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

FAQ

This FAQ provides information about "The Earliest Origins of Genetic Nurture: Prenatal Environment Mediates the Association Between Maternal Genetics and Child Development," a peer-reviewed journal article published in *Psychological Science*.

The context for our work

The standard approach for identifying regions of the genome that are associated with a given trait is known as a genome-wide association study (GWAS). GWAS approaches have been used to study both biomedical traits (e.g., height, body mass index, cardiovascular risk) and social traits (e.g., subjective well-being, cognitive ability, reproductive behavior). Several GWAS have been performed examining the genetic correlates of educational attainment (if you are unfamiliar with these GWAS, the FAQ for the most recent one would be a good place to start). One of the key insights from the past decade of GWAS is that most biomedical and social traits have a great number of genetic correlates scattered across the entire genome (i.e., these traits are *polygenic*). Educational attainment is no exception; researchers have used GWAS to identify a great number of locations in the genome that each have very small associations with years of schooling.

Naturally, researchers are interested in following up on GWAS results to better understand the mechanisms through which the identified genes come to be associated with various traits. However, studying each of these genetic variants individually would be impractical given their sheer quantity. One solution for studying traits which are influenced by many genes simultaneously has been to use "polygenic scores". As described in detail here, a polygenic score is a cumulative measure that summarizes information from across the genome into a single number. Such scores utilize millions of genetic variants that individually have tiny associations with the trait of interest but together account for a larger amount of variation. An individual's polygenic score conveys our best guess of an individual's genetic liability for some trait, but this best guess is not perfect. While the latest polygenic score for educational attainment predicts an individual's educational attainment at a level comparable to that of non-genetic predictors such as family income or the educational attainment of a parent (see Figure 4 here), it explains only a fraction of all genetic influences on educational attainment (see the discussion around Figure 3 here on this point). Nonetheless, polygenic scores meant to predict educational attainment have now been used in a variety of studies designed to further inform us about sociobehavioral processes related to educational attainment (that literature is discussed at length here).

Recently, researchers have identified a curious property of the polygenic score for educational attainment. The polygenic score that a mother has tends to predict how far her child goes in school even after we account for the genetics that the mother has transmitted directly to her child (Kong et al., 2018; Bates et al., 2018). This seems to be accounted for by the fact that an individual's genes influence the manner in which they act as parents; their parenting behaviors may then have effects on the educational outcomes of their children. For example, parental genetics for educational attainment have been associated with warm, stimulating parenting, which partially explained the positive association between parental genetics and offspring's educational attainment at age 18 (Wertz et al., 2019). This phenomenon has been termed "genetic nurture" (Kong et al., 2018). Research on genetic nurture has revealed that there is substantial "tangling" of genetic and environmental influences. A child's genes are inherited from his or her parents, and at the same time parental genes influence a child's rearing environment. This creates correlations between a child's genes and their rearing environment, complicating efforts to separate genetic and environmental influences.

In this study, we examine the first rearing environment that a child experiences: the environment in utero. The prenatal environment has been the subject of many scientific investigations and is known to be associated with subsequent health and development (Piccolo et al., 2018). The main question that we ask in this study is whether the maternal polygenic score designed to predict educational attainment is also associated with salient features of maternal health and behavior during pregnancy. Moreover, we test whether maternal behaviors during pregnancy can explain why children born to mothers with higher education polygenic scores tend to go further in their education.

What did we do?

In this study, we use information on (a) the genetics of mother and child and (b) features of the prenatal environment to study (c) development of the child when they start school. There are few studies that contain such data. We use data from the Born in Bradford study (BiB). This study is based in Bradford, in the United Kingdom. Pregnant women from 2007-2010 were enrolled in the study. During pregnancy, information on the mother's socio-economic status (e.g., neighborhood resources, maternal leave, family financial resources) and health behaviors (e.g., smoking behaviors, caffeine and drug use) were collected. Genotypes of both mother and any subsequent children were also derived from biospecimens taken during the study. Children of BiB mothers were followed-up when they enrolled in school. When these children were 4-5 years old, BiB collected a measure of child development based on national, standardized observational teacher reports (the Early Years Foundation Stage Profile). These reports ask about a child's progress in a range of domains (Early Learning Goals) that include both academic and personal development and check whether the child is showing the expected level of development for their age in these areas. When they were 6-7 years old, BIB collected a direct measure of academic performance based on national standardized exams (the Key Stage 1 Assessments).

What did we find?

We report three main findings.

1. Maternal polygenic scores are associated with maternal health and socioeconomic status during pregnancy. Mothers with higher polygenic scores for educational attainment had both better health and higher socioeconomic status during pregnancy. These findings are consistent with observations made in other studies of non-pregnant individuals (see, for example, this study on socioeconomic outcomes).
2. Maternal polygenic scores predicted their child's development and academic performance even after controlling for the child's polygenic score (i.e., directly transmitted genetics from mother to child). When they were 4-7 years of age, children of mothers with higher polygenic scores had higher scores on the child development and academic performance measures. Although children of mothers with higher polygenic scores tended to themselves have higher polygenic scores, the associations remained after accounting for the child's own polygenic score. These results suggest the presence of "genetic nurture" at far younger ages than have been observed in other studies (which have focused on older children, adolescents, or young adults).
3. Prenatal environmental exposures mediate nearly 1/3 of the association between maternal polygenic scores and the early outcomes reported in finding #2. The observed association between the maternal polygenic score for educational attainment and the child outcomes can be explained in part by environmental and behavioral differences—specifically, mothers with higher PGS tend to be more affluent and in higher SES surroundings and to generally have better health—experienced by the mothers during pregnancy. This association is incompletely mediated by these measures, however.

What does this study not mean?

Polygenic scores are NOT a measure of a child's "innate" or "inborn" potential to succeed in school. This study does not mean that children who have higher polygenic scores are innately "smarter" or "better" at school. It is not possible to accurately predict someone's education based on their genes. Rather, on a population level, polygenic scores are one tool that can be useful for helping researchers learn about individual differences in educational attainment, with small to moderate effect sizes (Morris et al., 2019).

What are its limitations?

As with any scientific study, ours has limitations. A central one is that our results are based on the respondents in the Born in Bradford Cohort that are of European ancestry. We restrict our analysis to this homogenous population for technical reasons described elsewhere (see, for example, the section entitled 'Predictable basis of disparities in PRS accuracy' in this paper). This limitation has scientific implications—we lack the capacity to study the Bradford residents of South Asian ancestry in the same manner, and our results may not generalize to this or other groups. It also speaks to the need for improvements in the data and techniques used in such studies such that analysis can take place in more heterogeneous groups. Even within a single ancestry group, the prediction accuracy of polygenic scores varies by specific demographic

characteristics of the individuals in which the GWAS was made, such as the age or sex distributions (Mostafavi et al., 2020).