ML, Schoemaker MM, Albaret JM, Geuze RH (2015): What is the evidence of impaired motor skills and motor control among children with attention deficit hyperactivity disorder (ADHD)? Systematic review of the literature. Res Dev Disabil 36C:338–357.
5. Johnson MH, Gliga T, Jones E, Charman T (2015): Annual Research Review: Infant development, autism, and ADHD – Early pathways to emerging disorders. J Child Psychol Psychiatry 56:228–247.
6. Landa RJ, Gross AL, Stuart EA, Bauman M (2012): Latent class analysis of early developmental trajectory in baby siblings of children with autism. J Child Psychol Psychiatry 53:986–996.
7. Nishimura T, Takei N, Tsuchiya KJ (2019): Neurodevelopmental trajectory during infancy and diagnosis of autism spectrum disorder as an outcome at 32 months of age. Epidemiology 30(suppl 1):S9–S14.
8. Guilmatre A, Dubourg C, Mosca AL, Legallic S, Goldenberg A, Drouin-Garraud V, *et al.* (2009): Recurrent rearrangements in synaptic and neurodevelopmental genes and shared biologic pathways in schizophrenia, autism, and mental retardation. Arch Gen Psychiatry 66:947–956.
9. Rujescu D, Ingason A, Cichon S, Pietiläinen OPH, Barnes MR, Toulopoulou T, *et al.* (2009): Disruption of the neurexin 1 gene is associated with schizophrenia. Hum Mol Genet 18:988–996.
10. 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. J Child Psychol Psychiatry 49:535–542.
11. Stergiakouli E, Davey Smith G, Martin J, Skuse DH, Viechtbauer W, Ring SM, *et al.* (2017): Shared genetic influences between dimensional ASD and ADHD symptoms during child and adolescent development. Mol Autism 8:18.
12. Morgan C, Fetters L, Adde L, Badawi N, Bancale A, Boyd RN, *et al.* (2021): Early intervention for children aged 0 to 2 years with or at high risk of cerebral palsy: International clinical practice guideline based on systematic reviews. JAMA Pediatr 175:846–858.
13. Austerberry C, Mateen M, Fearon P, Ronald A (2022): Heritability of psychological traits and developmental milestones in infancy: A systematic review and meta-analysis. JAMA Netw Open 5:e2227887.
14. Arden R, Trzaskowski M, Garfield V, Plomin R (2014): Genes influence young children's human figure drawings and their association with intelligence a decade later. Psychol Sci 25:1843–1850.
15. Katagiri M, Ito H, Murayama Y, Hamada M, Nakajima S, Takayanagi N, *et al.* (2021): Fine and gross motor skills predict later psychosocial maladaptation and academic achievement. Brain Dev 43:605–615.
16. Havmoeller SR, Thomsen PH, Lemcke S (2019): The early motor development in children diagnosed with ADHD: A systematic review. Atten Defic Hyperact Disord 11:233–240.
17. Choi B, Leech KA, Tager-Flusberg H, Nelson CA (2018): Development of fine motor skills is associated with expressive language outcomes in infants at high and low risk for autism spectrum disorder. J Neurodev Disord 10:14.
18. Cameron CE, Brock LL, Murrah WM, Bell LH, Worzalla SL, Grissmer D, Morrison FJ (2012): Fine motor skills and executive function both contribute to kindergarten achievement. Child Dev 83:1229–1244.
19. Grissmer D, Grimm KJ, Aiyer SM, Murrah WM, Steele JS (2010): Fine motor skills and early comprehension of the world: Two new school readiness indicators. Dev Psychol 46:1008–1017.
20. Klupp S, Möhring W, Lemola S, Grob A (2021): Relations between fine motor skills and intelligence in typically developing children and children with attention deficit hyperactivity disorder. Res Dev Disabil 110:103855.
21. van der Fels IMJ, te Wierike SCM, Hartman E, Elferink-Gemser MT, Smith J, Visscher C (2015): The relationship between motor skills and cognitive skills in 4–16 year old typically developing children: A systematic review. J Sci Med Sport 18:697–703.
22. Piek JP, Dawson L, Smith LM, Gasson N (2008): The role of early fine and gross motor development on later motor and cognitive ability. Hum Mov Sci 27:668–681.
23. Serdarevic F, Tiemeier H, Jansen PR, Alemany S, Xerxa Y, Neumann A, *et al.* (2020): Polygenic risk scores for developmental disorders, neuromotor functioning during infancy, and autistic traits in childhood. Biol Psychiatry 87:132–138.
24. Hannigan LJ, Askeland RB, Ask H, Tesli M, Corfield E, Ayorech Z, *et al.* (2023): Developmental milestones in early childhood and genetic liability to neurodevelopmental disorders. Psychol Med 53:1750–1758.
25. Askeland RB, Hannigan LJ, Ask H, Ayorech Z, Tesli M, Corfield E, *et al.* (2022): Early manifestations of genetic risk for neurodevelopmental disorders. J Child Psychol Psychiatry 63:810–819.
26. Riglin L, Tobarra-Sanchez E, Stergiakouli E, Havdahl A, Tilling K, O'Donovan M, *et al.* (2022): Early manifestations of genetic liability for ADHD, autism and schizophrenia at ages 18 and 24 months. JCPP Adv 2:e12093.
27. Leonard HC, Bedford R, Charman T, Elsabbagh M, Johnson MH, Hill EL, BASIS team (2014): Motor development in children at risk of autism: A follow-up study of infant siblings. Autism 18:281–291.
28. Leonard HC, Bedford R, Pickles A, Hill EL, BASIS team (2015): Predicting the rate of language development from early motor skills in at-risk infants who develop autism spectrum disorder. Res Autism Spectr Disord 13(14):15–24.
29. Bowler A, Ronald A: Infant fine motor skills and the longitudinal phenotypic and genetic associations with later child and adolescent psychopathology and educational outcomes. Available at: https://doi.org/10.17605/OSF.IO/EJ3R6. Accessed August 10, 2020.
30. Haworth CM, Davis OS, Plomin R (2013): Twins Early Development Study (TEDS): A genetically sensitive investigation of cognitive and behavioral development from childhood to young adulthood. Twin Res Hum Genet 16:117–125.
31. Demontis D, Walters RK, Martin J, Mattheisen M, Als TD, Agerbo E, *et al.* (2019): Discovery of the first genome-wide significant risk loci for attention deficit/hyperactivity disorder. Nat Genet 51:63–75.
32. Grove J, Ripke S, Als TD, Mattheisen M, Walters RK, Won H, *et al.* (2019): Identification of common genetic risk variants for autism spectrum disorder. Nat Genet 51:431–444.
33. Pardiñas AF, Holmans P, Pocklington AJ, Escott-Price V, Ripke S, Carrera N, *et al.* (2018): Common schizophrenia alleles are enriched in mutation-intolerant genes and in regions under strong background selection [no. 3]. Nat Genet 50:381–389.
34. International Obsessive Compulsive Disorder Foundation Genetics Collaborative (IOCDF-GC), OCD Collaborative Genetics Association Studies (OCGAS) (2018): Revealing the complex genetic architecture of obsessive-compulsive disorder using meta-analysis Mol Psychiatry 23:1181–1188.
35. Howard DM, Adams MJ, Clarke TK, Hafferty JD, Gibson J, Shirali M, *et al.* (2019): Genome-wide meta-analysis of depression identifies 102 independent variants and highlights the importance of the prefrontal brain regions. Nat Neurosci 22:343–352.
36. Purves KL, Coleman JRI, Meier SM, Rayner C, Davis KAS, Cheesman R, *et al.* (2020): A major role for common genetic variation in anxiety disorders. Mol Psychiatry 25:3292–3303.

37. Lee JJ, Wedow R, Okbay A, Kong E, Maghzian O, Zacher M, *et al.* (2018): Gene discovery and polygenic prediction from a genome-wide association study of educational attainment in 1.1 million individuals. Nat Genet 50:1112–1121.
38. Selzam S, Ritchie SJ, Pingault JB, Reynolds CA, O'Reilly PF, Plomin R (2019): Comparing within- and between-family polygenic score prediction. Am J Hum Genet 105:351–363.
39. Jansen AG, Dieleman GC, Jansen PR, Verhulst FC, Posthuma D, Polderman TJC (2020): Psychiatric polygenic risk scores as predictor for attention deficit/hyperactivity disorder and autism spectrum disorder in a clinical child and adolescent sample. Behav Genet 50:203–212.
40. Saudino KJ, Dale PS, Oliver B, Petrill SA, Richardson V, Rutter M, *et al.* (1998): The validity of parent-based assessment of the cognitive abilities of 2-year-olds. Br J Dev Psychol 16:349–362.
41. Revelle W (2023): psych: Procedures for Psychological. Psychometric, and Personality Research, version 2.3.3. Available at: https://CRAN.R-project.org/package=psych. Accessed March 24, 2023.
42. Rosseel Y, Jorgensen TD, Rockwood N, Oberski D, Byrnes J, Vanbrabant L, *et al.* (2023): lavaan: Latent variable analysis, version 0.6-16. Available at: https://cran.r-project.org/web/packages/lavaan/index.html. Accessed October 20, 2023.
43. Pain O, Glanville KP, Hagenaars SP, Selzam S, Fürtjes AE, Gaspar HA, *et al.* (2021): Evaluation of polygenic prediction methodology within a reference-standardized framework. PLoS Genet 17:e1009021.
44. Friedman J, Hastie T, Tibshirani R, Narasimhan B, Tay K, Simon N, *et al.* (2022): glmnet: Lasso and Elastic-Net Regularized Generalized Linear Models, version 4.1-4. Available at: https://CRAN.R-project.org/package=glmnet. Accessed September 13, 2022.
45. Mullen EM (1995): Mullen Scales of Early Learning. Circle Pines, MN: AGS.
46. Lim YH, Licari M, Spittle AJ, Watkins RE, Zwicker JG, Downs J, Finlay-Jones A (2021): Early motor function of children with autism spectrum disorder: A systematic review. Pediatrics 147:e2020011270.
47. West KL (2019): Infant motor development in autism spectrum disorder: A synthesis and meta-analysis. Child Dev 90:2053–2070.
48. Murray GK, Veijola J, Moilanen K, Miettunen J, Glahn DC, Cannon TD, *et al.* (2006): Infant motor development is associated with adult cognitive categorisation in a longitudinal birth cohort study. J Child Psychol Psychiatry 47:25–29.
49. Wu M, Liang X, Lu S, Wang Z (2017): Infant motor and cognitive abilities and subsequent executive function. Infant Behav Dev 49:204–213.
50. Oudgenoeg-Paz O, Volman MCJM, Leseman PP (2012): Attainment of sitting and walking predicts development of productive vocabulary between ages 16 and 28 months. Infant Behav Dev 35:733–736.
51. Flensborg-Madsen T, Mortensen EL (2018): Developmental milestones during the first three years as precursors of adult intelligence. Dev Psychol 54:1434–1444.
52. Robinson EB, St Pourcain B, Anttila V, Kosmicki JA, Bulik-Sullivan B, Grove J, *et al.* (2016): Genetic risk for autism spectrum disorders and neuropsychiatric variation in the general population. Nat Genet 48:552–555.
53. Denisova K, Zhao G (2017): Inflexible neurobiological signatures precede atypical development in infants at high risk for autism. Sci Rep 7:11285.
54. Koziol LF, Lutz JT (2013): From movement to thought: The development of executive function. Appl Neuropsychol Child 2:104–115.
55. Walle EA (2016): Infant social development across the transition from crawling to walking. Front Psychol 7:960A.
56. Bradshaw J, Klaiman C, Gillespie S, Brane N, Lewis M, Saulnier C (2018): Walking ability is associated with social communication skills in infants at high risk for autism spectrum disorder. Infancy 23:674–691.
57. Ronald A, Happé F, Plomin R (2008): A twin study investigating the genetic and environmental aetiologies of parent, teacher and child ratings of autistic-like traits and their overlap. Eur Child Adolesc Psychiatry 17:473–483.
58. Merwood A, Greven CU, Price TS, Rijsdijk F, Kuntsi J, McLoughlin G, *et al.* (2013): Different heritabilities but shared etiological influences for parent, teacher and self-ratings of ADHD symptoms: An adolescent twin study. Psychol Med 43:1973–1984.
59. von Stumm S, Malanchini M, Fisher HL (2023): The developmental interplay between the p-factor of psychopathology and the g-factor of intelligence from age 7 through 16 years [published online Jul 5]. Dev Psychopathol.
60. Francis ER, Tsaligopoulou A, Stock SE, Pingault JB, Baldwin JR (2023): Subjective and objective experiences of childhood adversity: A meta-analysis of their agreement and relationships with psychopathology. J Child Psychol Psychiatry 64:1185–1199.
61. Robbers SCC, Bartels M, van Oort FVA, Beijsterveldt CEM (Toos) van, Ende J van der, Verhulst FC, *et al.* (2010): A twin-singleton comparison of developmental trajectories of externalizing and internalizing problems in 6- to 12-year-old children. Twin Res Hum Genet 13:79–87.
62. Brouwer SI, van Beijsterveldt TCEM, Bartels M, Hudziak JJ, Boomsma DI (2006): Influences on achieving motor milestones: A twin–singleton study. Twin Res Hum Genet 9:424–430.
63. Christensen K, Petersen I, Skytthe A, Herskind AM, McGue M, Bingley P (2006): Comparison of academic performance of twins and singletons in adolescence: Follow-up study. BMJ 333:1095.
64. Day FR, Loh PR, Scott RA, Ong KK, Perry JRB (2016): A robust example of collider bias in a genetic association study. Am J Hum Genet 98:392–393.
65. Pingault JB, Allegrini AG, Odigie T, Frach L, Baldwin JR, Rijsdijk F, Dudbridge F (2022): Research Review: How to interpret associations between polygenic scores, environmental risks, and phenotypes. J Child Psychol Psychiatry 63:1125–1139.