SOC10000: Introduction to Sociology

Sociogenomics 2

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Let's review past week's concepts

Which of the following lines up closest with your understanding of heritability (h^2)?

1. It describes how much genes you have inherited from your parents.
2. It quantifies how much of your individual trait (e.g., height) can be explained by your genes.
3. It describes the proportion of variation in a trait (e.g., height) within a population that can be attributed to genetic factors.

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3. The researcher is spouting nonsense. Genes play absolutely no role in IQ, it's all social and environmental factors.
4. IQ differences are a product of the CHRM2 and other genes, but social/environmental factors matter too.

Let's review past week's concepts

What is the goal of a genome-wide association study (GWAS)?

1. To establish the genetic sequence of one's DNA
2. To determine which alleles appear at which SNPs
3. To identify SNPs that matter for a certain outcome (e.g., height)

Genes & Environments

There is (was?) an ongoing debate among sociologists/social scientists:

1. Nature: Genes matter for all outcomes. Even seemingly 'structural' factors (e.g., parental upbringing) are fundamentally genetic, and will have an effect on child's outcomes (e.g., educational levels).
2. Nurture: Genes only determine one's predisposition towards a certain outcome (e.g., education). But genetic effects are easily overwritten by structural factors (e.g., educational policies and school resources). 'Genetic effects' are ultimately just a function of social environments.

Well, which is it?

The case for nature: Education

The role of parental genotype in predicting offspring years of education: evidence for genetic nurture

Emily A. Willoughby[1] · Matt McGue[1] · William G. Iacono[1] · Aldo Rustichini[2] · James J. Lee[1]

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Abstract
Similarities between parent and offspring are widespread in psychology; however, shared genetic variants often confound causal inference for offspring outcomes. A polygenic score (PGS) derived from genome-wide association studies (GWAS) can be used to test for the presence of parental influence that controls for genetic variants shared across generations. We use a PGS for educational attainment (EA3; $N \approx 750$ thousand) to predict offspring years of education in a sample of 2517 twins and both parents. We find that within families, the dizygotic twin with the higher PGS is more likely to attain higher education (unstandardized $\beta = 0.32$; $p < 0.001$). Additionally, however, we find an effect of parental genotype on offspring outcome that is independent of the offspring's own genotype; this raises the variance explained in offspring years of education from 9.3 to 11.1% ($\Delta R^2 = 0.018$, $p < 0.001$). Controlling for parental IQ or socioeconomic status substantially attenuated or eliminated this effect of parental genotype. These findings suggest a role of environmental factors affected by heritable characteristics of the parents in fostering offspring years of education.

The case for nature: Mental Health

How important are parents in the development of child anxiety and depression? A genomic analysis of parent-offspring trios in the Norwegian Mother Father and Child Cohort Study (MoBa)

Rosa Cheesman[1*], Espen Moen Eilertsen[2], Yasmin I. Ahmadzadeh[1], Line C. Gjerde[2,3], Laurie J. Hannigan[4,5], Alexandra Havdahl[2,3,4,5], Alexander I. Young[1,6], Thalia C. Eley[1,7], Pål R. Njølstad[8,9], Per Magnus[10], Ole A. Andreassen[11,12], Eivind Ystrom[2,3,13†] and Tom A. McAdams[1,3†]

Abstract

Results: Parental genetic nurture explained 14% of the variance in depression symptoms at age 8. Subsequent analyses suggested that maternal anxiety and depression partially mediated this effect. The genetic nurture effect was mirrored by the finding of family environmental influence in our pedigree model. In contrast, variance in anxiety symptoms was not significantly influenced by common genetic variation in children or parents, despite a moderate pedigree heritability.

Conclusions: Genomic methods like RDR represent new opportunities for genetically sensitive family research on complex human traits, which until now has been largely confined to adoption, twin and other pedigree designs. Our results are relevant to debates about the role of parents in the development of anxiety and depression in children, and possibly where to intervene to reduce problems.

Keywords: Genomics, Environment, Genetic nurture, Anxiety, Depression, Children, MoBa

The case for nurture: Education

Heritability of education rises with intergenerational mobility

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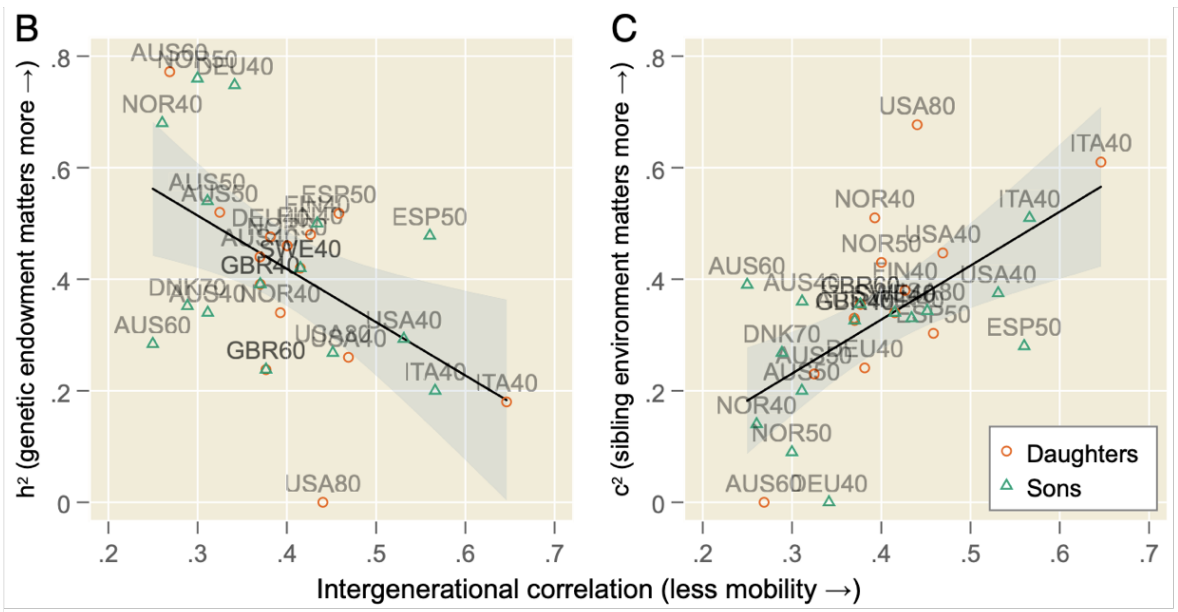

The Nature of Nurture

Today, the general consensus is that outcomes are the product of **both** nature and nurture!

- Many social structures (nurture) are influenced by genes.
- How much one 'lives up' to their genetic potential (nature) depends heavily on social structures.

The Nature of Nurture [Kong et al., 2018]

Quite possibly my favourite sociogenomics paper!

HUMAN GENOMICS

The nature of nurture: Effects of parental genotypes

Augustine Kong,[1,2,3]* Gudmar Thorleifsson,[1] Michael L. Frigge,[1] Bjarni J. Vilhjalmsson,[4,5] Alexander I. Young,[1,2,6] Thorgeir E. Thorgeirsson,[1] Stefania Benonisdottir,[1] Asmundur Oddsson,[1] Bjarni V. Halldorsson,[1] Gisli Masson,[1] Daniel F. Gudbjartsson,[1,3] Agnar Helgason,[1,7] Gyda Bjornsdottir,[1] Unnur Thorsteinsdottir,[1,8] Kari Stefansson[1,8]*

Sequence variants in the parental genomes that are not transmitted to a child (the proband) are often ignored in genetic studies. Here we show that nontransmitted alleles can affect a child through their impacts on the parents and other relatives, a phenomenon we call "genetic nurture." Using results from a meta-analysis of educational attainment, we find that the polygenic score computed for the nontransmitted alleles of 21,637 probands with at least one parent genotyped has an estimated effect on the educational attainment of the proband that is 29.9% ($P = 1.6 \times 10^{-14}$) of that of the transmitted polygenic score. Genetic nurturing effects of this polygenic score extend to other traits. Paternal and maternal polygenic scores have similar effects on educational attainment, but mothers contribute more than fathers to nutrition- and heath-related traits.

The Nature of Nurture [Kong et al., 2018]

Table 1. Decomposition of the observed effect of the polygenic score into direct, genetic nurturing, and confounding effects. Traits: educational attainment (EA), age at first child (AGFC), high-density lipoprotein level (HDL), body mass index (BMI), fasting glucose level (FG), height (HT), cigarettes per day for smokers (CPD), and composite health trait (HLTH). Traits are standardized to have a variance of 1. *N*: number of probands with at least one parent genotyped; N_{NTP}: number with father genotyped; N_{NTM}: number with mother genotyped. $\hat{\theta}_T$ and $\hat{\theta}_{NT}$: estimated effects of the polygenic scores computed for the transmitted and nontransmitted alleles, respectively, when they are analyzed jointly. $\hat{\delta} = (\hat{\theta}_T - \hat{\theta}_{NT})$: estimated direct effect of the polygenic score. R^2: estimated variance accounted for by the transmitted polygenic score, which captures both the direct effect and the genetic nurturing effect. R^2_δ: estimated variance accounted for by the direct effect alone. These fractions of variance explained are for trait values adjusted for sex, yob (year of birth), and PCs. Corresponding values for unadjusted trait values would be somewhat smaller (*13*). $\hat{\phi}_\delta$, $\hat{\eta}$, and $\hat{\phi}_\eta$: estimates, respectively, of the assortative mating–induced confounding effect for the direct effect component, the genetic nurturing effect, and the confounding effect of the genetic nurturing component.

Trait	*N*	N_{NTP}	N_{NTM}	Transmitted T ($T = T_P + T_M$)			Nontransmitted NT ($NT = NT_P + NT_M$)		R^2_δ (%)	$\hat{\delta}/\hat{\theta}_T$	$\hat{\phi}_\delta/\hat{\theta}_T$	$\hat{\eta}/\hat{\theta}_T$	$\hat{\phi}_\eta/\hat{\theta}_T$
				$\hat{\theta}_T$	*P*	R^2 (%)	$\hat{\theta}_{NT}$	*P*					
EA	21637	13948	19012	0.223	1.6×10^{-174}	4.98	0.067	1.6×10^{-14}	2.45	0.701	0.046	0.224	0.029
AGFC	54372	35294	47052	0.108	9.7×10^{-110}	1.17	0.039	2.9×10^{-13}	0.48	0.640	0.052	0.264	0.043
HDL	46872	30855	40788	0.065	9.0×10^{-29}	0.42	0.027	6.0×10^{-6}	0.14	0.586	0.046	0.319	0.050
BMI	39078	26433	34533	−0.060	1.0×10^{-22}	0.36	−0.017	0.0077	0.19	0.718	0.055	0.197	0.030
FG	34767	22959	30222	−0.051	7.6×10^{-18}	0.26	−0.018	0.0059	0.11	0.655	0.052	0.252	0.040
HT	39270	26563	34703	0.052	6.6×10^{-14}	0.28	0.030	1.5×10^{-5}	0.05	0.422	0.031	0.476	0.071
CPD	18887	12371	16589	−0.055	1.4×10^{-12}	0.31	−0.030	5.3×10^{-4}	0.06	0.461	0.035	0.439	0.066
HLTH	62328	41996	54546	0.082	2.7×10^{-60}	0.67	0.033	8.9×10^{-11}	0.23	0.592	0.051	0.305	0.052

Isn't it curious that even non-transmitted genes affect children's outcomes??

The Nature of Nurture [Kong et al., 2018]

Let's have a think: why might non-transmitted genes affect children outcomes? Grab your closest neighbour (or don't)

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Let's have a think: why might non-transmitted genes affect children outcomes? Grab your closest neighbour (or don't)

- Non-transmitted genes might still shape how parents 'behave' around their children
- Even if parents did not transmit their 'smart' genes to their children, they might still nurture children in ways that are genetically influenced
- e.g., Higher aspirations for their children, buying more books, investing more resources into children

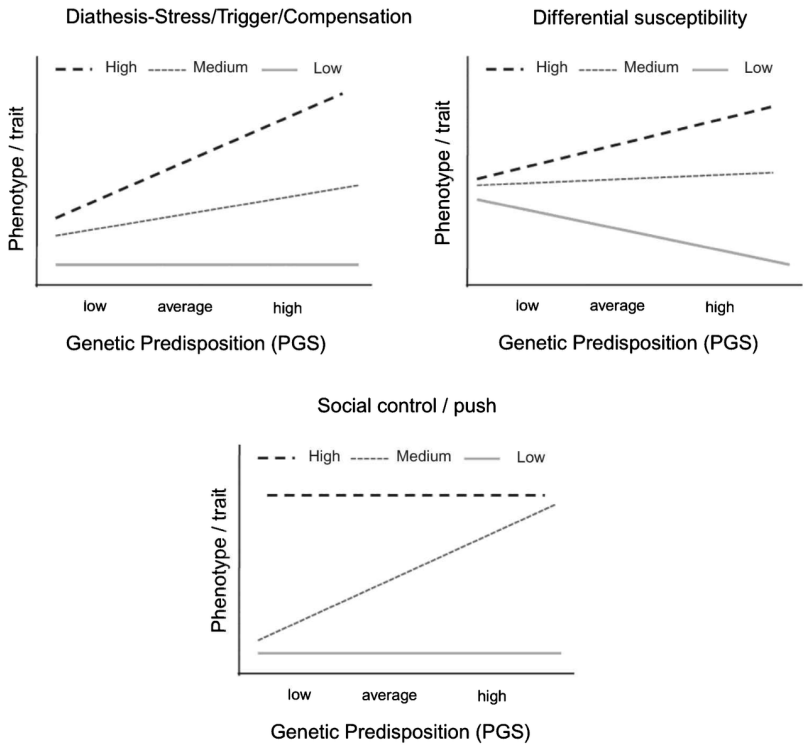
The Nature of Nurture [Kong et al., 2018]

So what are we really saying ?

- It is undeniable that social environments like parental upbringing affect our outcomes
- But even such environments are influenced by genes *not directly related to children outcomes*
- In other words, nurturing effects also have a genetic component to them
- Hence, the **nature of nurture!**

Gene-environment interactions

Genes may exert **differential effects** depending on environments!



Three models commonly discussed:

1. Diathesis-stress
2. Differential susceptibility
3. Social push

Gene-environment correlation (rGE)

Three types of rGE

1. Passive rGE: Children not only inherit genetic material from parents, but also environments related to these genetic dispositions – Kong et al.'s *nature of nurture*
   (e.g., educated parents are more likely to cultivate 'academic environments' for children)
2. Evocative rGE: People tend to 'respond' to individuals and their associated genetic predispositions
   (e.g., parents tend to invest more in children who are 'academically capable')
3. Active rGE: Individuals tend to 'select into' environments that best match their genetic predispositions
   (e.g., individuals tend to qualify and opt into more competitive and resourceful universities)

Gene-environment correlation (rGE)

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Comparison of Adopted and Nonadopted Individuals Reveals Gene–Environment Interplay for Education in the UK Biobank

Rosa Cheesman[1], Avina Hunjan[1,2], Jonathan R. I. Coleman[1,2], Yasmin Ahmadzadeh[1], Robert Plomin[1], Tom A. McAdams[1], Thalia C. Eley[1,2], and Gerome Breen[1,2]

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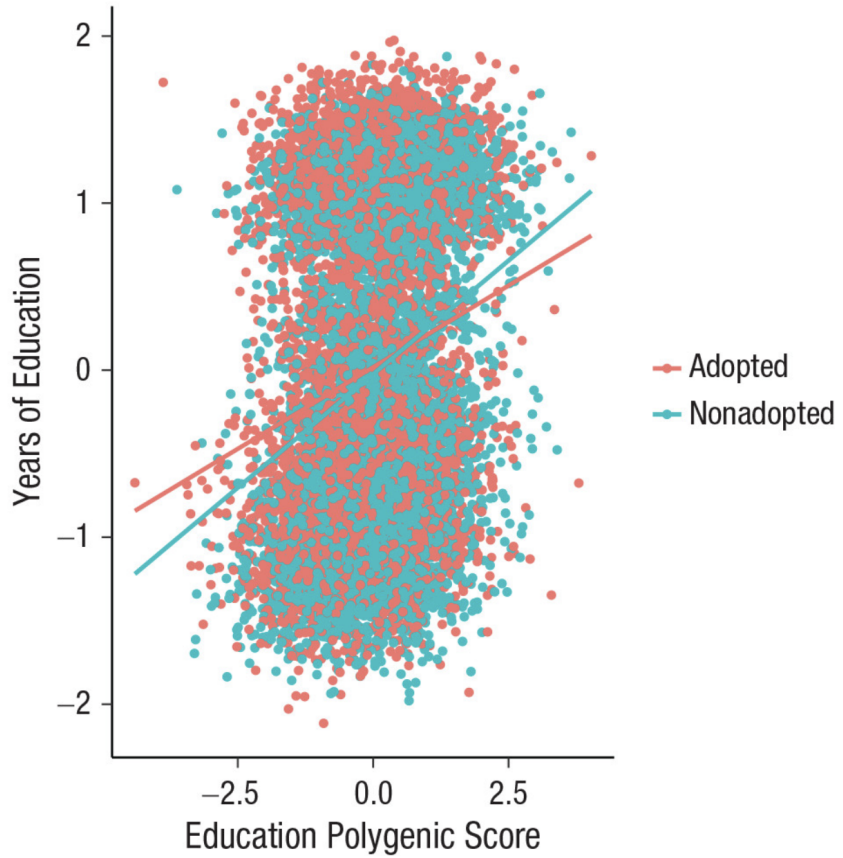
Abstract

Polygenic scores now explain approximately 10% of the variation in educational attainment. Howeve not only genetic propensity but also information about the family environment. This is because of environment correlation, whereby the correlation between offspring and parent genotypes results in between offspring genotypes and the rearing environment. We measured passive gene–environm using information on 6,311 adoptees in the UK Biobank. Adoptees' genotypes were less correlated wi environments because they did not share genes with their adoptive parents. We found that polyger twice as predictive of years of education in nonadopted individuals compared with adoptees (R^2s = .0 8.23×10^{-24}). Individuals in the lowest decile of polygenic scores for education attained significantly mo they were adopted, possibly because of educationally supportive adoptive environments. Overall, these that genetic influences on education are mediated via the home environment.



Interaction vs Correlation

Point of clarification: Difference between GxE and rGE?

- GxE describes how genetic effects are amplified/dampened as a result of environmental factors
  - e.g., Educational outcomes of 'genetically bright' students in **rich vs poor** families
- rGE describes the process by which genes tend to correlate with their environments
  - e.g., Individuals tend to select into environments that best cultivate their genetic dispositions (*active rGE*)
  - e.g., Children tend to 'inherit' environments shaped by their parents (*passive rGE*)
  - e.g., Parents tend to construct environments that align with child's genetic dispositions (*evocative rGE*)

Implications

Much literature revolves around GxE because it is empirically more interesting. rGE is equally important, but often treated as the 'annoying child' in Sociogenomics. Why?

- If environments and genes are correlated, then many empirical claims about 'genetic effects' really contain some degree of environmental effects – (aka environments are endogenous to genetic effects)
- Constrains the range of answerable research questions (like mine).

Implications

Think about why this is problematic:

How do parental educational aspirations for their child interact with children's 'academic predisposition' to affect their educational outcomes? (Parental Aspirations $\times$ Edu PGS)

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- (sigh) time to think of a new research topic
- Orrrrrr... get rid of this endogeneity

How? Easier said than done.

Getting rid of endogeneity

Two ways that I can think of:

1. Random 'shocks' in environments such that they are independent of children genetic effects (instrumental variable)
   - e.g., For instance *maybe* if a mother has suffered a miscarriage before, her aspirations for her child would be independent of his/her academic potential
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2. Within-family designs
   - Environments of sibling 1 and sibling 2 *within any one family* are similar. Therefore any resulting difference are due to genetic effects
   - Robust against passive and evocative rGE – but not active rGE

My head hurts. Let's move on.

Other problems with causal claims

What other 'annoying children' are there in Sociogenomics?

1. Linkage disequilibrium (LD)
   - SNPs that are close together tend to be inherited together from parents (i.e., they are correlated)
   - This means that certain SNPs might still show up in GWAS as 'significant' even though they technically do not predict certain outcomes
   - Solution: LD Score Regression (not included in this lecture, but happy to chat)

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   - Solution: LD Score Regression (not included in this lecture, but happy to chat)
2. Assortative mating
   - People tend to choose partners similar to themselves (e.g., educated folks tend to get together with educated folks)
   - Children are more likely to (1) inherit 'smart' genes; (2) be 'smart'. This falsely inflates the strength of association between genes and educational attainment
   - Solution: Within-family analysis (not included in this lecture, but happy to chat)

Thank you for your attention!

Please feel very free to reach out anytime for any questions, comments, or coffee (preferably tea)!

Email: wang6429@purdue.edu
Github: https://github.com/wesleywj/SOC10000

References I

Kong, A., Thorleifsson, G., Frigge, M. L., Vilhjalmsson, B. J., Young, A. I., Thorgeirsson, T. E., Benonisdottir, S., Oddsson, A., Halldorsson, B. V., Masson, G., Gudbjartsson, D. F., Helgason, A., Bjornsdottir, G., Thorsteinsdottir, U., and Stefansson, K. (2018). The nature of nurture: Effects of parental genotypes. *Science*, 359(6374):424–428.