Research Article

Transpersonal Genetic Effects Among Older U.S. Couples: A Longitudinal Study

Aniruddha Das, PhD*,

Department of Sociology, McGill University, Montreal, Quebec, Canada.

*Address correspondence to: Aniruddha Das, PhD, Department of Sociology, McGill University, Room 712, Leacock Building, 855 Sherbrooke Street West, Montreal, Quebec H3A 2T7, Canada. E-mail: aniruddha.das@mcgill.ca

Received: July 13, 2019; Editorial Decision Date: November 16, 2019

Decision Editor: Deborah Carr, PhD

Abstract

Background: Emerging social genetics research suggests one's genes may influence not just one's own outcomes but also those of close social alters. Health implications, particularly in late life, remain underexplored. Using combined genetic and survey data, this study examined such transpersonal genetic associations among older U.S. couples.

Method: Data were from married or cohabiting couples in the 2006–2016 waves of the Health and Retirement Study, nationally representative of U.S. adults over 50. Measures included a polygenic score for educational attainment, and self-rated health. Analysis was through parallel process latent growth models.

Results: Women's and men's genetic scores for education had transpersonal linkages with their partner's health. Such associations were solely with life-course variations and not late-life change in outcomes. Moreover, they were indirect, mediated by educational attainment itself. Evidence also emerged for individual-level genetic effects mediated by the partner's education.

Discussion: In addition to the subject-specific linkages emphasized in extant genetics literature, relational contexts involve multiple transpersonal genetic associations. These appear to have consequences for a partner's and one's own health. Life-course theory indicates that a person is never not embedded in such contexts, suggesting that these patterns may be widespread. Research is needed on their implications for the life-course and gene–environment correlation literature.

Keywords: Polygenic, Educational attainment, Dyads, HRS, Self-rated health

Health effects of educational stratification have long been recognized (Crimmins & Saito, 2001; Kitagawa & Hauser, 1973). Recent findings indicate that these influences may partly be rooted in the genetic antecedents of education (Lin et al., 2018; Marioni et al., 2016; Zhu et al., 2018). A less explored possibility is that of “genetic externalities”—influences of one's genes on the health of close social alters. Such effects may exist in any closely linked interpersonal system and may be central to an alter's life trajectory. A growing “gene–environment correlation” (rGE) literature, in particular, suggests a person's genes may be linked to behaviors and dispositions of partners in social interactions (Avinun & Knafo, 2014). These latter traits may,

from the focal person's perspective, also constitute “environments” with potential downstream implications for his/her own health outcomes.

In late life, perhaps the most consequential relationship is with one's spouse or intimate partner (Waite & Das, 2010). Especially if concordance in genetic propensities exists between partners, accurately characterizing externalities as well as individual-level effects requires information on both partners' genetic endowments. The availability of dyadic genetic scores for education in the Health and Retirement Study—nationally representative of U.S. adults over 50—offers an unprecedented opportunity to explore such patterns.

Genetic Antecedents of Education and Dyadic Health Effects

Evidence is accumulating on the genetic roots of educational attainment. Overall, heritability may account for about 40% of the variation across individuals—with substantial variation in estimates across settings (Branigan, McCallum, & Freese, 2013). These effects are best conceptualized as polygenic—reflecting the aggregate influences of many different genes of very small effect. These “common variants” may include single-nucleotide polymorphisms (SNPs) and copy number variants. A recent genome-wide association study (GWAS) of approximately 1.1 million individuals identified 1,271 independent genome-wide significant SNPs (Lee et al., 2018). In the HRS data, the sample-size-weighted mean incremental R^2 for the corresponding polygenic score or PGS was 10.6%. The score used in the present study was based on this GWAS.

Variants of this genetic aggregate display strong “pleiotropy”—seemingly influencing a range of outcomes besides education. In particular, they have been linked to multiple health dimensions—including longevity (Marioni et al., 2016), impaired neurobiological profiles (Lin et al., 2018), Alzheimer’s disease (Zhu et al., 2018), and smoking (Wedow et al., 2018). An established approach to capturing such multidimensional outcomes in surveys is through self-rated health (Singh-Manoux et al., 2006). Accordingly, a recent cross-sectional study links an older version of the HRS polygenic score with this “global” health measure, among white and black participants (Das, 2019).

What is often ignored in the individual-focused human genetics literature is the embeddedness of life trajectories in “convoys” of close social relationships (Antonucci, Birditt, & Ajrouch, 2011). In such closely “linked lives” (Bengtson, Elder, & Putney, 2005), one’s genetically rooted traits may clearly be linked to an alter’s outcomes in addition to one’s own. Moreover, associations with life-course variations in these outcomes may differ from those with late-life change in them. The aging and stress process literature offer multiple frameworks for such divergent influences. First, an “age as leveler” model indicates a closing of between-person gaps in multiple mental and physical health dimensions in later life (House et al., 1994). Mortality selection does not fully explain the pattern. Although the process remains to be fully clarified, proposed mechanisms include universal frailty in old age and equalization of health-relevant resources due to government support to the older adults (Beckett, 2000). An “age as maturity” perspective in social gerontology also suggests elevations in multiple traits that may buffer against stressors and hence possibly enhance health perceptions. These include self-integration, insight, skill, psychosocial propensities, and self-esteem (Mirowsky & Ross, 1992). Both models imply weakening effects of earlier disadvantages with age. Whether the pattern applies to genetic influences—of one’s own genes or those of an alter’s—remains unclear. Such effects, however, may also strengthen with time. Education-related cognitive

capacities or personality traits—and especially socioeconomic resources—may become increasingly important as health challenges mount in late life. A substantial literature on “cumulative disadvantage” suggests an accelerated senescence process among those without such resources (Ferraro & Morton, 2018; Rehnberg, Fors, & Fritzell, 2019). As explained below, such assets are shared within family systems and especially partnerships, such that their lack can influence all members.

In addition, however, such contexts may involve genetic concordance with one’s alters. “Passive” sharing of transmitted alleles with one’s parents—and, to a lesser extent, siblings and other close relatives—is well recognized (Kong et al., 2018). Concordance may also occur in voluntary ties, not just due to direct phenotypic assortment (active choice of alters with traits similar to oneself) but also through individuals interacting and forming ties according to social or environmental background (Domingue et al., 2018; Robinson et al., 2017). In such situations, accurately identifying genetic externalities requires controlling the alters’ own genes. High data requirements have thus been a major impediment to genetic analysis of interpersonal systems—especially those involving alters who are not consanguineal (blood) kin.

A growing literature on human “social genetics” or “metagenomics” is beginning to examine such patterns. Two non-kin network studies—both based on the National Longitudinal Study of Adolescent to Adult Health (Add Health)—stand out. The first uses data from 5,500 adolescents to demonstrate that polygenic scores of an individual’s friends and schoolmates predict his/her own educational attainment and obesity (Domingue et al., 2018). A second finds that peers’ genetic propensity to smoke predicts one’s own smoking behavior, net of one’s genotype (Sotoudeh et al., 2019). This emerging body of work borrows from a long tradition of social genetics research in animals (Baud et al., 2017; Domingue & Belsky, 2017).

In late life, perhaps the most important locus of genetic externalities is the marriage or intimate partnership. Individuals at these ages experience fundamental changes in the structure of both their families and their broader social network. Children leave home; retirement uproots individuals from their social networks at work; parents and older adults pass away; and health problems begin impeding social interaction. During this period, one’s most health-relevant relationship is with the spouse or partner (Lindau, Laumann, Levinson, & Waite, 2003). In turn, dyadic theory increasingly suggests that couples form “systems” wherein members are critically interdependent in a range of ways. This symbiosis occurs through repeated small exchanges and specialization of roles within the relationship and serves to maximize efficiency and efficacy, thereby becoming self-perpetuating (Waite & Das, 2010). Such interdependency is particularly strong in late life when the process has had time to cumulate and become entrenched. An influential “interactive biopsychosocial model” thus posits an intricate interweaving of older couples’ lives, such

that successful aging becomes a jointly produced outcome, dependent on each partner's characteristics and on the nature of the partnership itself (Lindau et al., 2003).

As with individual-specific genetic effects, externalities may be direct or routed through one's education. Indirect effects seem supported by the large literature on education's influence on health and longevity (Marioni et al., 2016; Zajacova, Hummer, & Rogers, 2012). Such effects may reflect greater knowledge or awareness of health issues—or simply higher socioeconomic resources to buffer against health risks and enable health maintenance. Because these assets are shared between partners, they may influence health outcomes among both. Educational attainment also requires and rewards cognitive ability (Deary et al., 2007) and traits such as conscientiousness, agreeableness, and sense of mastery (Herd, 2010; Shiner et al., 2003; Wedow et al., 2018). Such attributes may conceivably have direct linkages with one's own and a partner's health, via health behaviors. A couple's dietary and physical activity patterns are, for instance, jointly determined (Waite & Das, 2010). Similarly, maintenance of a partner's health given pre-existing health conditions is dependent on one's monitoring and behavioral control (Umberson, 1992), which are in turn contingent on one's own cognitive and personality traits. (It is noted that “direct” and “indirect” are used here per their standard meanings in mediation analysis. In much of the social genetics literature, by contrast, direct genetic effects refer to influences of a focal person's genotype on his/her own traits or outcomes, whereas indirect influences denote those of an alter's genotype on one's phenotype.)

The dyadic context, however, suggests one's genes may also be linked to a partner's health through the *partner's* education. Specifically, under assortative mating (phenotypic similarity between partners), correlations can arise between a person's genes and a partner's traits (Robinson et al., 2017). Such associations may exist net of concordance in genes or family background, potentially reflecting selection into the tie (or the social locus of partnership) due to one's own genetically rooted propensities. As such, they can mediate apparent genetic “effects” of one's genes on the partner's late-life health. Such selection-based paths would not, however, constitute genetic externalities as defined above. Finally, a partner's education may influence one's own downstream health—suggesting a path for apparently individual-level genetic effects that is routed through the relational context.

Accordingly, this study used panel data from eight HRS waves (2006–2016) to address five questions: (a) Is a person's genetic propensity for education associated with a partner's health? (b) Are such linkages mediated by one's own education? (c) Are they mediated by the partner's education? (d) Are there direct genetic effects on a partner's health, after accounting for his/her education? (e) Does a partner's education mediate associations of one's genes with one's own health? Both level and trend effects were examined.

Data

HRS is an ongoing longitudinal survey of the U.S. population, nationally representative of those aged over 50, and conducted every 2 years since 1992. Overall response rate is about 87%. The survey uses multistage sampling of households with an oversample of Blacks and Hispanics (Sonnega et al., 2014). Genetic data collection began with Wave 8 (2006), with sampling at the household level, such that both members of a couple were selected. Accordingly, married or cohabiting couples in that wave comprised the baseline for the present study. Trends in self-rated health among members of these dyads were followed from that point through Wave 13 (2016).

HRS genetic principal components, crucial to the polygenic analyses, are specific to African or European ancestry groups (see below). The longitudinal sample for the former was too small to yield robust results: lack of significant associations could have been due to low statistical power rather than absent empirical linkages. Moreover, SNP weights for the educational attainment PGS were derived from an external GWAS of European ancestry individuals, such that the score may not have the same predictive power among other groups (Ware et al., 2018). Accordingly, analysis was restricted to couples with genetic data in which both members were white (comprising 90.0% of all such dyads). The original race measure in the survey was a self-assessment. Respondents were able to identify themselves as part of more than one racial category. Those who indicated multiple races were asked, “Do you consider yourself primarily (first mention, second mention, etc.)?” This “primary” race was then used as the identification. In a second stage, the HRS team used principal component analysis (PCA) of genome-wide SNP data to more deeply investigate population structure. For several of the subjects for whom self-identified race (black or white) strongly contrasted with the PCA results, the self-assessment was corrected after review by the HRS group (Health and Retirement Study, 2012). To minimize population stratification (see below), the present study used this corrected identification.

To optimize statistical power, subjects aged 50 and younger in the 2006 wave were retained in the analysis. These were partners of age-eligible (over 50) HRS participants. About 14% of white dyads had such members. Finally, 24 couples (0.40% of all 2006 white dyads) were of the same sex. For analytic simplicity, they were excluded—the sole deletions from the baseline sample. The remaining sample comprised 11,860 older white adults in 5,930 dyads. Estimation was through a robust weighted least squares approach that maximized observed data retention while simultaneously maintaining population representativeness.

Measures

All variables below were partner-specific. [Supplementary Table S1](#) shows summary statistics. Health perceptions

were assessed over six successive HRS waves (2006–2016). All other variables were at baseline (2006).

Self-rated Health

The HRS measure for *worse self-rated health* was a five-category Likert item, ranging from 1 (“excellent”) to 5 (“poor”).

Polygenic Scores

As with all genetic scores in HRS, the *educational attainment* PGS was standardized within ancestry group. It ranged from –3.21 to 3.25 among women and –3.25 to 3.37 among men, with higher scores denoting a greater genetic propensity for education.

DNA data collection in HRS were through the Oragene DNA Collection Kit (Ware et al., 2018). Genotyping was conducted by the Center for Inherited Disease Research in 2011, 2012, and 2015. Construction of genetic measures followed current best practices. For each phenotype, the polygenic score was based on a replicated and externally validated GWAS. Scores were calculated using the PRSice and PLINK software packages. As noted, SNP weights for the education PGS came from a 2018 study by the Social Science Genetic Association Consortium (Lee et al., 2018). The meta-analysis included 405,073 individuals in the discovery sample and 726,808 in the replication group. Genome-wide significant SNPs were identified in 1,271 loci. The corresponding European ancestry score used in this study contained 1,274,056 SNPs that overlapped between the HRS genetic database and the GWAS meta-analysis. To clarify, the original GWAS included the HRS. To compute PGSs for HRS participants, the SSGAC provided SNP weights with HRS and 23andMe results removed (due to data use agreements; Ware et al., 2018). As such, estimates do not fully align with the Lee and colleagues’ (2018) publication.

Educational Attainment

A participant’s self-reported *educational attainment* was capped at 17 years of schooling.

Control Variables

Adjustments were made only for factors likely not to be “post-treatment” (Pearl, 2009). In other words, those that could have been influenced by the genetic scores—or potentially on causal pathways from education to current self-rated health—were left out. This included life-course or recent experiences, and diagnosed health conditions.

Among viable controls, *age* at baseline (2006) was entered linearly as a continuous variable. *Father’s* and *mother’s education* were, as with a participant’s own,

capped at 17 years of schooling. An additional dichotomous item indexed *foreign* (non-U.S.) *birth*. Finally, population stratification—systematic differentials in allele frequencies across subgroups due to distinct histories—is a known confounder of gene–trait associations (Conley, 2016). To adjust for this factor, models included 10 HRS-provided and ancestry-group-specific *genetic principal components* for each partner (Ware et al., 2018).

Analytic Strategy

Analysis was through parallel process latent growth models that simultaneously incorporated both partners’ attributes. In the measurement part of each model, women’s and men’s growth factors were linked to the Likert scales of self-reported health through ordered probit models. As in any growth analysis, each partner’s intercept growth factor indexed between-person variation in this outcome at baseline (2006) and proxied life-course differentials. The slope growth factor captured within-person change over the study period (through 2016; Bollen & Curren, 2006). In the structural submodel, these continuous latent variables were regressed on covariates of interest through OLS. Across-partner covariances were specified for growth factors to account for additional sources of nonindependence such as family effects (Cook & Kenny, 2005). Two separate sets of analyses were run. Model 1 addressed the first research question, testing baseline associations of a person’s genes with a partner’s health outcomes and one’s own. [Supplementary Figure S1](#) presents a reduced path diagram. Model 2 then added each partner’s educational attainment ([Supplementary Figure S2](#)). In addition to growth factors, covariances between partners’ education were also specified in this analysis. [Figure 1](#) depicts the underlying conceptual logic in simple format. Direct and indirect genetic effects from this second model were then used to address the remaining four research questions.

Figure 1. Simplified illustration of structure of proposed linkages. Thick solid lines represent theoretically important paths. Curved lines denote covariances. In addition to variables shown, the model adjusted each partner’s age at baseline, father’s and mother’s educational attainment, foreign birth, and 10 genetic principal components. Effects on levels (indexed by intercept growth factors) and trends (slope growth factors) in self-rated health were examined.

Over-time attrition presented a selection problem, given the 10-year study period. Initial full-information maximum likelihood (FIML) analysis failed to reach convergence due to the complexity of the model. Instead, as noted, estimation was through a robust weighted least squares estimator. The approach yielded precisely the same sample size as, and handled missingness in a manner similar to, FIML (Asparouhov & Muthén, 2010).

Because all analysis was conducted within the dyadic sample; however, individual-level selection into the 2006 dyadic pool could not be so handled. Specifically, 33.3% of participants (and 31.1% of white respondents) in that wave had no partners. Preliminary investigation indicated that they were likely to be older, less educated, and with more depressive symptoms. Inverse-probability weighting is an increasingly standard solution to such issues. The approach separates the model of substantive interest from the one used to account for missingness. Assumptions underlying the two are therefore not conflated, and model compatibility problems or other types of misspecification are avoided (Sun et al., 2018). Accordingly, individual-level logistic regression was first used to fit predictive models of partnership among all 2006 participants. Covariates included participants' demographic and health attributes—age, gender, race, education, a count of diagnosed health conditions, and depressive symptoms. Based on predicted probabilities from these analyses, stabilized inverse-probability weights (IPWs) were created. The same approach was used to generate weights for individual-level genetic data missingness (39.4% overall, 29.5% among white respondents)—for which selection issues have already been reported (Domingue et al., 2017).

Growth models were then weighted by the cumulative product of the female and the male partner's IPWs, and HRS-provided household-level cross-sectional weights. The first two components ensured that individuals with a lower likelihood of selection into the 2006 dyadic pool and/or of providing genetic data were assigned larger weights, "compensating" for their under-representation in the analytic sample. In turn, the household weights ensured baseline generalizability to all U.S. households containing at least one person in the age-eligible range and included a nonresponse adjustment based on age, gender, race/ethnicity, and geography. The American Community Survey and the Current Population Survey were used for poststratification correction (Ofstedal, Weir, Chen, & Wagner, 2011). SE were adjusted for sample stratification (sampling strata independently) and clustering (sampling households within primary sampling units).

Results

Given the range of estimates, the focus below is on those important for pattern inference. All coefficients are standardized. To condense exposition, growth factor covariances are shown

in [Supplementary Material](#), for Model 1 ([Supplementary Table S2](#)) and Model 2 ([Supplementary Table S3](#)).

Model 1: Genetic Associations With Self-rated Health

First stage analysis did not suggest any individual-level genetic associations with late-life change in health ([Table 1](#)). For instance, the coefficient for effects of women's PGS on their own slope growth factor was 0.07 and not statistically significant. Women's PGS, however, did have a counterintuitive positive linkage with men's slope growth factor (coefficient = 0.10, $p < .05$). Consistent with previous literature, the polygenic score was uniformly associated with baseline between-person variation in one's own worse health. This was true among women (coefficient = -0.11 , $p < .001$) and men (coefficient = -0.11 , $p < .01$). In keeping with conceptions of genetic externalities above, women's (coefficient = -0.08 , $p < .001$) and men's (coefficient = -0.05 , $p < .05$) PGS also seemed linked to a *partner's* intercept growth factor. In other words, the answer to the first study question was affirmative: these genetic aggregates apparently did have transpersonal rather than just subject-specific associations.

Model 2: Additive Model With Genes and Educational Attainment

As noted, the second analytic stage added partners' educational attainment to the model ([Table 2](#)). Results for slope growth factors were uniformly null—except for a counterintuitive positive linkage between women's educational attainment and their own health change (coefficient = 0.12, $p < .05$). Genetic associations with intercept growth factors were patterned differently than in Model 1: only women's PGS retained a direct association with their baseline worse health (coefficient = -0.07 , $p < .05$). Unsurprisingly, educational attainment had strong individual-specific linkages with this outcome—among women (coefficient = -0.11 , $p < .001$) and men (coefficient = -0.26 , $p < .001$). Moreover, it was also associated with a partner's intercept growth factor, among both women (coefficient = -0.10 , $p < .01$) and men (coefficient = -0.23 , $p < .001$).

In the education submodel, consistent with previous GWAS, individual-specific PGS effects were found among women (coefficient = 0.17, $p < .001$) and men (coefficient = 0.15, $p < .001$). Finally, in keeping with selection arguments above, both women's (coefficient = 0.09, $p < .001$) and men's (coefficient = 0.11, $p < .001$) genetic scores were associated with the *partner's* educational attainment.

Direct and Indirect Genetic Effects on Intercept Growth Factors

[Table 3](#) presents mediation results derived from Model 2. As above, the focus is on theoretically important findings

Table 1. Model 1: Dyadic Associations of Polygenic Score for Educational Attainment With Self-rated Health Among Older U.S. Couples: Standardized Coefficients (95% Confidence Intervals)

	Women's worse self-rated health		Men's worse self-rated health	
	Intercept growth factor	Slope growth factor	Intercept growth factor	Slope growth factor
Polygenic scores				
Women's PGS	-0.11*** (-0.16, -0.05)	0.07 (-0.04, 0.17)	-0.08*** (-0.12, -0.04)	0.10* (0.01, 0.19)
Men's PGS	-0.05* (-0.10, 0.00)	0.04 (-0.08, 0.15)	-0.11** (-0.17, -0.04)	0.00 (-0.09, 0.10)
Control variables: women's attributes				
Age	0.04 (-0.07, 0.15)	-0.01 (-0.18, 0.17)	0.01 (-0.09, 0.10)	-0.16** (-0.27, -0.05)
Father's education	-0.08** (-0.13, -0.02)	0.05 (-0.06, 0.16)	-0.01 (-0.07, 0.05)	-0.06 (-0.18, 0.06)
Mother's education	-0.08* (-0.14, -0.01)	-0.08 (-0.18, 0.01)	-0.09** (-0.14, -0.04)	0.04 (-0.05, 0.13)
Foreign birth	-0.01 (-0.05, 0.03)	0.02 (-0.08, 0.12)	-0.06** (-0.10, -0.01)	0.04 (-0.04, 0.13)
Control variables: men's attributes				
Age	0.04 (-0.07, 0.13)	-0.07 (-0.22, 0.08)	0.06 (-0.03, 0.15)	0.16* (0.02, 0.31)
Father's education	-0.15*** (-0.22, -0.09)	0.03 (-0.08, 0.14)	-0.12*** (-0.18, -0.06)	0.13* (0.02, 0.24)
Mother's education	-0.06 (-0.13, 0.00)	0.08 (-0.04, 0.20)	-0.11** (-0.18, -0.04)	-0.03 (-0.16, 0.10)
Foreign birth	0.03 (-0.02, 0.08)	0.00 (-0.09, 0.09)	0.01 (-0.04, 0.06)	-0.04 (-0.13, 0.05)
R ²	0.13***	0.06*	0.13***	0.08**
CFI	1.00			
TLI	.99			
RMSEA	.00			
N	5,930			

Notes: PGS = polygenic score; CFI = comparative fit index; TLI = Tucker–Lewis index; RMSEA = root mean square error of approximation. [Supplementary Figure S1](#) presents a reduced path diagram. In addition to those shown, controls included 10 genetic principal components for each partner. Estimates are from parallel process latent growth models weighted to adjust for differential probabilities of selection and nonresponse. Analysis was restricted to white adults with available genetic data. Figures in bold represent estimates significant at least $p < .05$.

* $p < .05$; ** $p < .01$; *** $p < .001$.

(i.e., those relevant to study questions 2–5). Results suggested the apparent genetic externalities in Model 1 were indirect rather than direct. They were partly mediated by one's own education. Such a pattern held for women's (indirect effect coefficient = -0.02 , $p < .01$) and men's (coefficient = -0.03 , $p < .001$) genetic scores. In part, however, they seemed channeled through the partner's education—a selection-based path that would not meet the definition of genetic externalities proposed above. Such indirect “effects” were found for both women's (coefficient = -0.02 , $p < .001$) and men's PGS (coefficient = -0.01 , $p < .01$). Results also suggested that individual-level genetic effects routed through the relational context. Specifically, women's (coefficient = -0.02 , $p < .001$) and men's (coefficient = -0.01 , $p < .05$) genetic scores were linked to their own baseline health status through the *partner's* education.

Finally, while reweighting through IPWs is now a standard way of handling selection issues ([Perkins et al., 2018](#)), the procedure may conceivably have led to bias in the HRS data. [Supplementary Tables S4–S6](#) present results without such weighting. Only one estimate relevant to the study questions changed: men's PGS no longer had a “total effect” on women's intercept growth factor ([Supplementary Tables S4 and S6](#)).

Discussion

This article began by noting that in closely connected social systems, one's genetically rooted traits may influence not just one's own but also an alter's outcomes. Such “genetic externalities” remain underexplored in the individual-focused genetics literature. Moreover, such influences are substantively distinct from selection-based paths routed

Table 2. Model 2: Additive Associations of Partners' Polygenic Scores and Educational Attainment With Self-rated Health: Standardized Coefficients (95% Confidence Intervals)

	Women		Men	
	Worse self-rated health			
	Intercept growth factor	Slope growth factor	Intercept growth factor	Slope growth factor
Polygenic scores				
Women's PGS	-0.07* (-0.13, -0.01)	0.03 (-0.08, 0.14)	-0.04 (-0.08, 0.00)	0.08 (-0.02, 0.18)
Men's PGS	0.00 (-0.05, 0.04)	0.01 (-0.11, 0.13)	-0.06 (-0.12, 0.01)	-0.05 (-0.14, 0.04)
Educational attainment (years)				
Women	-0.11*** (-0.16, -0.06)	0.12* (0.03, 0.22)	-0.10** (-0.16, -0.04)	-0.05 (-0.16, 0.05)
Men	-0.23*** (-0.28, -0.18)	0.05 (-0.06, 0.16)	-0.26*** (-0.32, -0.21)	0.01 (-0.11, 0.13)
R ²	0.19***	0.07**	0.20***	0.09**
Educational attainment (years)				
Polygenic scores				
Women's PGS	0.17*** (0.14, 0.21)		0.09*** (0.05, 0.13)	
Men's PGS	0.11*** (0.07, 0.15)		0.15*** (0.11, 0.19)	
R ²	0.29***		0.27***	
CFI	1.00			
TLI	1.00			
RMSEA	.01			
N	5,930			

Notes: PGS = polygenic score; CFI = comparative fit index; TLI = Tucker–Lewis index; RMSEA = root mean square error of approximation. [Figure 1](#) depicts the specified structure of linkages. [Supplementary Figure S2](#) presents a reduced path diagram. In addition to estimates shown, control variables were added to both stages of the model—the one regressing growth factors on the PGS and educational attainment, and the submodels regressing educational attainment on the PGS. These included each partner's age, father's and mother's educational attainment, foreign birth, and 10 genetic principal components. These results are presented in [Supplementary Table S7](#). Estimates are from parallel process latent growth models weighted to adjust for differential probabilities of selection and nonresponse. Analysis was restricted to white adults with available genetic data. Figures in bold represent estimates significant at least $p < .05$.

* $p < .05$; ** $p < .01$; *** $p < .001$.

through the alter's traits—paths that may also mediate genetic effects on one's own outcomes. At least with marriage or intimate partnership—perhaps the most important interpersonal context in late life—the availability of genetic data from both members of a couple in the nationally representative HRS provides an opportunity to parse these linkages. Accordingly, this study used six waves of dyadic HRS data to address five study questions: (a) Is a person's genetic propensity for education associated with a partner's health? (b) Are such linkages mediated by one's own education? (c) Are they mediated by the partner's education? (d) Are there direct genetic effects on a partner's health? (e) Does a partner's education mediate associations of one's genes with one's own health?

Per the findings, the answer to the first study question seemed “yes.” Consistent with the externalities argument, women's and men's education PGS had modest associations their partner's health ([Table 1](#)). The latter estimate, however, may possibly have been a false positive because it dropped below significance in sensitivity tests.

In addition, these linkages were with life-course variations rather than late-life changes in outcomes. Put simply, the genetic externalities examined did seem to fade in late life. Indeed, women's genetic scores were linked to *sharper* health declines in their male partners. Absent other plausible mechanisms, such connections are tentatively ascribed to “leveling” of male health differences with age—that is, steeper decline among those with better health at baseline. The interpretation is also supported by the strong negative covariance between men's intercept and slope growth factors (coefficient = -0.58 , $p < .001$; [Supplementary Table S2](#)). These results were net of each partner's family background (their father's and mother's education and nativity). Given model specification ([Figure 1](#)), they were also not artifacts of concordance in partners' polygenic scores (Pearson's $r = .15$, $p < .001$ in separate analysis). Indeed, to the extent such concordance was itself produced by genetically influenced choice, rather than common social or geographic background, partner effects were overadjusted and underestimated.

Table 3. Direct and Indirect Genetic Effects on Intercept Growth Factors Based on Model 2: Standardized Coefficients (95% Confidence Intervals)

	Women's worse self-rated health (intercept growth factor)	Men's worse self-rated health (intercept growth factor)
Effects of women's PGS		
Indirect effects		
Women's PGS → women's education → outcome	-0.02*** (-0.03, -0.01)	-0.02** (-0.03, -0.01)
Women's PGS → men's education → outcome	-0.02*** (-0.03, -0.01)	-0.02*** (-0.04, -0.01)
Total indirect effects	-0.04*** (-0.05, -0.03)	-0.04*** (-0.05, -0.03)
Direct effects of women's PGS	-0.07* (-0.13, -0.01)	-0.04 (-0.08, 0.00)
Total effects of women's PGS	-0.11*** (-0.16, -0.05)	-0.08*** (-0.12, -0.04)
Effects of men's PGS		
Indirect effects		
Men's PGS → women's education → outcome	-0.01** (-0.02, 0.00)	-0.01* (-0.02, 0.00)
Men's PGS → men's education → outcome	-0.03*** (-0.05, -0.02)	-0.04*** (-0.05, -0.03)
Total indirect effects	-0.05*** (-0.06, -0.03)	-0.05*** (-0.07, -0.03)
Direct effects of men's PGS	0.00 (-0.05, 0.04)	-0.06 (-0.12, 0.01)
Total effects of men's PGS	-0.05* (-0.10, 0.00)	-0.10** (-0.17, -0.04)

Notes: PGS = polygenic score. Figures in bold represent estimates significant at least $p < .05$.

* $p < .05$; ** $p < .01$; *** $p < .001$.

Results also suggested an affirmative answer to the second question—and a negative one to the fourth. Both genders' genetic scores were indirectly but not directly linked to their partner's baseline health, through their own educational attainment (Tables 2 and 3). In other words, consistent with dyadic theory, the proximal mechanism was arguably a sharing of education-related health resources among couples. As noted, such assets may include greater knowledge or awareness of health issues—or simply higher socioeconomic resources to buffer against health risks and enable health maintenance. Genetically rooted cognitive or other precursors of education, on the other hand, did not seem to generate unmediated externalities for the partner. To the extent, these genes have cross-partner health effects, then, they appear to do so largely through the social process of education.

As noted, dyadic contexts may also involve linkages of one's genes with a partner's health through the partner's education. Such sorting- or selection-based paths—distinct from externalities—were indeed found, for both women's and men's genetic scores. The answer to the third study question, then, was unambiguously “yes.” More intriguingly, results also yielded a consistently affirmative answer to the fifth question. Among both genders, selection-based paths

through a partner's education linked a person's genetic score with his/her *own* baseline health. The extent to which genetically influenced social affiliation or “active rGE” (Avinun & Knafo, 2014)—and late-life assets conferred by such ties—channels ostensibly individual-level genetic effects remains underexplored. A fundamental insight of life-course theory is that a person is never *not* embedded in relationships (Bengtson et al., 2005). Research is thus needed on the filtering of person-specific genetic influences through such “voluntary” contexts—both to distinguish such paths from biological processes and for their intrinsic scientific importance. In the given case, total genetic effects and hence their indirect components were modest, and perhaps more important for their conceptual relevance than their health implications. Whether the same is true of other genetic scores—such as those directly connected to health outcomes—and/or relationships other than those with a spouse or partner remains unknown.

Limitations

This study had several limitations. The 10-year study period may not have been sufficient to capture longer-term cumulative trends. Positive associations of men's baseline age

with their slope growth factor also suggested differential developmental trajectories in late life (Table 2). Examining such patterns more deeply would have required analysis explicitly in the multilevel framework. With parallel process models, this leads to convergence problems, especially when observed outcomes are categorical. Nor were nonlinear effects investigated—whether genetic or educational. Next, due to small sample sizes and specificity of genetic measures, black participants could not be included. Nor were genetic data available for Hispanic or other ethnicities. Within the white subsample, inverse probability weights were used to address selection into dyads and genetic data collection. However, predictive models for these weights may well have excluded factors crucial to these processes. Moreover, the approach does not adjust for “missingness not at random”. Next, controls were limited to those likely not to be post-treatment (Pearl, 2009). Adjustments were avoided for factors that could have been influenced by the genetic scores—or on causal pathways from education to self-rated health. Omitted variable bias remained a concern, especially given the scarcity of valid “pre-treatment” controls in HRS. To elaborate, a person’s genome contains fine-grained information about their place in the intricate structure of a population (Trejo & Domingue, 2019). Thus, GWASs for complex traits such as education may simply identify genes linked to confounding environmental variables such as ancestry, geography, or socioeconomic status. Standard methods to control for biases due to population structure and environmental heterogeneity, such as principal component analysis (used in this study), work well in simulations but may be insufficient in practice (Barton, Hermisson, & Nordborg, 2019). In addition, the polygenic measures were additive indexes. Empirical genetic influences, however, may also involve interactions between SNPs—both within (dominance) and across loci (epistasis; Lin & Wu, 2006). Environmental moderation (i.e., $G \times E$) is also possible. These interactions may be a major reason “SNP heritability” is uniformly and substantially lower than “twin heritability” (Cheesman et al., 2017). Moreover, GWAS-based scores are limited to common alleles and do not incorporate rare genetic variants with potentially large influences. Most importantly, this was a one-sample analysis. A previous generation of “candidate gene” studies lost credibility due to nonreplication of findings (Conley, 2016). Although polygenic scores are promoted partly as a solution to this issue, cross-sample consistency in their effects remains poorly explored. Pending replication in independent samples, then, inferences above remain tentative.

Conclusion

Data from a nationally representative sample of older U.S. adults suggested that in addition to subject-specific ones, dyadic contexts involve a range of transpersonal genetic associations. These include, in particular, genetic externalities—effects of a person’s genes on the partner’s

outcomes. Moreover, individual-level linkages themselves seem partly channeled through the relational context, through selective affiliation. Although the present study established such patterns for the polygenic antecedents of educational attainment, and self-rated health outcomes, theory suggests they may be widespread. Broadening this line of inquiry is an important next step in advancing and synthesizing the life-course and rGE literature.

Supplementary Material

Supplementary data are available at *The Journals of Gerontology, Series B: Psychological Sciences and Social Sciences* online.

Funding

None reported.

Acknowledgments

The HRS (Health and Retirement Study) is sponsored by the National Institute on Aging (grant number NIA U01ACG009740) and is conducted by the University of Michigan. The author thanks the editor and three anonymous reviewers for their thorough and insightful comments.

Author Contributions

All work for this study—including conception, analysis, and writing—was performed by A. Das.

Conflict of Interest

None reported.

References

- Antonucci, T. C., Birditt, K. S., & Ajrouch, K. (2011). Convoys of social relations: Past, present, and future. In K. L. Fingerman, C. A. Berg, J. Smith, & T. C. Antonucci (Eds.), *Handbook of life-span development* (pp. 161–182). New York, NY: Springer Publishing Company.
- Asparouhov, T., & Muthén, B. (2010). *Weighted least squares estimation with missing data* (Technical appendix). Los Angeles, CA: Muthén & Muthén.
- Avinun, R., & Knafo, A. (2014). Parenting as a reaction evoked by children’s genotype: A meta-analysis of children-as-twins studies. *Personality and Social Psychology Review*, 18, 87–102. doi:10.1177/1088868313498308m
- Barton, N., Hermisson, J., & Nordborg, M. (2019). Why structure matters: Great care is needed when interpreting claims about the genetic basis of human variation based on data from genome-wide association studies. *eLife*, 8, e45380. doi:10.7554/eLife.45380
- Baud, A., Mulligan, M. K., Casale, F. P., Ingels, J. F., Bohl, C. J., Callebort, J., . . . Stegle, O. (2017). Genetic variation in the social

- environment contributes to health and disease. *PLoS Genetics*, 13, e1006498. doi:10.1371/journal.pgen.1006498
- Beckett, M. (2000). Converging health inequalities in later life – an artifact of mortality selection. *Journal of Health and Social Behavior*, 41, 106–119.
- Bengtson, V. L., Elder, G. H., Jr., & Putney, N. (2005). The life course perspective on aging: Linked lives, timing, and history. In M. L. Johnson (Ed.), *The Cambridge handbook of age and ageing* (pp. 9–17). Cambridge, UK: Cambridge University Press.
- Bollen, K. A. & Curran, P. J. (2006). *Latent curve models: A structural equation perspective*. Hoboken, NJ: Wiley.
- Branigan, A. R., McCallum, K. J., & Freese, J. (2013). Variation in the heritability of educational attainment: An international meta-analysis. *Social Forces*, 92, 109–140. doi:10.1093/sf/sot076
- Cheesman, R., Selzam, S., Ronald, A., Dale, P. S., McAdams, T. A., Eley, T. C., & Plomin, R. (2017). Childhood behaviour problems show the greatest gap between DNA-based and twin heritability. *Translational Psychiatry*, 7, 1284. doi:10.1038/s41398-017-0046-x
- Conley, D. (2016). Socio-genomic research using genome-wide molecular data. *Annual Review of Sociology*, 42, 275–299. doi:10.1146/annurev-soc-081715-074316
- Cook, W. L., & Kenny, D. A. (2005). The actor-partner interdependence model: A model of bidirectional effects in developmental studies. *International Journal of Behavioral Development*, 29, 101–109. doi:10.1080/0165025044000405
- Crimmins, E. M., & Saito, Y. (2001). Trends in healthy life expectancy in the United States, 1970–1990: Gender, racial, and educational differences. *Social Science and Medicine*, 52, 1629–1641. doi:10.1016/S0277-9536(00)00273-2
- Das, A. (2019). Social integration, self rated health...and genes? *Journal of Aging and Health*. Advance online publication. doi:10.1177/0898264319831513
- Deary, I. J., Strand, S., Smith, P., & Fernandes, C. (2007). Intelligence and educational achievement. *Intelligence*, 35, 13–21. doi:10.1016/j.intell.2006.02.001
- Domingue, B. W., & Belsky, D. W. (2017). The social genome: Current findings and implications for the study of human genetics. *PLoS Genetics*, 13, e1006615. doi:10.1371/journal.pgen.1006615
- Domingue, B. W., Belsky, D. W., Fletcher, J. M., Conley, D., Boardman, J. D., & Harris, K. M. (2018). The social genome of friends and schoolmates in the National Longitudinal Study of Adolescent to Adult Health. *Proceedings of the National Academy of Sciences of the United States*, 115, 702–707. doi:10.1101/107045
- Domingue, B. W., Belsky, D. W., Harrati, A., Conley, D., Weir, D. R., & Boardman, J. D. (2017). Mortality selection in a genetic sample and implications for association studies. *International Journal of Epidemiology*, 46, 1285–1294. doi:10.1093/ije/dyx041
- Ferraro, K. F., & Morton, P. M. (2018). What do we mean by accumulation? Advancing conceptual precision for a core idea in gerontology. *Journals of Gerontology, Series B: Psychological Sciences and Social Sciences*, 73, 269–278. doi:10.1093/geronb/gbv094
- Health and Retirement Study. (2012). *Quality control report for genotypic data*. Seattle, WA: University of Washington.
- Herd, P. (2010). Education and health in late-life among high school graduates: Cognitive versus psychological aspects of human capital. *Journal of Health and Social Behavior*, 51, 478–496. doi:10.1177/0022146510386796
- House, J. S., Lepkowski, J. M., Kinney, A. M., Mero, R. P., Kessler, R. C., & Herzog, A. R. (1994). The social stratification of aging and health. *Journal of Health and Social Behavior*, 35, 213–234. doi:10.2307/2137277
- Kitagawa, E. M., & Hauser, P. (1973). *Differential mortality in the United States: A study in socioeconomic epidemiology*. Cambridge, MA: Harvard University Press.
- Kong, A., Thorleifsson, G., Frigge, M. L., Vilhjalmsdottir, B. J., Young, A. I., Thorgeirsson, T. E., . . . Stefansson, K. (2018). The nature of nurture: Effects of parental genotypes. *Science*, 359, 424–428. doi:10.1126/science.aan6877
- Lee, J. J., Wedow, R., Okbay, A., Kong, E., Maghzian, O., Zacher, M., . . . Cesarini, D. (2018). Gene discovery and polygenic prediction from a genome-wide association study of educational attainment in 1.1 million individuals. *Nature Genetics*, 50, 1112–1121. doi:10.1038/s41588-018-0147-3
- Lin, M., & Wu, R. (2006). Detecting sequence-sequence interactions for complex diseases. *Current Genomics*, 7, 59–72. doi:10.2174/138920206776389775
- Lin, Y. F., Chen, C. Y., Öngür, D., Betensky, R., Smoller, J. W., Blacker, D., & Hall, M. H. (2018). Polygenic pleiotropy and potential causal relationships between educational attainment, neurobiological profile, and positive psychotic symptoms. *Transl Psychiatry*, 8, 97. doi:10.1038/s41398-018-0144-4
- Lindau, S. T., Laumann, E. O., Levinson, W., & Waite, L. J. (2003). Synthesis of scientific disciplines in pursuit of health: The Interactive Biopsychosocial Model. *Perspectives in Biology and Medicine*, 46, S74–S86. doi:10.1353/pbm.2003.0055
- Marioni, R. E., Ritchie, S. J., Joshi, P. K., Hagenaars, S. P., Okbay, A., Fischer, K., . . . Deary, I. J. (2016). Genetic variants linked to education predict longevity. *Proceedings of the National Academy of Sciences of the United States of America*, 113, 13366–13371. doi:10.1073/pnas.1605334113
- Mirowsky, J., & Ross, C. E. (1992). Age and depression. *Journal of Health and Social Behavior*, 33, 187–205. doi:10.2307/2137349
- Ofstedal, M. B., Weir, D., Chen, K.-T., & Wagner, J. (2011). *HRS documentation report: Updates to HRS sample weights*. Ann Arbor, MI: Survey Research Center, University of Michigan.
- Pearl, J. (2009). *Causality: Models, reasoning, and inference*. New York, NY: Cambridge University Press.
- Perkins, N. J., Cole, S. R., Harel, O., Tchetgen Tchetgen, E. J., Sun, B., Mitchell, E. M., & Schisterman, E. F. (2018). Principled approaches to missing data in epidemiologic studies. *American Journal of Epidemiology*, 187, 568–575. doi:10.1093/aje/kwx348
- Rehnberg, J., Fors, S., & Fritzell, J. (2019). Divergence and convergence: How do income inequalities in mortality change over the life course? *Gerontology*, 65, 313–322. doi:10.1159/000494082
- Robinson, M. R., Kleinman, A., Graff, M., Vinkhuyzen, A. A. E., Couper, D., Miller, M. B., . . . Visscher, P. M. (2017). Genetic

- evidence of assortative mating in humans. *Nature Human Behaviour*, 1, 0016. doi:10.1038/s41562-016-0016
- Shiner, R. L., Masten, A. S., & Roberts, J. M. (2003). Childhood personality foreshadows adult personality and life outcomes two decades later. *Journal of Personality*, 71, 1145–1170. doi:10.1111/1467-6494.7106010
- Singh-Manoux, A., Martikainen, P., Ferrie, J., Zins, M., Marmot, M., & Goldberg, M. (2006). What does self rated health measure? Results from the British Whitehall II and French Gazel cohort studies. *Journal of Epidemiology and Community Health*, 60, 364–372. doi:10.1136/jech.2005.039883
- Sonnega, A., Faul, J. D., Ofstedal, M. B., Langa, K. M., Phillips, J. W., & Weir, D. R. (2014). Cohort Profile: The Health and Retirement Study (HRS). *International Journal of Epidemiology*, 43, 576–585. doi:10.1093/ije/dyu067
- Sotoudeh, R., Harris, K. M., & Conley, D. (2019). Effects of the peer metagenomic environment on smoking behavior. *Proceedings of the National Academy of Sciences of the United States of America*, 116, 16302–16307. doi:10.1073/pnas.1806901116
- Sun, B., Perkins, N. J., Cole, S. R., Harel, O., Mitchell, E. M., Schisterman, E. F., & Tchetgen Tchetgen, E. J. (2018). Inverse-probability-weighted estimation for monotone and nonmonotone missing data. *American Journal of Epidemiology*, 187, 585–591. doi:10.1093/aje/kwx350
- Trejo, S., & Domingue, B. W. (2019). Genetic nature or genetic nurture? Quantifying bias in analyses using polygenic scores. *BioRxiv* 069187 [Preprint]. doi:10.1101/524850
- Umberson, D., (1992). Gender, marital status and the social control of health behavior. *Social Science and Medicine*, 34, 907–917. doi:10.1016/0277-9536(92)90259-S
- Waite, L., & Das, A. (2010). Families, social life, and well-being at older ages. *Demography*, 47 (Suppl), S87–S109. doi:10.1353/dem.2010.0009
- Ware, E., Schmitz, L., Gard, A., & Faul, J. (2018). *HRS polygenic scores – Release 3: 2006–2012 genetic data*. Ann Arbor, MI: Survey Research Center, University of Michigan.
- Wedow, R., Zacher, M., Huibregtse, B. M., Harris, K. M., Domingue, B. W., & Boardman, J. D. (2018). Education, smoking, and cohort change: Forwarding a multidimensional theory of the environmental moderation of genetic effects. *American Sociological Review*, 83, 802–832. doi:10.1177/0003122418785368
- Zajacova, A., Hummer, R. A., & Rogers, R. G. (2012). Education and health among U.S. working-age adults: A detailed portrait across the full educational attainment spectrum. *Biodemography and Social Biology*, 58, 40–61. doi:10.1080/19485565.2012.666122
- Zhu, Z., Zheng, Z., Zhang, F., Wu, Y., Trzaskowski, M., Maier, R., . . . Yang, J. (2018). Causal associations between risk factors and common diseases inferred from GWAS summary data. *Nature Communications*, 9, 224. doi:10.1038/s41467-017-02317-2