The Economics and Econometrics of Gene-Environment Interplay

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Frequently Asked Questions

This FAQ provides information about "The Economics and Econometrics of Gene-Environment Interplay," a scientific paper published in *The Review of Economic Studies*. The FAQ may change in response to feedback from the scholarly community, journalists, and members of the public. Questions and comments about the paper or this FAQ can be sent to Hans van Kippersluis at hvankippersluis@ese.eur.nl.

What is Gene-Environment interplay?

It is very well established that both genes (or more accurately genetic variants) as well as the environment (think about which country, city, neighborhood you grew up in; your upbringing from your parents, etc.) play a role in virtually all individual outcomes and behaviors. What is less well known is how genes and the environment jointly shape our outcomes: Do people with a certain genetic "predisposition" thrive in specific environments? Can certain environments compensate for a genetic disadvantage? Are individuals who are genetically "predisposed" to some trait more likely to grow up in different environments (for example, through choosing to move)?

The joint role of genes, environments, and their interaction in shaping lifetime outcomes is what constitutes gene-environment interplay. Our research above has focused on the role of gene-environment interactions (GxE): whether environments protect or exacerbate genetic effects, or vice versa, whether one's genetic variation increases or reduces the impact of the environment.

Why is it interesting to study Gene-Environment interplay?

Gene–Environment interplay is relevant for several reasons that go beyond genetics. It can deepen scientific understanding and inform the public debate around policies and interventions. In particular:

- **Advancing basic science**: Gene-environment interplay studies may advance basic science by improving our understanding of the role of nature and nurture in shaping human lives. This knowledge contributes to foundational science with potential long-term relevance.
- **Understanding treatment effect heterogeneity**: When social scientists study the effect of a treatment (like an educational reform), they are often interested in whether it has different effects on different kinds of people. For example, depending on the goals of policymakers, it may be important to understand whether a policy has bigger effects on people with more or less social advantage. In our context, people with different genetic profiles may respond differently to the same environmental exposure. GxE research can help identify who benefits most (or least) from specific policies or interventions, and which interventions increase or reduce the influence of genetic factors.
- **Clarifying moral intuitions about inequality**: People often view inequalities arising from genetics differently than those due to early-life environments (e.g., Sandel, 2020; Harden, 2021). Some consider genetic gradients a signal of meritocracy (e.g., Rimfeld et al., 2018); others view genetic differences as another layer of inequality of opportunity, since genes are unchosen and unearned (e.g., Harden, 2021; Kweon et al., 2020). GxE studies help identify whether policies mitigate or amplify genetic differences, informing debates about fairness and meritocracy.
- **Testing economic theory:** Economic theories of skill formation often assume that abilities and endowments are complements with parental investments (e.g., Ben-Porath, 1967; Becker and Tomes, 1986; Cunha and Heckman, 2007). Since endowments and abilities are typically hard to measure, testing such predictions can be challenging. Observable genetic variation – especially random variation within families – offers a new and powerful way to measure such characteristics, and test theoretical predictions.
- **Identifying mechanisms:** G×E evidence can help uncover how genetic predispositions influence outcomes—e.g., through self-esteem, teacher interactions, or financial decision-making—providing insights into behavioral or economic pathways. For example, access to defined benefit pension plans can weaken the link between genetic predispositions and household wealth (Barth et al., 2020), suggesting that genetics influences wealth not only via earnings and savings, but also through financial decision-making and portfolio choice.
- **Potential for personalized decision-making**. While *institutional* use of genetic data raises substantial ethical and practical concerns, well-identified G×E results may inform *household-level* decisions, such as which medical treatment to pursue or when to start school. Genetic data are already used in medicine for diagnostic and

treatment purposes. Their application in social and economic domains remains more controversial due to cost, privacy and ethical issues (Meyer et al., 2023). Moreover, the currently limited predictive power of composite measures of genetic variants, so-called polygenic scores/polygenic indices (Morris et al., 2020; Turley et al., 2021), limit their usefulness for individual-level recommendations. Even if enthusiasm for such applications may be premature—and institutional adoption unlikely and arguably unwanted—well-identified G×E studies remain essential for evaluating their long-run viability in household-level decision making. Depending on preferences and constraints, there might be a future where households on the margin use genetic information as one input among many in selecting suitable environments for their children.

I'm new to GxE research. How can this paper help me get started?

This paper provides both conceptual guidance and practical tools for researchers interested in studying gene–environment interplay in the social sciences.

- **Conceptual overview**: We introduce key definitions of the essential components of G×E research—such as genetic variants, alleles, polygenic indices, quasi-exogenous variation—and explain common sources of bias in the estimation of gene-environment interactions—such as assortative mating, dynastic effects, and measurement error in polygenic indices. We also discuss how to interpret G×E estimates and the conditions under which they can be interpreted using a causal framework.
- **Framework for empirical design**: We present a typology of study designs, based on whether genetic and environmental variables are exogenous or endogenous. This classification (summarized in Table 1) helps researchers evaluate the credibility of G×E estimates and understand trade-offs in different empirical strategies.
- **Practical checklist for applied work**: Appendix E includes a practical checklist for conducting G×E research, covering topics such as power calculations, the construction and interpretation of polygenic indices, choice of environmental variables, identification strategies, and reporting standards. This is intended as a resource for researchers planning new studies or reviewing existing work.
- **Illustrative application**: The paper includes a worked example based on school-starting age in the UK, showing how quasi-random environmental variation and genetic data can be combined to study treatment effect heterogeneity.

Together, these components make the paper a useful entry point for economists and social scientists who are new to G×E research and seek methodological orientation.

What makes it difficult to study Gene-Environment interactions?

Studying G×E is challenging due to the complex ways in which genes and environments are related. Key difficulties include:

- **Genes and environments are not independent:** Individuals do not inherit genes and environments independently. For example, parents who enjoy reading may pass on both genetic variants related to language ability and a home filled with books. This creates gene–environment correlation (rGE), making it hard to understand whether observed associations between genes and outcome are driven by causal genetic effects, environmental effects, or both.
- **Gene–environment correlation can take many forms:** A child's genetic traits can influence the environments they are exposed to—either by actively seeking certain settings (active rGE) or by eliciting responses from others (evocative rGE). Additionally, environments may reflect parental traits that are themselves genetically influenced (passive rGE). For example, a child who has a genetic predisposition for being introvert may actively seek a quieter environment, might be differentially treated by peers and parents, and might come from an introvert household. These correlations can complicate the interpretation of G×E interactions.
- **Identifying causal G×E effects requires quasi-random variation in both genes and environments**: What we call "the ideal experiment" for studying G×E would combine random genetic variation (e.g., from Mendelian segregation within families) with exogenous variation in environments (e.g., from natural experiments or policy changes). Such designs are rare, and failing to meet these conditions can lead to biased estimates of GxE interaction.
- **Measurement challenges**: The most common way of measuring genetic differences is to create polygenic indices, which are noisy proxies for genetic propensities and have limited predictive power. Measurement error in such indices can attenuate estimated effects, particularly in within-family designs.
- **Data requirements**: Studying G×E credibly often requires family-based genetic data (e.g., parents-offspring or sibling pairs) linked to high-quality environmental measures and longitudinal outcomes. Such data remain scarce, especially outside of European-ancestry populations.

How did you measure genes?

All humans are identical in over 99% of their DNA. Yet, at specific loci in the DNA there is variation across humans. The most common type of variation is called a Single Nucleotide Polymorphism (SNP, pronounced "snip"), which is a one-letter variation at a specific point in DNA. The variant (allele) that is less common in the population is called the minor allele. Since one inherits two copies of each chromosome (one from the father, one from the mother), one can inherit 0, 1 or 2 copies of the minor allele. What researchers have done is to link these allele frequencies (0, 1 or 2) of a specific genetic variant to educational attainment. Basically, one compares the average years of education for someone with 0, 1 or 2 minor alleles at a specific SNP to obtain a regression coefficient (weight) for that SNP. Since the predictive power of a single SNP is tiny, researchers aggregate the tiny SNP effects of all available SNPs into an additive index: the sum of each SNP multiplied by their weights. This is called a polygenic index, also referred to as polygenic score, or polygenic risk score.

It is this polygenic index that we use in our analysis to measure "genetic endowment" or "genetic predisposition". It should be interpreted as the best linear genetic predictor of educational attainment. An excellent blog post by Paige Harden and Dan Belsky gives further information on the interpretation of polygenic indexes.

Which (quasi-)random variation in genes and environments is used in this study?

Regarding **genes**, random variation is ensured by exploiting Mendel's Law stating that children randomly inherit one allele from each parent. This means that children's genetic variants are random *conditional* on the genes of the parents. The data that we use in this study contain genetic information on both parents and children, providing us with random variation in the child's genetic variants.

For the **environment**, we exploit the UK school starting-age policy, which creates quasi-random variation in children's age at school entry. Children begin school in the school year in which they turn five. As a result, a child born on August 31 starts school at age 4 years and 1 day, while a child born just one day later, on September 1, starts at age 5. These children differ by nearly a full year in age when they enter school, but are otherwise very similar in terms of their genetic, socioeconomic, and demographic characteristics. This cut-off generates a natural experiment: children born in August and before are young-for-grade, while those born in September and later are old-for-grade. The treatment of being old-for-grade represents a multi-faceted change in the educational environment, inducing differences in maturity for grade-level, teacher expectations, peer dynamics, etc.

What are the main empirical findings?

Earlier studies have already established that being old-for-grade leads to better test performance, and that genetic endowments matter too. This study adds to the literature in showing that the effect of being old-for-grade on standardized test scores in school is larger for children with a lower genetic predisposition towards education.

What explains this finding? What is the mechanism?

Our data and empirical analyses do not allow us to conclusively pinpoint the exact mechanisms through which this interaction arises. In the paper we speculate about two plausible explanations:

(i) First, it could be that age-for-grade is associated with certain traits and skills that can substitute for genetic "predisposition". Children with a higher genetic predisposition for education might find schoolwork easier, and may be better able to learn skills on their own. At the same time, those who are old-for-grade may have greater maturity or self-confidence. These traits might allow students who need extra help to better communicate with teachers and peers and thus to more easily get support. Since children with higher a genetic predisposition might need less help to begin with, these advantages of being old-for-grade could disproportionately help children with a lower genetic predisposition.

(ii) Second, the interaction could arise from how teachers target their time and attention in class. Those who are young-for-grade tend to lag behind their older peers. Knowing this, teachers may devote more time and attention to young-for-grade students, regardless of their genetic "predisposition". However, this extra attention from teachers could be more productive in boosting the skills of students with a higher genetic predisposition if teacher attention is complementary with genetic predisposition. Being young-for-grade would then be particularly detrimental for children with a lower genetic predisposition since they benefit less from efforts being made by teachers to help younger students.

We should note that both explanations could be true, and there could be other explanations. This deserves further study.

What are the implications of this study?

Our findings have several implications for research, policy, and household decision-making:

- **Schools can reduce genetic inequalities**: We find that children with a lower genetic "predisposition" for education benefit more from being old-for-grade when looking at performance on standardized tests taken in school. This result is all the more noteworthy because we find the opposite interaction when looking at student skills at the time of school entry. At the very start of the first year of schooling, we find a positive interaction between age-at-test and the polygenic index for education in the production of skills. A reasonable assumption would be that this pattern would continue once students enter school. But we find a striking reversal in this pattern – once in school, being old relative to your peers benefits students with a lower genetic predisposition more than those with a higher predisposition. At the very least, this suggests that the school environment can fundamentally alter relationships between age, genetic endowments, and skill accumulation. Moreover, it suggests that how students move through formal schooling (e.g., whether they are old or young for grade) can significantly moderate the effects of genetic endowments on academic outcomes. Our findings thus provide evidence that the structure of formal schooling can act as an equalizing force, reducing differences that arise from genetic variation.
- **Implications for theories of skill formation**: The results challenge strong complementarities between genetic endowments and environmental inputs. In this setting, being old-for-grade may substitute for genetic advantage during the school years, implying a more nuanced interaction between early endowments and educational environments.
- **Informing household choices**: In education systems that allow some flexibility in school entry timing, genetic information could, in principle, help families make more informed decisions—particularly those near the margin. While it is not clear whether current polygenic indices have sufficient predictive power for individualized guidance, G×E evidence may eventually support such applications.
- **Relevance for personalized policy or interventions:** Although it is unlikely that institutions will tailor schooling based on genetic information in the near term—due to cost, privacy, and ethical concerns (Meyer et al., 2023)—G×E research remains essential for evaluating whether such personalization could ever be feasible or beneficial.

Who are the people in this study, and why does that matter?

Our analysis is based on the Avon Longitudinal Study on Parents and their Children (ALSPAC), a study among parents and their children who were born in the early 1990s in the British Avon region.

Since allele frequencies differ across people from different ancestry, and school policies differ from country to country, our study is most relevant to people from European-ancestry in the UK.

If genetic research is to truly help improve lives, it's important to ensure that its benefits are accessible to all communities. Fortunately, efforts are underway for genetic research to be more inclusive.

What does this study not mean? (draws heavily from Paige Harden's blogpost)

Genetic research has a long history of being misinterpreted and misused to argue that social inequality is inevitable, that social programs designed to improve people's lives are bound to fail, and that some people are "naturally" inferior to other people. **We wholeheartedly reject these claims on both scientific and moral grounds.**

A high or low polygenic index does **not** mean someone is destined to show a particular trait—it's **not** a fortune teller. It's simply one influencing factor, or predictor. For example, high cholesterol increases the risk of a heart attack but doesn't guarantee one, and lifestyle changes can reduce that risk. Likewise, a high polygenic index suggests a slightly higher likelihood of completing more years of education—assuming similar environments as in the original study—but it doesn't determine anyone's future.

Genetic associations with education do not mean that environment doesn't matter, nor that policies to improve education are futile. Just as a genetic predisposition to poor eyesight doesn't make eyeglasses useless, genetics and intervention can coexist. We already know that high-quality early childhood programs can boost education with lasting effects, and nothing in this study challenges those findings.

These associations within a population also tell us nothing about average differences between racial or ethnic groups or why such differences, if they exist, occur. This distinction matters because racist and classist claims of genetic "inferiority" have long been used to justify harmful policies. The current study offers no support for such ideas.

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