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The Earliest Origins of Genetic Nurture: The Prenatal Environment Mediates the Association Between Maternal Genetics and Child Development

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Abstract

Observed genetic associations with educational attainment may be due to direct or indirect genetic influences. Recent work highlights *genetic nurture*, the potential effect of parents' genetics on their child's educational outcomes via rearing environments. To date, few mediating childhood environments have been tested. We used a large sample of genotyped mother–child dyads ($N = 2{,}077$) to investigate whether genetic nurture occurs via the prenatal environment. We found that mothers with more education-related genes are generally healthier and more financially stable during pregnancy. Further, measured prenatal conditions explain up to one third of the associations between maternal genetics and children's academic and developmental outcomes at the ages of 4 to 7 years. By providing the first evidence of prenatal genetic nurture and showing that genetic nurture is detectable in early childhood, this study broadens our understanding of how parental genetics may influence children and illustrates the challenges of within-person interpretation of existing genetic associations.

Keywords

genetics, childhood development, prenatal

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Psychologists have long understood that genetic and environmental influences interact to shape human development and produce individual differences (Turkheimer, 2000). However, as genome-wide association studies over the past decade have created new avenues for the study of genetics at the molecular level (Visscher et al., 2017), the line between genetic and environmental influences has begun to blur. There is increasing appreciation that humans are shaped by both *direct genetic effects*, the influence of their own genes, and *social genetic effects*, the indirect influences that other people's genes have through affecting the shared environment (Domingue & Belsky, 2017).

Social genetic effects represent a novel mechanism through which individual differences may be transmitted from parents to children. Consider recent genetic discoveries for educational attainment (Lee et al., 2018; Okbay et al., 2016), which correlate with numerous related behavioral and social phenotypes: more prestigious occupations and upward social mobility (Belsky et al., 2018; Trejo et al., 2018); intelligence, self-control, and interpersonal skills (Belsky et al., 2016); personality (Mõttus, Realo, Vainik, Allik, & Esko, 2017; Smith-Woolley, Selzam, & Plomin, 2019; Stephan, Sutin, Kornadt, & Terracciano,

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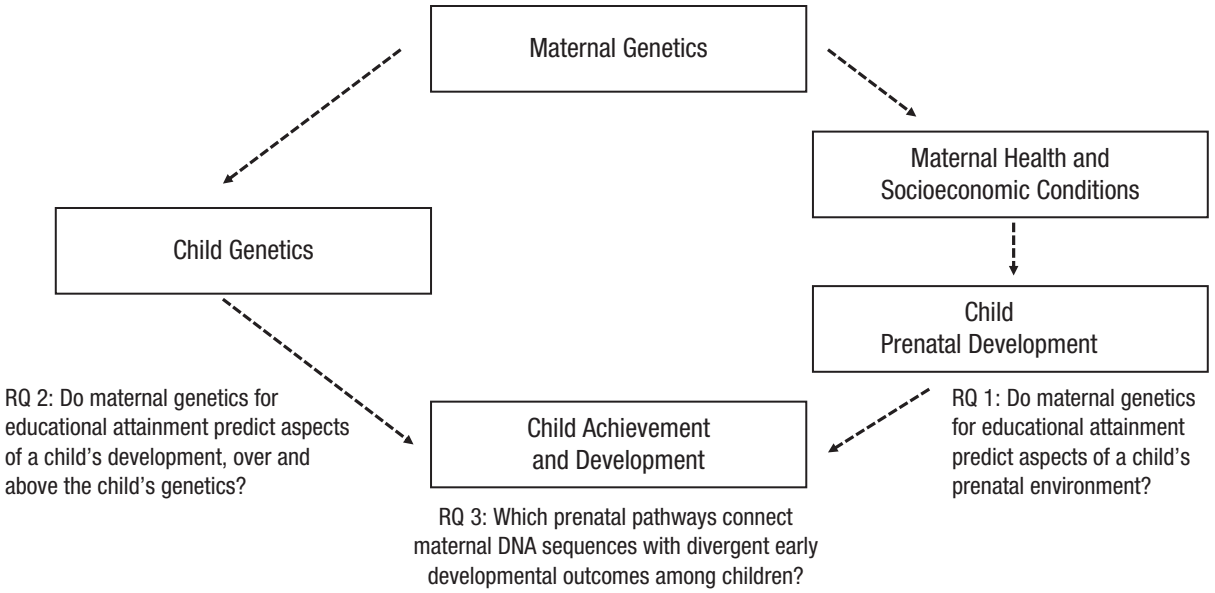

Fig. 1. Conceptual model linking maternal genetics with child achievement and development through both a direct pathway (left) and an indirect pathway (child environment; right). Our three primary research questions (RQs) are also shown.

2019); brain development (Elliott et al., 2019; Okbay et al., 2016); attention (de Zeeuw et al., 2014); and prosocial behavior (Wertz et al., 2018). Parental genes related to educational attainment may be associated with children's educational attainment because of the correlation between maternal and child genetics that results from genetic inheritance (Ayorech, Krapohl, Plomin, & von Stumm, 2017; Conley et al., 2015). However, parental genes related to educational attainment may also become associated with children's educational attainment as a result of an environmentally mediated social genetic effect, whereby parental genes causally influence their children's educational outcomes via genetically associated parental behaviors or environmental exposures. Recently, nontransmitted parental genes have been used to document such social genetic influences from parents to their children, an effect described as *genetic nurture* (Kong et al., 2018). Because genome-wide association studies do not discriminate among the various pathways through which genes become associated with outcomes, recent genetic discoveries from such studies capture both direct genetic effects and genetic-nurture effects (Trejo & Domingue, 2019).

Genetic nurture allows genes to be used as a lens for the study of the social processes through which parents influence their children. For example, new research has found that parental genetics for educational attainment are associated with warm, stimulating parenting, which partially explains the association between parental genetics and children's educational attainment at age 18 (Wertz et al., 2019). However, it is also possible that genetic-nurture processes begin even earlier. In particular, we consider the possibility of such a phenomenon occurring at the earliest stage of development, when the child is still in utero.

The prenatal period is a promising site for genetic nurture for two reasons. First, the prenatal environment is critical for human development, and prenatal adversity (e.g., maternal stress, poverty, and toxicants) is a well-documented developmental risk factor (Piccolo & Noble, 2019). Second, the mother's womb is the predominant environment for the developing child. External environments may influence the child in utero, but even those are mediated by the mother's biology. This is not true for the postnatal environment, where many environmental processes that affect a child are independent of the mother.

Figure 1 presents a conceptual model for how maternal genetics could influence child development in utero. Maternal genetics are related to both the mother's behaviors and her environmental exposures while pregnant; these collectively affect the child in utero and impact the child's downstream outcomes. Identifying the exact causal flows in this graph is challenging, but we note one crucial point. If maternal genetics have a causal effect on child outcomes (independently of genetic transmission), the association between an individual's prenatal environmental exposures and downstream outcomes will be confounded by both direct genetic and social genetic influences. Put plainly, influences on children's development that stem from their own genetics, maternal genetics, and independent aspects of the prenatal environment will be challenging to separate.

Investigating genetic nurturance during the prenatal period is complicated by the paucity of genetically informed studies that contain both information on a

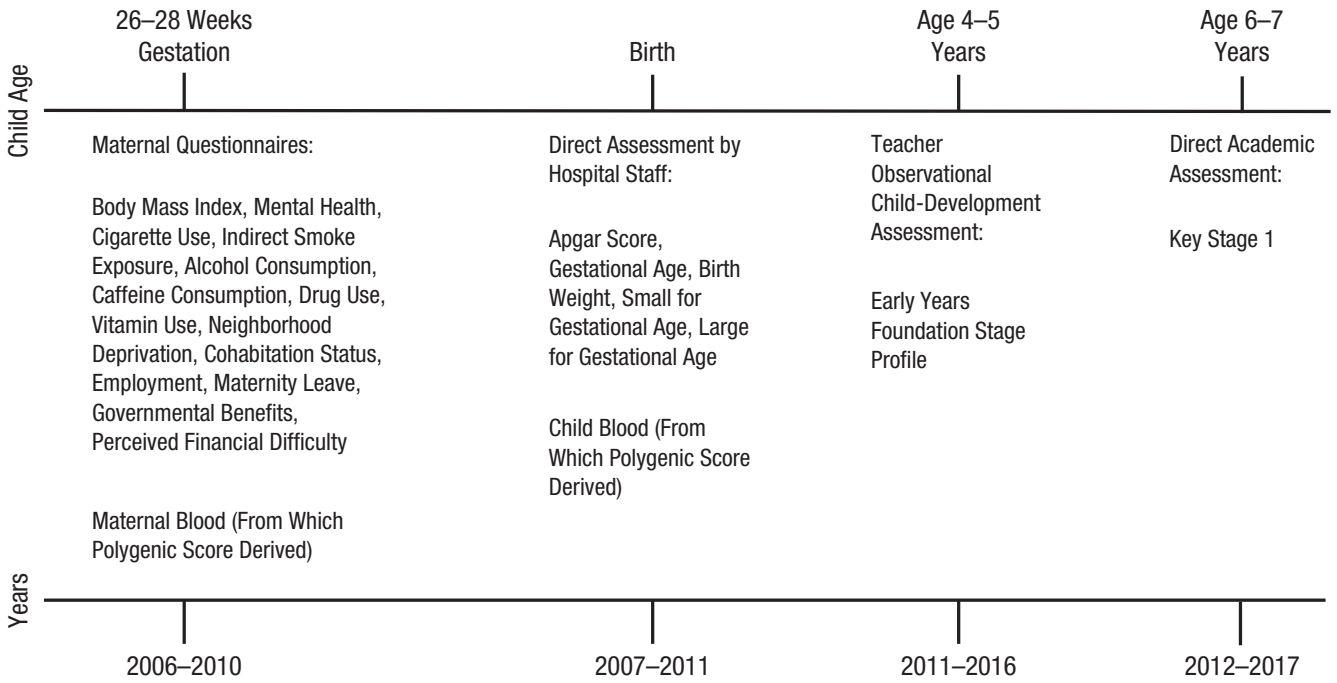

Fig. 2. Timeline of procedures for the Born in Bradford cohort.

mother's behaviors and environmental exposures during pregnancy and measures of the subsequent cognitive and social development of her children. The study of genetic nurture has been further constrained by the timing of developmental and cognitive outcome measures. Previous research has focused on offspring outcomes later in life (e.g., at ages 17 and 18; Bates et al., 2018; Wertz et al., 2019), but a complete accounting of genetic nurture would naturally begin earlier in the life course. Can such effects be observed when young children are just entering school?

To investigate (a) whether the prenatal environment is a pathway for genetic nurture and (b) whether these associations are observed early in a child's life, we asked three main questions. First, do maternal genetics for educational attainment predict aspects of a child's prenatal environment? Second, do maternal genetics for educational attainment predict aspects of a child's development in early and middle childhood, over and above the child's own genetics for educational attainment (i.e., genetic transmission)? Third, which social, behavioral, and psychological prenatal pathways connect maternal genetics with divergent early developmental outcomes among children?

To address these questions, we used rich, prospective data from the Born in Bradford (BiB) birth cohort (Wright et al., 2012). To index maternal genetics, we used a maternal polygenic score for educational attainment (Lee et al., 2018). By controlling for children's genotype, we isolated genetic nurture from direct genetic influences and clarified the contribution of each. Further, we used a high-quality multi-informant method drawing on parent-reported indexes of prenatal environments, teacher observations of child development, and direct assessments of children's academic achievement during their first 3 years of schooling (ages 4–7 years). With these robust measures, we offer evidence that maternal genetics are associated with a variety of prenatal exposures and that genetically associated differences in exposure are predictive of downstream differences in educational development early in a child's life.

Method

Sample

Our analytic sample is drawn from the BiB study, a longitudinal multiethnic birth-cohort study conducted in northern England (Wright et al., 2012). Compared with national averages, the BiB cohort is more ethnically diverse and has higher levels of socioeconomic deprivation; the cohort is broadly characteristic of the city's maternal population (Wright et al., 2012). BiB enrolled pregnant mothers at 26 to 28 weeks' gestation and has followed them longitudinally. The full study recruited 12,453 women and 3,353 of their partners across 13,776 pregnancies and 13,858 children from 2007 to 2010. Figure 2 shows a timeline of BiB procedures. After being enrolled during pregnancy, women completed an extensive questionnaire that included

information on health behaviors and socioeconomic factors. At the child's birth, genetic samples were assayed from both mother and child, and measures of neonatal health were taken. Administrative educational records were collected for children, including a structured, teacher-led observational assessment of development at the end of the first year of schooling, when students were 4 to 5 years old (the Early Years Foundation Stage Profile), and an exam-based direct assessment of academic performance at the end of their third year, when students were 6 to 7 years old (Key Stage 1). Genetic data were available for 6,256 mother–child dyads, and valid data for prenatal, academic and developmental measures were available for 6,124 out of the 13,858 children in the BiB cohort.

The cohort was 33.65% White British, 60.35% Pakistani, and 6.00% other ethnicities. Although a strength of the cohort, diversity raises issues in studies of genetic prediction (Martin et al., 2017). Because the polygenic score for educational attainment was derived from genome-wide association studies of 1 million individuals of European ancestry (Lee et al., 2018), we restricted our sample to mother–child dyads in which the mother self-identified as British and was also of European ancestry (N = 2,077, as identified via the first two principal components; see Section 1B in the Supplemental Material available online). We briefly report on preliminary analyses in a Pakistani-ancestry subsample of the BiB cohort (see Section 3 in the Supplemental Material).

Genotyping and polygenic scoring

We used Illumina HumanCore Exome 12 and 24 BeadChip arrays (Version 1/1.1; Illumina, Hayward, CA) to assay common variation in single-nucleotide polymorphism (SNP) in the genomes of our cohort members. As with many traits of interest (Chabris, Lee, Cesarini, Benjamin, & Laibson, 2015), education is highly polygenic. To capture information from across the dispersed loci, we constructed polygenic scores (Dudbridge, 2013) using Plink software (Version 1.9; Chang et al., 2015). We matched mother and child genotypes from the BiB data with the most recent results of genome-wide association studies for educational attainment (Lee et al., 2018; note that the BiB data were not used in this genome-wide association study). We used 216,542 matched SNPs from BiB members to construct polygenic scores. For each genotype, we counted the number of education-associated alleles (0, 1, or 2), multiplied this count by the effect size estimated in the original genome-wide association study, and then summed weighted counts across all genotypes to calculate each BiB participant's polygenic score. All matched SNPs were used to compute polygenic scores, irrespective of nominal significance for their association with educational attainment. In all analyses, we controlled for maternal age and the first 10 principal components of European-ancestry genotype to account for population stratification and increase the robustness of our findings (Price et al., 2006).

Measures

Additional information for all variables used in the study is available in the Supplemental Material (Section 1).

Prenatal environment. To index salient aspects of the child's prenatal environment, we measured the mother's health and socioeconomic status (SES) during pregnancy. Maternal health during pregnancy was indexed via body mass index (BMI; directly assessed by hospital staff), mental health, cigarette use, indirect smoke exposure, alcohol consumption, caffeine consumption, drug use, vitamin use, and sleep problems (via maternal self-report). SES during pregnancy was indexed by maternal education, cohabitation status, employment, maternity leave, governmental benefits, perceived financial difficulty (via maternal self-report), and neighborhood-level socioeconomic neighborhood deprivation (via governmental index). On the basis of the variables separately described for prenatal health and SES, we constructed two composites via principal components analysis. To maximize sample size in downstream analyses, we used an algorithm designed to allow for missing data (Stacklies, Redestig, Scholz, Walther, & Selbig, 2007); additional details on the composites' construction can be found in Section 1 in the Supplemental Material.

Child outcomes. To index child development, we used children's scores on the Early Years Foundation Stage Profile, a teacher-led observational assessment with six subscales that indexes physical, personal, social, and emotional development relative to the average child at the end of the first year of schooling (Whitaker, 2014). We created a single composite measure by first standardizing each subscale and then calculating a mean total score (higher scores indicate greater development). To index children's academic performance, we used their scores on the Key Stage 1, a standardized school-based exam that includes math, reading, and science subscales (Standards and Testing Agency, 2016). We again created a single composite by standardizing each subscale and calculating the total mean (higher scores indicate greater academic performance). Early achievement at the age of 7 years has been shown to have enduring effects on individuals' downstream educational attainment, SES, and well-being (Ritchie & Bates, 2013).

Analytic sample

Our analytic sample was restricted to mothers and children of European ancestry for whom genetic data and test scores are available (N = 2,077 dyads). Our analytic sample differed from the full BiB sample in several

ways (see Section 1C in the Supplemental Material for additional details on sample comparisons); this is to be expected given the diversity of the BiB sample. Given our focus on a genetically homogeneous sample, we concentrated on comparisons within the full set of self-reported White British BiB respondents. Only a small portion of this group is not in the analytic sample (6% of this subsample). Both child and maternal characteristics were largely similar across these two samples (see Table S2A in the Supplemental Material). Within our analytic sample, further data were missing for children's polygenic scores and developmental and academic outcomes. This is largely due to either children having left the BiB study or students having been too young to be eligible for the Key Stage 1 (see Section 1D in the Supplemental Material for additional details).

Statistical analysis

We conducted linear regressions with standard errors clustered at the mother level (74 mothers had two pregnancies) to test how maternal genetics predict both children's prenatal conditions and their early academic and developmental outcomes. We conducted a power analysis to probe our ability to detect associations between mothers' polygenic scores and children's outcomes (see Section 1E in the Supplemental Material). Given our sample size, our study was well powered to detect association estimates (βs) larger than 0.06; note that previous work has suggested much larger association estimates of around 0.2 (Wertz et al., 2019).

To test possible prenatal pathways through which maternal genetics may be associated with child outcomes, we then considered mediation models—using a recently developed framework (Imai, Keele, & Tingley, 2010)—to test the extent to which maternal-genetics-related differences in early-childhood academic performance and development are explained by prenatal conditions and behaviors. We focused on models in which the composites of prenatal health and SES were separately included as potential mediators linking mothers' polygenic scores and children's outcomes (controlling for children's polygenic scores). We computed confidence intervals on the basis of the bootstrap method. In analyses, all continuous measures were standardized ($M = 0$, $SD = 1$).

We refrain from extensive reliance on p values in discussion of our results. However, for the core analyses involving the prenatal composites and the child outcomes, we guard against spurious findings by commenting on p values relative to the recently suggested conservative threshold of $p < .005$ (Benjamin et al., 2018). Code used for our analysis is publicly available (see Section 4 in the Supplemental Material).

Ethical approvals and data sharing

The research project used only existing, deidentified data; institutional review determined that this project's study protocol did not meet the definition of human-subjects research. The Bradford Leeds NHS Research Ethics Committee provided ethical approval for the BiB study (15/YH/0455), and adult participants provided written consent before data collection. When participants were children, their parents gave informed consent. Researchers retrieved the sensitive biological, medical, and educational records through a managed-access process approved by the BiB executive board.

Results

Maternal genotypes are associated with maternal health and SES during pregnancy

We first tested whether the mothers' polygenic score for educational attainment was associated with the mothers' health composite scores during pregnancy (Table 1). In this model, we did not control for child polygenic score; these are measures derived from data collected before the child's birth and should thus be largely unaffected by a child's genetics. We found that, on average, maternal polygenic score was positively associated with greater health ($\beta = 0.089$, 95% confidence interval, or CI = [0.046, 0.132], $z = 4.077$, $p < .005$). To further investigate this, we also tested each prenatal health factor separately in independent models. We found that a greater maternal polygenic score was associated with lower levels of caffeine consumption, smoking, and indirect smoke exposure and with higher levels of vitamin use (effect sizes ranged from $\beta = 0.07$ to $\beta = 0.10$). This suggests that a larger polygenic score was generally associated with more optimal health behaviors during pregnancy; however, associations with alcohol consumption were the opposite: mothers with higher polygenic scores were more likely to have drunk alcohol in the last few months than were mothers with lower polygenic scores.

We then tested whether the mothers' polygenic score for educational attainment was associated with the mothers' SES composite scores during pregnancy. We found that, on average, maternal polygenic score was positively associated with greater SES ($\beta = 0.156$, 95% CI = [0.114, 0.198], $z = 7.261$, $p < .005$). This association was greater in magnitude than that observed for maternal health. To investigate this further, we also tested each prenatal SES factor separately in independent models. Unsurprisingly, the maternal polygenic score was positively associated with maternal education.

Table 1. Associations Between Mother's and Children's Polygenic Score (PGS) for Educational Attainment and Prenatal Exposures (From Separate Models)

	Maternal PGS		Child PGS		
Outcome	β	95% CI	β	95% CI	*n*
Health composite	0.089	[0.046, 0.132]	0.048	[–0.002, 0.097]	1,986
Body mass index	–0.030	[–0.077, 0.017]	–0.021	[–0.074, 0.032]	1,903
Mental health	–0.009	[–0.056, 0.038]	–0.001	[–0.055, 0.053]	1,910
Vitamin use	0.060	[0.014, 0.107]	0.092	[0.042, 0.143]	1,986
Indirect smoke exposure	–0.076	[–0.118, –0.034]	–0.050	[–0.099, –0.002]	1,984
Smoking	–0.108	[–0.151, –0.065]	–0.048	[–0.096, 0.000]	1,986
Alcohol consumption	0.067	[0.021, 0.113]	0.034	[–0.017, 0.085]	1,986
Caffeine use	–0.070	[–0.118, –0.023]	–0.008	[–0.056, 0.040]	1,742
Drug use	–0.013	[–0.056, 0.031]	0.014	[–0.040, 0.069]	1,923
Sleep problems	–0.005	[–0.051, 0.041	0.001	[–0.052, 0.053]	1,907
SES composite	0.156	[0.114, 0.198]	0.096	[0.048, 0.143]	1,986
Maternal education	0.206	[0.162, 0.250]	0.070	[0.019, 0.121]	1,809
Single	–0.081	[–0.123, –0.039]	–0.086	[–0.135, –0.037]	1,985
Employed	0.092	[0.049, 0.136]	0.036	[–0.015, 0.086]	1,986
Maternal leave	–0.019	[–0.069, 0.031]	–0.026	[–0.080, 0.029]	1,554
Neighborhood deprivation	–0.067	[–0.112, –0.022]	–0.044	[–0.094, 0.006]	1,935
Financial difficulty	–0.030	[–0.076, 0.017]	–0.058	[–0.112, –0.004]	1,984
Receipt of governmental benefits	–0.102	[–0.145, –0.059]	–0.052	[–0.104, –0.001]	1,984

Note: The rightmost column shows individual *n*s. For associations with maternal PGS, analyses controlled for age and 10 principal components. For associations with child PGS, analyses controlled for maternal PGS, age, and 10 principal components. CI = confidence interval; SES = socioeconomic status.

Greater maternal polygenic score was associated with lower likelihood of the mother being single, being unemployed, and receiving governmental benefits (effect sizes ranged from 0.08 to 0.1). Echoing previous findings, our results showed that higher polygenic score was also associated with living in a neighborhood with lower levels of deprivation (Belsky et al., 2019; Domingue, Belsky, Conley, Harris, & Boardman, 2015).

As shown in Table 1, these models also revealed that child polygenic score uniquely contributed to aspects of the prenatal environment, even after we controlled for maternal polygenic score. With respect to health, child polygenic score was weakly associated with greater health composite scores, as well as with increased vitamin usage and decreased smoke exposure. With respect to SES, child polygenic score was positively associated with the SES composite and with the mother's education, and it was negatively associated with the likelihood of the mother being single and experiencing financial difficulty. These results provide further evidence for gene–environment correlation.

Maternal genotypes predict offspring development after analyses control for offspring genes

To examine the possibility of genetic nurture among young children, we next tested whether maternal genetics for educational attainment predicted child development (at age 4–5 years) and academic performance (at age 6–7 years) over and above the child's genetics. As shown in Table 2 and Figure 3, maternal polygenic score was positively associated with offspring development (β = 0.114, 95% CI = [0.058, 0.171], z = 4.002, $p < .005$) and academic performance (β = 0.087, 95% CI = [0.020, 0.154], z = 2.748, p = 0.006; note that this is marginal in that it is above a conservative threshold of p = .005). In this model, child polygenic score also uniquely predicted greater academic performance (β = 0.083, 95% CI = [0.016, 0.150], z = 2.639, p = .008) and marginally greater child development (β = 0.058, 95% CI = [0.002, 0.133], z = 2.020, p = .043; Table 2).

Because the distributions of child outcome variables were highly centralized (see Fig. S2 in the Supplemental Material), we also considered analyses based on outcomes converted to percentiles of their respective distributions. Results were qualitatively similar; a 1-standard-deviation increase in the mother's polygenic score predicted a gain of around 3 percentile points in the outcome distribution (β = 0.034 for development, β = 0.030 for academic performance). We also tested whether our findings were potentially due to individual differences in child characteristics measured at birth (see Section 2A in the Supplemental Material). Associations between mothers' polygenic score and children's gestational age, Apgar score, and birth weight were null.

Table 2. Results of Regression Analyses Predicting Children's Development and Academic Performance From Mother's and Children's Polygenic Score (PGS)

	Child development (n = 1,611, r^2 = .044)		Child academic performance (n = 1,267, r^2 = .056)	
Outcome	Mother PGS	Child PGS	Mother PGS	Child PGS
Standardized	0.114 [0.058, 0.171]	0.058 [0.002, 0.113]	0.087 [0.020, 0.154]	0.083 [0.016, 0.150]
Percentile ranked	0.034 [0.017, 0.050]	0.017 [0.001, 0.033]	0.030 [0.011, 0.049]	0.025 [0.006, 0.044]

Note: Standardized coefficients are shown, with robust 95% confidence intervals in brackets. The *n*s are for mother–child dyads. Child development was indexed by scores on the Early Years Foundation Stage Profile; child academic performance was indexed by scores on the Key Stage 1.

As other researchers have observed (Bates et al., 2018; Kong et al., 2018; Wertz et al., 2019), these results are consistent with the hypothesis that mothers' education-associated genetics shape environments that affect offspring outcomes independently of direct mother-child genetic transmission. Our results suggest that such processes are observable during early childhood.

Prenatal environmental exposures mediate associations between maternal genetics and outcomes in early childhood

We next examined whether the observed associations between maternal polygenic score and offspring development and academics were explained by conditions experienced during the prenatal period. To do this, we created mediation models, first with child development as the outcome and next with academic performance as the outcome (see Table 3). Each model separately included the prenatal health and SES composites as mediators (each model additionally controlled for child polygenic score). Note that both the health and SES composites were themselves strongly and positively associated with child development and academic performance (see Section 2B in the Supplemental Material).

For child development, maternal SES during pregnancy explained 27.3% (p < .005) of the variance in the association between higher maternal polygenic score

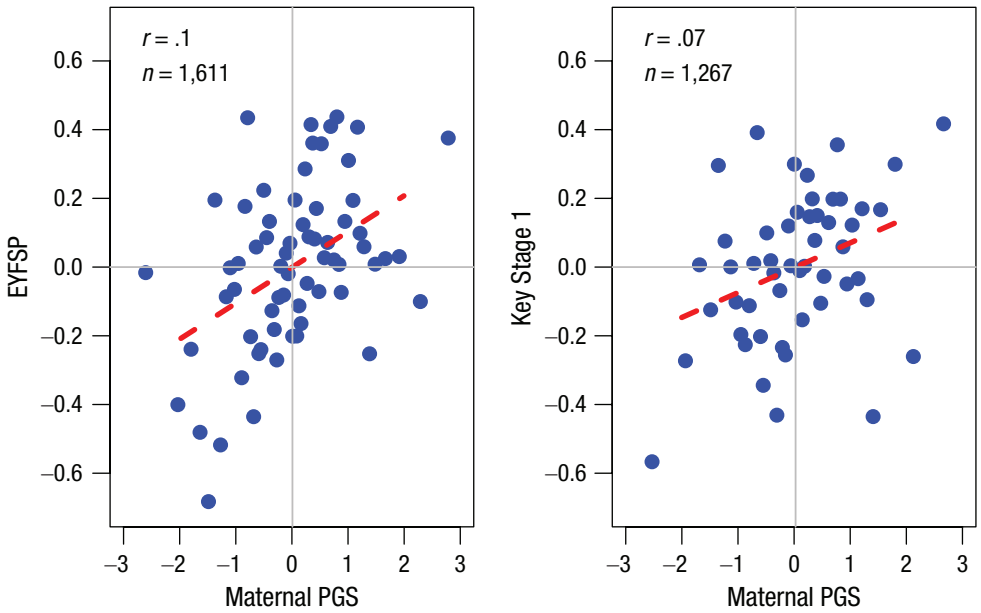

Fig. 3. Binned scatterplots showing the associations between the Born in Bradford's mothers' polygenic score (PGS) and their children's developmental outcomes (left) and academic outcomes (right). Children's developmental outcomes are indexed by scores on the Early Years Foundation Stage Profile (EYFSP), and their academic outcomes are indexed by scores on the Key Stage 1. Maternal polygenic score was residualized on child polygenic score, maternal age, and the first 10 principal components of individual genotype. Maternal polygenic score and both developmental outcomes were standardized within sample (M = 0, SD = 1). Each point represents roughly 25 mother–child pairs. The red line represents the best linear fit from a regression on the underlying, unbinned data.

Table 3. Mediation Analysis: Total Effect of Maternal Polygenic Score (PGS) and Proportion of Total Effect Due to Mediator (Controlling for Child PGS and the Alternative Prenatal Composite)

Outcome and mediator	Total effect (maternal PGS on outcome)	95% CI	Proportion mediated	95% CI	*n*
Early Years Foundation Stage Profile					
SES principal component	0.113	[0.057, 0.164]	.273	[.138, .548]	1,611
Health principal component	0.115	[0.058, 0.169]	.112	[.039, .252]	1,611
Key Stage 1					
SES principal component	0.087	[0.025, 0.146]	.321	[.134, .980]	1,267
Health principal component	0.087	[0.024, 0.150]	.131	[.038, .484]	1,267

Note: Total effects are given as standardized coefficients. The rightmost column shows individual *n*s. CI = confidence interval; SES = socioeconomic status.

and greater child development, and maternal health during pregnancy explained 11.2% ($p < .005$) of the variance.

For child academic performance, results were similar. Maternal SES during pregnancy explained 32.1% ($p < .005$) of the variance in the association between higher maternal polygenic score and greater child academic performance, and maternal health during pregnancy explained 13.1% ($p < .005$) of the variance.

We considered a supplemental analysis wherein each individual prenatal environmental variable was entered as a mediator, instead of the two composites (see Section 2C in the Supplemental Material). Maternal education was an especially salient mediator. One interpretation of these results could be that observed differences were largely mediated by prenatal maternal behaviors that are themselves associated with educational attainment.

Discussion

We investigated whether mothers' education-associated genetics are associated with offspring's early development and whether prenatal environmental factors explain variance in these associations. We drew on a large sample of mother–child dyads followed from 28 weeks' gestation through the first 7 years of life. Our results indicate that mothers with more education-associated alleles tended to be healthier (with the exception of alcohol consumption) and more economically secure during pregnancy. Further, these prenatal factors explained about 30% of the positive association between maternal-education-associated genetics and children's school readiness and early academic performance, even after analyses accounted for direct genetic transmission. Together, our results suggest that prenatal exposures are salient environmental pathways through which maternal genetics may influence children's early development and education.

Recent work documents associations between mothers' genetics and their adolescents' education (Bates et al., 2018; Kong et al., 2018; Wertz et al., 2019). We showed that maternal genetics are similarly associated with young children's academic success and broader developmental milestones and that these associations are detectable as early as ages 4 to 5 years. The effect size of the association we observed between maternal polygenic score and child academic achievement was smaller than effect sizes from recent studies of adolescent outcomes ($\beta = 0.12$ compared with $\beta = 0.23$, as observed by Bates et al., 2018, and Wertz et al., 2019, respectively). Our finding adds to growing evidence that genetic variation linked to educational attainment also predicts a constellation of different behaviors and social circumstances across the life course, and it even spills into the next generation.

This study suggests that genetic nurture may occur during the prenatal period and leave detectable traces earlier in the child's life than previously observed. Our findings highlight prenatal genetic nurture as a novel pathway through which genetics can confound the observed relationship between prenatal circumstances and child development. For the prenatal environment to be a period of concern for social policymakers, the documented association between prenatal circumstances and life-course development must reflect, at least in part, a causal relationship. However, because a mother's genetics are both transmitted to her offspring and predict her prenatal circumstances, the degree to which the relation between prenatal circumstances and child development is correlational versus causal is unclear. Most perniciously, such confounding may continue to exist even after analyses control for the genetics a child inherits (Rice et al., 2010; Stein et al., 2014). Researchers interested in exploring the causal chain that connects prenatal circumstances to human development would benefit from controlling for the specific pathways we have identified. In particular, we note the crucial role played by the mother's social environment during pregnancy. That said, a mother's SES and other environmental exposures are likely to be relatively

unchanging throughout the life course; features of the mother's pregnancy will become the child's environmental surroundings in the first few years of life and beyond. This "stickiness" offers further challenges to research connecting prenatal circumstances to later-life outcomes.

Our research expands on the budding phenotypic-annotation literature in which a top-down approach is used for unpacking genetic discoveries (Belsky & Harden, 2019). We showed that this technique can be applied to indirect genetic influences in addition to direct genetic influences. Although findings from genome-wide association studies tend to be a black box, researchers can use data from whole genomes and take a life-course-development approach to explore how genetics for the discovery of specific phenotypes relate to broader nomological networks (Cronbach & Meehl, 1955). Our analyses embody this approach; we utilized a genome-wide polygenic score for educational attainment as a starting point for exploring the broader nomological network of child development that extends beyond purely educational attainment. This is important because children's socioemotional skills are associated with school readiness and later achievement and well-being (Duncan et al., 2007). Consequently, our results highlight the possibility that maternal genetics may predict a child's capacity to cope and thrive during the transition into formal education.

We acknowledge limitations of our study. Prenatal environmental measures may be correlated with environmental exposures occurring both before and after pregnancy; for example, the mother's SES may be relatively stable throughout the life course. Thus, prenatal exposures may also inadvertently capture the effect of, say, persistent exposure to relatively high levels of neighborhood deprivation. Another limitation is that the existing educational-attainment polygenic score contains substantial amounts of measurement error resulting from the finite sample used to obtain the underlying allelic weights. This measurement error attenuates the association between maternal polygenic score and child outcomes, potentially obscuring relevant prenatal pathways. However, this measurement error does not lead to false positives; because mother and child polygenic scores are constructed using the same allelic weights, the child polygenic score indexes the same genetic pathways as the maternal polygenic score, and unmeasured child genetics do not confound the association between maternal polygenic score and child outcomes. In addition, given the complications of interpreting genetic differences across ancestry groups (Martin et al., 2017), our findings only pertain to individuals of White British ancestry. Finally, though we attempted to reduce confounding through the inclusion of control variables, the findings are observational in nature and do not definitively indicate causal pathways.

The present study illustrates ways in which maternal genetics are interwoven in a complex tapestry of health behaviors and social circumstances. Although genes are often used to partition variance in a given outcome into genetic and environmental influences, they also characterize features of the environments that individuals are exposed to. We use genetics to illuminate the important and complex influences on the prenatal environment that in turn shape children's early development and downstream outcomes. Genetic-nurture influences blur the line between genetic and environmental influences, reminding us that genetic influences are not immutable and environments are rarely exogenous.

Transparency

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Author Contributions

E. Armstrong-Carter and S. Trejo contributed equally to this article. E. Armstrong-Carter, S. Trejo, and B. W. Domingue conducted the analysis and wrote the manuscript. L. J. B. Hill, K. L. Crossley, and D. Mason edited the manuscript and provided support.

Declaration of Conflicting Interests

The author(s) declared that there were no conflicts of interest with respect to the authorship or the publication of this article.

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Open Practices

Data access can be requested via the Born in Bradford website (https://borninbradford.nhs.uk/). The design and analysis plans for this study were not preregistered.

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Supplemental Material

Additional supporting information can be found at http://journals.sagepub.com/doi/suppl/10.1177/0956797620917209

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The Earliest Origins of Genetic Nurture:
Prenatal Environment Mediates the Association Between
Maternal Genetics and Child Development

Supplemental Information

1. Additional Methods

1A. Measures

Measures used in this study are described in Table S1. Additional details are available via the BiB website, https://borninbradford.nhs.uk/research/documents-data/.

Our health and SES composites were computed after separately standardizing all variables used for construction of each composite. Loadings for the components of the composites are:

- SES composite. Single -0.39, neighborhood deprivation -0.39, financial difficulties -0.36, government benefits -0.30, maternal leave -0.01, education 0.46, employment status 0.51.
- Health composite. cigarette use -0.51, smoke exposure -0.46, mental health composite -0.41, sleep problems -0.35, caffeine -0.29, illicit drug use -0.26, alcohol consumption -0.18, BMI 0.01, vitamin usage 0.23.

1B. Genetic Diversity amongst BiB participants

Figure S1 shows the first two PCs with color indicating self-reported ancestral background. Our main analytic sample consisted of those respondents who both (a) self-reported British ancestry

and (b) had their first two PCs fall within the red box (i.e., these are the red dots in the red box). A similar procedure was used to identify Pakistani respondents (i.e., blue dots in the blue box).

1C. Sample Comparisons

Table S2A compares the full BiB sample to the self-reported white British sample and our analytic sample (which is comprised of respondents with genetic data that we included based on the rules described above in 1B). Our analytic sample clearly differs from the full sample, which is expected given that it is an ancestrally homogenous subsample pulled from a diverse cohort. Differences between the two samples are potentially reflective of cultural differences that may fall along ancestral lines (i.e., the analytic sample is not uniformly "healthier" for example). For example, mothers in the analytic sample live in neighborhoods of lower disadvantage but are more likely to smoke than mothers in the full BiB sample. Children in the analytic sample have higher levels of both development and academic performance compared to those in the full BiB sample.

Focusing just on a comparison of the analytic sample (n=2077) to the full sample of respondents who self-report British ancestry (n=2210), our analytic sample is similar in terms of the child outcomes and maternal characteristics.

1D. Further description of Analytic Sample

Descriptive statistics are available in Table S2. Histograms for key variables in analytic sample are shown in Figure S2. Correlations amongst all variables are given in Figure S3.

As can be seen in Table S2, there are different levels of missingness in our variables. We further discuss missingness on three crucial variables in our analytic sample: child PGS, EYFSP, and KS1.

- In the analytic sample, 91 children did not have genetic data from which to compute a polygenic score. We did not observe a significant difference in the means of the maternal polygenic scores comparing those mothers whose children do have genetic data to those who do not.
- We did not observe EYFSP scores for 387 students. Missingness on the EYFSP is driven largely by students moving outside of the Bradford area. We did not observe a significant difference in the means of the maternal polygenic scores comparing those mothers whose children do EYFSP scores as compared to those who do not.
- We did not observe KS1 scores for 742 students. Missingness on the KS1 is due to both moving (as with the EYFSP) and also to the fact many BiB children were not yet old enough to have yet taken the KS1. Of the 742 students missing the KS1, nearly half (n=306, 41.2%) started school in 2015/2016 and thus would not have yet taken the KS1 by the time relevant data collection was complete.

Additional comparisons of the analytic sample to our minimum complete data sample are shown in Table S2 Panel B. There are a few differences (e.g., the full analytic sample had a slightly higher mean EYFSP than those in the minimum data sample), but the two groups are comparable across many dimensions (e.g., similar profiles of maternal education).

1E. Power Analysis

We conducted a sensitivity power analysis meant to determine our statistical power, given the BiB sample size, to detect associations of different size. In particular, we analyzed our power to detect associations in the presence of a covariate with known correlation structure (i.e., can we detect associations between the maternal PGS and some outcome given the fact that we also control for the child PGS which is correlated with the mother PGS at roughly 0.5). Figure S4 shows results of this analysis. Even for our analyses of KS1 in Table 2 (with N=1267), we have reasonable power (>0.8) to detect associations starting if effect sizes are larger than roughly 0.06.

2. Ancillary Analyses on British respondents

2A. Associations with outcomes measured at birth

In Table S3, we examined associations between polygenic scores and outcomes measured at birth in parallel to Table 2 of main text. We considered gestational age, APGAR scores, birthweight in grams and a low birth indicator (additional information on measures in Table S1); results were null.

2B. Associations between prenatal exposures and child development and academic performance

Our composite measures of prenatal exposures are highly associated with child development and academic performance (Table S4). The SES composite has estimated associations of around 0.28 with both the EYFSP and the KS1. The health composite has estimated associations with both measures of around 0.15.

2C. Mediation via individual environmental pathways

Table S5 replicates results along the lines of Table 3 from the main text including each environmental variable separately. Maternal education is an especially important mediator. Note that maternal education has, as expected, strong associations with the maternal PGS (Figure S5). However, we do note that the direct effect of maternal PGS on offspring development (b=0.082, 95% CI=[0.025, 0.140], p<0.005) remained highly significant in our mediation model. For academic performance, associations were weaker (b=0.055, 95% CI=[-0.003, 0.120], p=0.074).

3. Analysis of a Pakistani ancestry subsample of the BiB cohort

We considered analysis of the genetically identified respondents of Pakistani ancestry (e.g., the blue dots in the blue box in Figure S1). We first computed health and SES prenatal composites in the same manner as before. We then looked at associations between the maternal education PGS and the prenatal composites net of the first 10 PCs computed in the entire genetic sample. Results were null. The PGS for the mothers in the Pakistani sample was not robustly predictive of either the health or SES prenatal composite (see Table S6). We then looked at associations between the maternal education PGS and the child outcomes net of both the PCs and the child PGS. Results were again null. The maternal PGS was not associated with either child development or academic performance.

4. Syntax

In the interest of reproducibility, we provide the syntax for all of our statistical analyses at https://github.com/ben-domingue/prenatal_genetic_nurture. Note that we prepared data using Stata Version 14 (StataCorp, 2015) and analyzed data using R (Version 3.5.2).

Table S1. Description of study variables.

Measures	Description
Prenatal health	
Body Mass Index (BMI)	BMI was directly assessed at the hospital by nursing staff during upon study enrollment
Mental Health	General Health Questionnaire (GHQ; Goldberg & Hillier, 1979) is 28-item scaled questionnaire that assessed mother's somatic symptoms, anxiety and insomnia, social dysfunction and depression. A General Health factor score was the mean of all items and standardized.
Cigarette use	A single item "do you smoke cigarettes?" indexed mother's cigarette use. Mothers responded yes or no.
Indirect Smoke Exposure	A single item index: "During pregnancy have you been exposed to other peoples' cigarette smoke at work or at home?" Mothers responded yes or no.
Alcohol use	A single item: "Have you drunk alcohol in the past 3 months? Mothers responded yes or no
Caffeine consumption.	Mothers responded to 28 items of decaffeinated and caffeinated
Drug use	A single item index: "Have you used any drugs like marijuana or ecstasy during pregnancy or in the three months before pregnancy?" Mothers indicated yes or no.
Vitamin use	A single item index: "Have you taken any dietary supplements including vitamins or iron tablets in the last 4 weeks of pregnancy?" Mothers indicated yes or no.
Sleep problems	Sleep problems were assessed with two items: "have you Lost much sleep over worry?" and "have you had difficulty staying asleep once you are off?". Mothers responded on a Likert-type scale from 1 (not at all) to 4 (much more than usual).
Prenatal socio-economic conditions	
Single	A single item index: Mothers responded whether they were currently living with the baby's father, living with another partner, or not living with another partner. If mothers lived with a partner of any kind, they were coded as 0 = not single. If they did not live with a partner, they were coded as 1 = single (N_{single} = 505, $N_{partnered}$ = 1486).
Employment	A single item index: "are you currently employed?". Mothers responded yes or no
Maternal leave	A single item index: "Are you currently on maternity/sick leave?". Mothers indicated yes or no
Neighborhood deprivation	The Index of Multiple Deprivation (IMD) is an official measure of neighborhood affluence in England based on income, employment, health and disability, education, barriers to housing and services, crime, and living environment. IMD rankings within Bradford only were included in order to illuminate the full variation among Bradford neighborhoods. There were ten neighborhoods ranked from one to ten in Bradford, with 10 indicating relatively more deprived neighborhoods.
Governmental benefits	Checklist of ten governmental benefits, indicating which ones they received and their partner received (e.g., child tax credit, income support, disability living allowance). Mothers responded yes or no to each item. Principle components analysis was used to create a composite score with higher scores indicating more governmental benefits received
Perceived financial difficulty	A single item: "How well are you and your partner managing financially?" Mothers responded on a 5-item response set ranging from "living comfortably" to "finding it very difficult".
Characteristics at birth of child	
APGAR score	APGAR scores at birth were determined by a hospital nurse. Two scores were provided for each child: one within the first minute of life, and the other within the first five minutes of life. We calculated an average score.
Gestational age	Child's gestational age was obtained from medical records.
Gestational weight	Birth weight was directly assessed by hospital staff and was recorded in grams.
Small for gestational age	Small for gestational age was coded yes/no: Yes if birthweight is below 10th percentile on UK WHO fetal growth charts for sex and gestational week at birth. This measure was only calculated for singletons.

Large for gestational age	Large for gestational age was coded yes/no: Yes if birthweight was above 90th percentile on UK WHO fetal growth charts for sex and gestational week at birth. This measure was only calculated for singletons.
Child outcomes	
Child development	We used children's scores on the Early Years Foundation Stage Profile (EYFSP), a teacher-led observational assessment conducted towards the end of the child's first year at school. The version of this assessment analysed was used from the start of the 2012/2013 academic year onwards in English schools, and is completed at the end of the child's first year in school, when they are usually 4-5 years old. The profile measures children's attainment in seven main areas of learning: communication and language; expressive arts and design; literacy, mathematics; physical development; personal, socio and emotional development and understanding the world. The assessment is designed not as an academic test but to assess children's development in these areas, compared to the average child at the end of one year's schooling. Teachers completed the assessment for each child based on their knowledge and observations of that child. The measure is intended to provide a complete picture of children's development, not just a snapshot of what happens at school. We standardized each subscale and calculated a mean composite score for child development, with higher scores indicating relatively greater development.
Academic performance	We used children's scores on the Key Stage 1 Assessment, a standardized test conducted under exam conditions and set by the Standards and Testing Agency in England. This version was used from the start of the 2015/2016 academic year onwards, and is completed towards the end child's third year in school when the child was 6-7 years old. The Key Stage 1 Assessment includes math, reading and science subscales. For math and reading, children were graded on a five-point scale: level 1, just into level 2, securely at level 2, top end of level 2, and level 3. For science, children were graded on a three-point scale: levels 1, 2 and 3. We standardized each subscale and calculated a mean composite score for academic performance, with higher scores indicating relatively better performance.

Table S2. Sample Comparisons

A. Comparison between full BiB cohort, the white British sample, and our analytic sample (dyads for whom genetic and test data were available and European ancestry only).

	Full Sample (N=6124)			Self-reported White British (N=2210)			Analytic sample (genotyped respondents of British ancestry, N=2077)			p-value of test of difference in means between full British sample (N=2210) and analytic sample (N=2077)
	Mean	SD	N	Mean	SD	N	Mean	SD	N	
Child Characteristics										
Child Development (EYSFP)	0	1	5056	0.184	0.955	1800	0.18	0.955	1690	9.10E-01
Academic Performance (Key Stage 1)	0	1	4023	0.029	0.967	1424	0.021	0.971	1335	8.34E-01
Maternal Characteristics										
Mom's Education			4087			2014			1892	
GCSE 1	0.285	0.451		0.216	0.412		0.22	0.414		8.50E-01
GCSE 2	0.316	0.465		0.382	0.486		0.379	0.485		8.80E-01
GCSE 3	0.185	0.389		0.2	0.4		0.198	0.398		9.24E-01
University Degree	0.215	0.411		0.202	0.402		0.203	0.403		9.45E-01
Maternal Age	27.499	5.608	5405	26.844	6.121	2210	26.856	6.102	2077	8.77E-01
BMI	26.344	5.732	5163	27.131	6.031	2115	27.139	6.029	1987	9.11E-01
Mental Health	0.082	0.815	5042	0.033	0.798	2102	0.042	0.801	1989	7.64E-01
Vitamin use	0.411	0.492	5392	0.295	0.456	2209	0.295	0.456	2077	9.99E-01
Indirect Smoke Exposure	0.316	0.465	5382	0.423	0.494	2207	0.425	0.494	2075	9.49E-01
Cigarette Use	0.153	0.36	6124	0.338	0.473	2210	0.339	0.474	2077	9.29E-01
Alcohol Consumption	0.175	0.38	6124	0.423	0.494	2210	0.428	0.495	2077	8.02E-01
Caffeine Consumption (mg)	61.403	99.138	4598	90.323	130.255	1929	89.892	130.742	1813	2.50E-01
Drug Use	0.011	0.104	5211	0.02	0.141	2118	0.021	0.145	2002	9.21E-01
Single	0.162	0.368	5397	0.268	0.443	2208	0.268	0.443	2076	9.89E-01
Employed	0.396	0.489	6124	0.644	0.479	2210	0.644	0.479	2077	9.88E-01
Maternal Leave	0.074	0.262	3213	0.055	0.229	1736	0.058	0.233	1632	8.90E-01

Neighborhood Deprivation	7.119	2.369	5332	6.152	2.519	2154	6.153	2.515	2023	9.92E-01
Sleep Problems	0	1.217	5037	0.075	1.167	2099	0.085	1.171	1986	7.67E-01
Financial Difficulties	2.124	0.934	5385	2.134	0.932	2207	2.13	0.934	2074	9.06E-01
Receipt of Governmental Benefits	0	1.368	5394	-0.085	1.412	2207	-0.07	1.415	2075	6.83E-01

Table S2B. Comparison of analytic sample to minimal complete data sample.

	Analytic sample (genotyped respondents of British ancestry, N=2077)			Analytic sample with both child PGS and KS1 (n=1267)			p-value of test of difference in means between analytic sample (N=2077) and complete data sample (n=1267)
	Mean	SD	N	Mean	SD	N	
Child Characteristics							
Child Development (EYSFP)	0.18	0.955	1690	0.088	0.927	1257	1.09E-02
Academic Performance (Key Stage 1)	0.021	0.971	1335	0.012	0.974	1267	8.09E-01
Maternal Characteristics							
Maternal Education			1892			1145	
GCSE 1	0.22	0.414		0.236	0.425		5.12E-01
GCSE 2	0.379	0.485		0.396	0.489		5.24E-01
GCSE 3	0.198	0.398		0.188	0.391		6.73E-01
University Degree	0.203	0.403		0.181	0.385		3.33E-01
Maternal Age	26.856	6.102	2077	26.721	6.11	1267	1.24E-01
BMI	27.139	6.029	1987	27.358	6.12	1218	1.49E-02
Mental Health	0.042	0.801	1989	0.039	0.794	1211	9.44E-01
Vitamin use	0.295	0.456	2077	0.272	0.445	1267	3.39E-01
Indirect Smoke Exposure	0.425	0.494	2075	0.439	0.496	1267	5.70E-01
Cigarette Use	0.339	0.474	2077	0.364	0.481	1267	3.22E-01
Alcohol Consumption	0.428	0.495	2077	0.424	0.494	1267	8.67E-01
Caffeine Consumption (mg)	89.892	130.742	1813	96.112	135.13	1075	1.95E-44
Drug Use	0.021	0.145	2002	0.023	0.15	1218	9.14E-01
Single	0.268	0.443	2076	0.292	0.455	1266	3.07E-01
Employed	0.644	0.479	2077	0.641	0.48	1267	8.93E-01
Maternal Leave	0.058	0.233	1632	0.055	0.228	1033	8.99E-01

Neighborhood Deprivation	6.153	2.515	2023	6.083	2.523	1262	2.22E-01
Sleep Problems	0.085	1.171	1986	0.079	1.158	1208	8.82E-01
Financial Difficulties	2.13	0.934	2074	2.148	0.92	1266	6.09E-01
Receipt of Governmental Benefits	-0.07	1.415	2075	0.029	1.445	1265	1.98E-02

Table S3. Estimated associations between maternal PGS and child PGS with birth characteristics (controlling for 10 PCs and maternal age)

	Maternal PGS		Child PGS		
	Estimate	95% CI	Estimate	95% CI	N
Gestational Age (days)	0.024	-0.026, 0.075	0.002	-0.047, 0.051	1985
APGAR Score	0.016	-0.035, 0.067	-0.036	-0.087, 0.015	1975
Birthweight (g)	0.044	-0.008, 0.096	0.042	-0.007, 0.091	1984
Small for gestational age	-0.066	-0.116, -0.015	0.000	-0.046, 0.045	1951

Table S4. Associations between prenatal composites & child academic and developmental outcomes (net of 10 PCs and maternal age).

Outcome	Predictor	Estimate	95% CI
EYFSP	SES Composite	0.290	0.241, 0.339
	Health Composite	0.159	0.111, 0.207
KS1	SES Composite	0.279	0.223, 0.335
	Health Composite	0.143	0.088, 0.199

Table S5. Mediation Analysis: Proportion of maternal PGS association on outcome (EYFSP or KS1) mediated by individual environmental measures.

A. Child development (EYFSP)

Mediator	Total Effect (maternal PGS on outcome)	95% CI	Proportion mediated	95% CI	N
BMI	0.118	0.060, 0.171	0.013	-0.018, 0.066	1539
Mental Health	0.110	0.054, 0.165	0.001	-0.014, 0.024	1549
Indirect Smoke Exposure	0.115	0.061, 0.168	0.078	0.008, 0.185	1610
Cigarette use	0.115	0.061, 0.177	0.099	0.033, 0.219	1611
Alcohol Consumption	0.115	0.060, 0.173	0.000	-0.028, 0.026	1611
Caffeine Consumption	0.115	0.053, 0.172	0.060	0.011, 0.179	1408
Drug use	0.112	0.054, 0.169	0.000	-0.022, 0.027	1562
Vitamin use	0.115	0.061, 0.171	0.031	-0.020, 0.097	1611
Sleep Problems	0.110	0.054, 0.166	0.006	-0.025, 0.051	1546
Maternal Education	0.121	0.063, 0.176	0.319	0.188, 0.627	1470
Single	0.114	0.057, 0.168	0.029	-0.003, 0.095	1610
Employed	0.115	0.058, 0.173	0.092	0.014, 0.204	1611
Maternal Leave	0.125	0.056, 0.184	0.000	-0.017, 0.025	1258
Subjective Financial Difficulty	0.114	0.056, 0.171	0.004	-0.050, 0.053	1610
Neighborhood Deprivation	0.114	0.062, 0.167	0.078	-0.012, 0.212	1602
Receipt of Governmental Benefits	0.114	0.059, 0.171	0.139	0.050, 0.307	1609

B. Academic Performance (KS1)

Mediator	Total Effect (maternal PGS on outcome)	95% CI	Proportion mediated	95% CI	N
BMI	0.096	0.032, 0.162	0.010	-0.044, 0.087	1218
Mental Health	0.083	0.020, 0.147	0.008	-0.051, 0.084	1211
Indirect Smoke Exposure	0.087	0.021, 0.148	0.066	-0.003, 0.283	1267
Cigarette use	0.087	0.026, 0.151	0.113	0.035, 0.405	1267
Alcohol Consumption	0.088	0.025, 0.152	0.008	-0.020, 0.083	1267
Caffeine Consumption	0.115	0.051, 0.183	0.049	-0.002, 0.169	1075
Drug use	0.084	0.021, 0.146	0.001	-0.058, 0.045	1218
Vitamin use	0.088	0.026, 0.147	0.015	-0.018, 0.095	1267
Sleep Problems	0.080	0.020, 0.143	0.015	-0.039, 0.112	1208
Maternal Education	0.097	0.037, 0.162	0.432	0.224, 1.053	1145
Single	0.087	0.023, 0.148	0.012	-0.042, 0.112	1266
Employed	0.087	0.027, 0.146	0.111	-0.023, 0.398	1267
Maternal Leave	0.081	0.012, 0.150	0.000	-0.040, 0.065	1033
Subjective Financial Difficulty	0.087	0.028, 0.148	-0.009	-0.117, 0.069	1266
Neighborhood Deprivation	0.089	0.030, 0.152	0.089	-0.003, 0.323	1262
Receipt of Governmental Benefits	0.087	0.025, 0.144	0.174	0.031, 0.532	1265

Table S6. Association estimates in East Asian subsample.

Outcome	Controls	Association	95% CI	N
SES Composite	10 PCs & Age	0.050	0.008, 0.091	2196
Health Composite	10 PCs & Age	-0.035	-0.078, 0.007	2196
EYFSP	10 PCs, Age, and Child PGS	0.007	-0.049, 0.063	1852
KS1	10 PCs, Age, and Child PGS	0.023	-0.039, 0.085	1473

Figure S1. Principle components plots for polygenic scores in genetic sample.

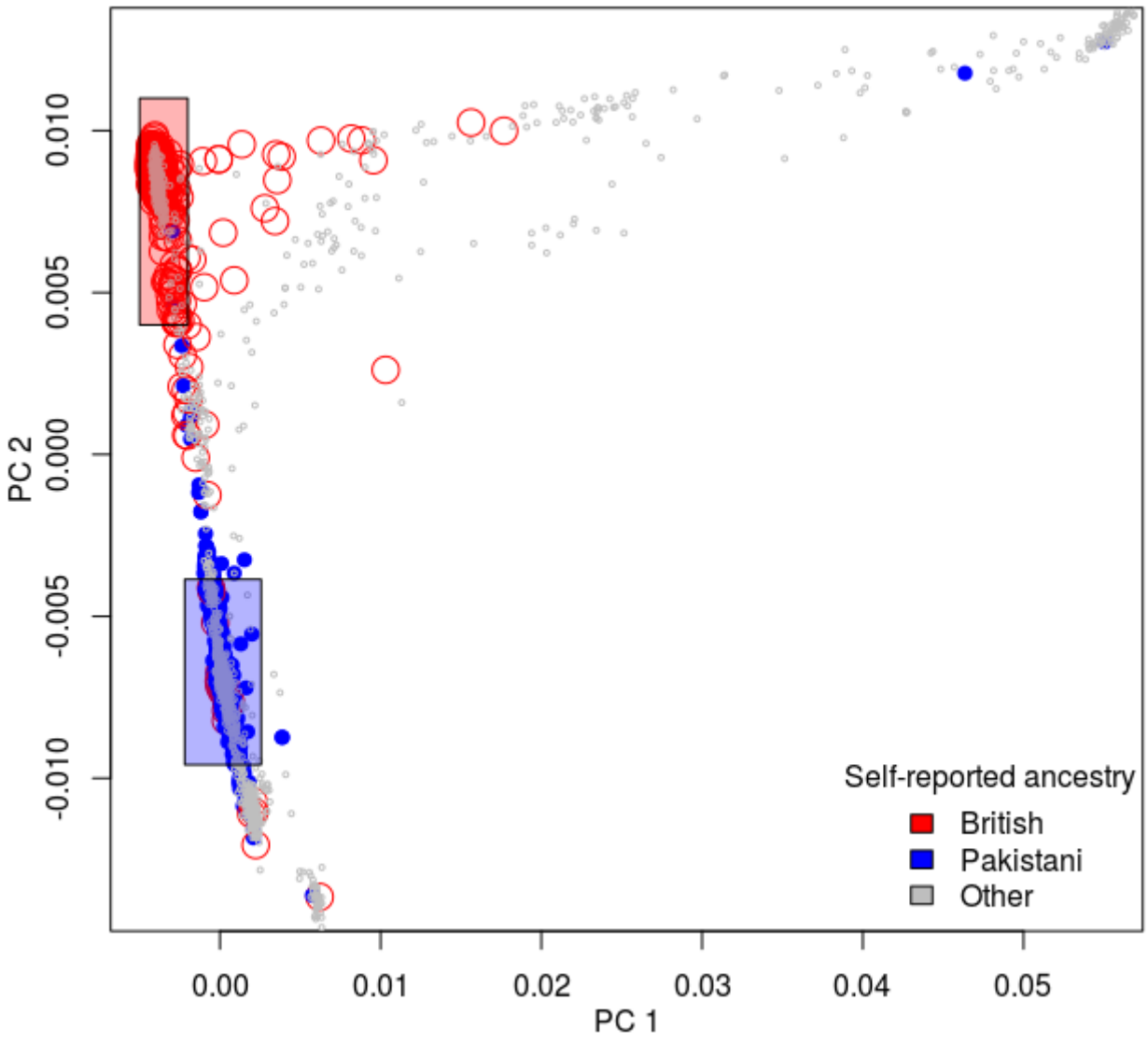

Figure S2. Histograms of (top row) children's development and academic performance and (bottom row) prenatal health and SES composites.

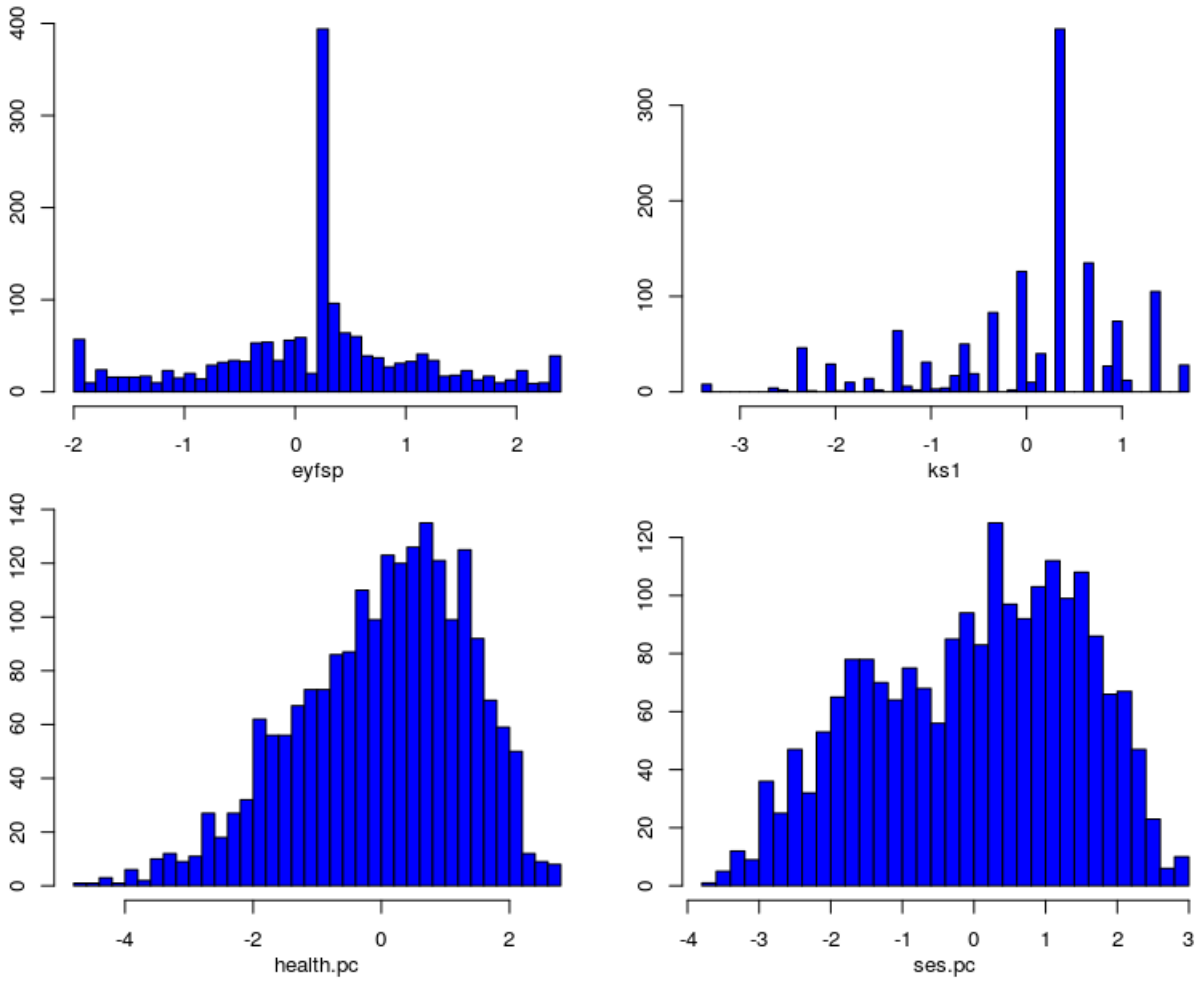

Figure S3. Correlations between key study variables.

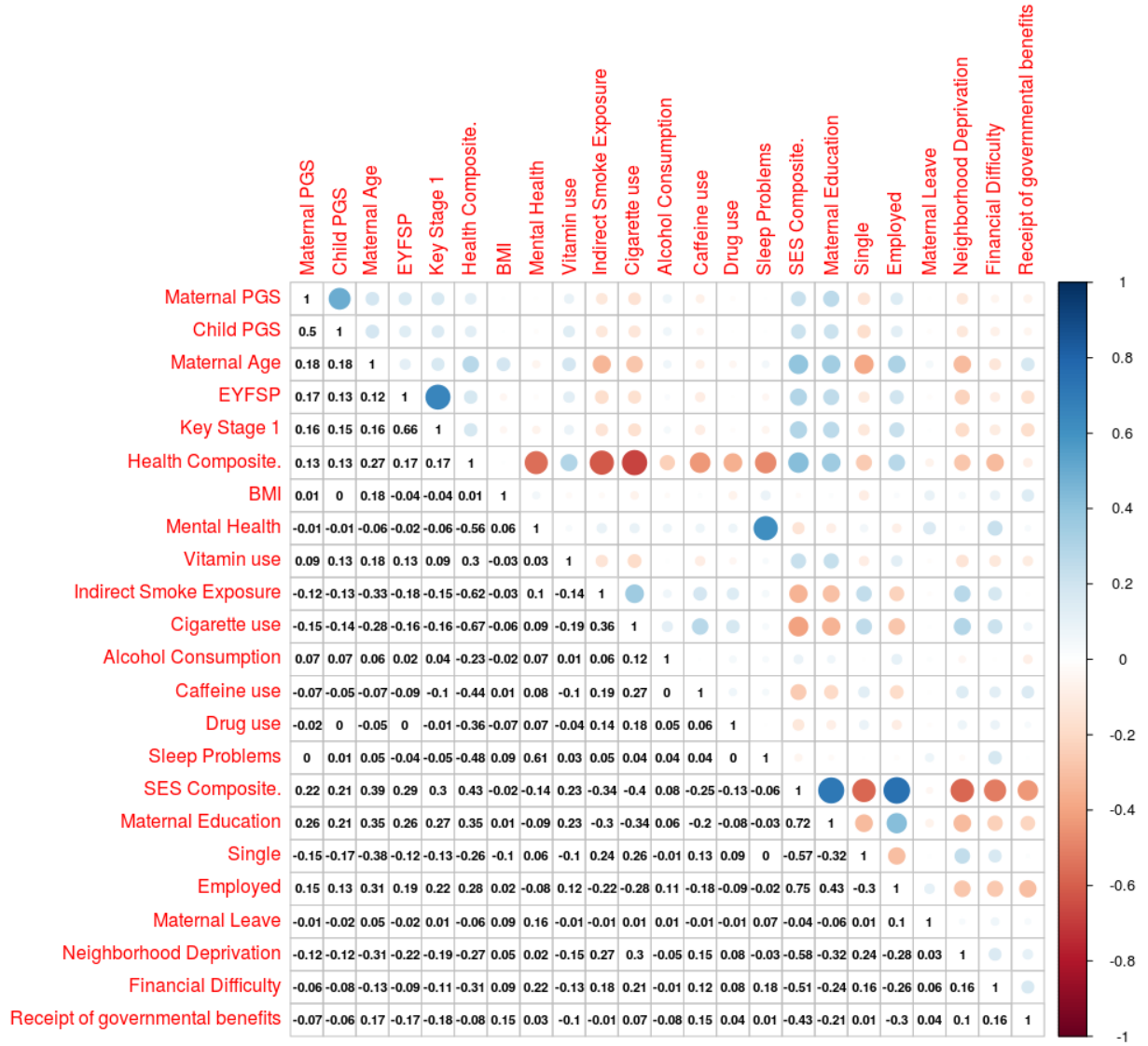

Figure S4. Power Analysis

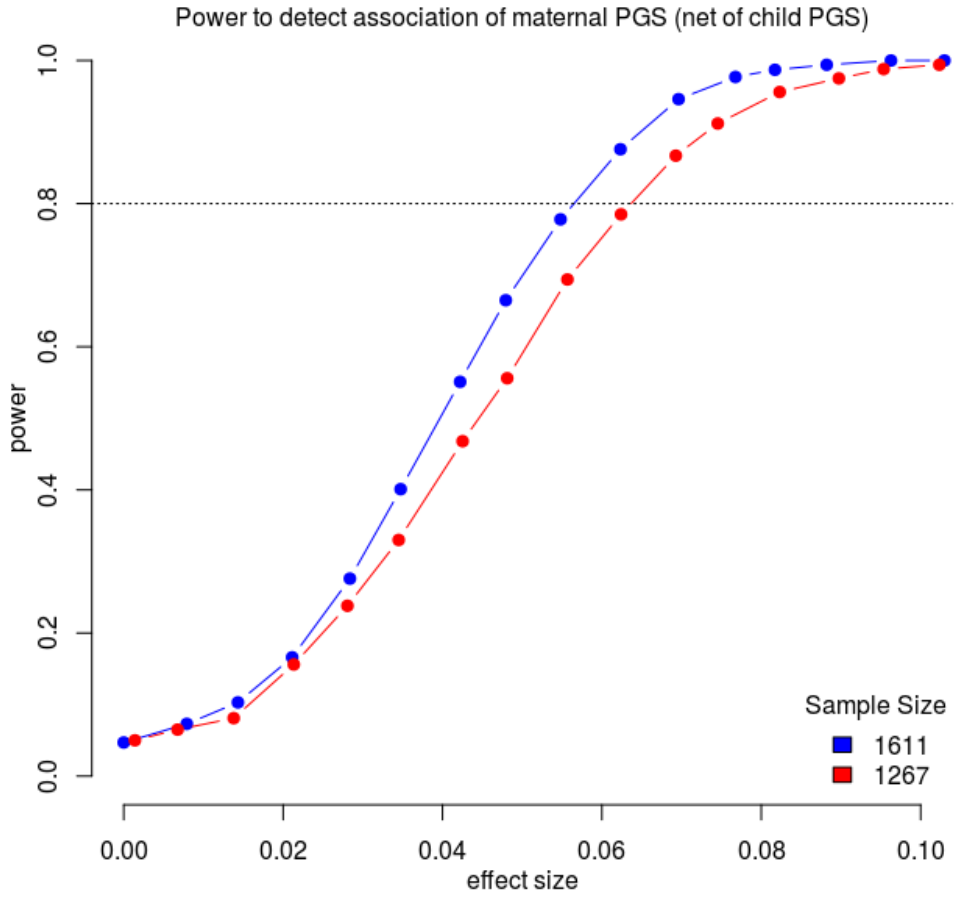

Figure S5. Mean polygenic scores as a function of level of maternal education.