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ORIGINAL ARTICLE

Genetic link between family socioeconomic status and children's educational achievement estimated from genome-wide SNPs

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One of the best predictors of children's educational achievement is their family's socioeconomic status (SES), but the degree to which this association is genetically mediated remains unclear. For 3000 UK-representative unrelated children we found that genome-wide single-nucleotide polymorphisms could explain a third of the variance of scores on an age-16 UK national examination of educational achievement and half of the correlation between their scores and family SES. Moreover, genome-wide polygenic scores based on a previously published genome-wide association meta-analysis of total number of years in education accounted for ~ 3.0% variance in educational achievement and ~ 2.5% in family SES. This study provides the first molecular evidence for substantial genetic influence on differences in children's educational achievement and its association with family SES.

Molecular Psychiatry advance online publication, 10 March 2015; doi:10.1038/mp.2015.2

INTRODUCTION

After health care, education is society's largest and most expensive environmental intervention, consuming > 6% of gross domestic product in OECD (Organization for Economic Co-operation and Development) countries.[1] Understanding the etiology and correlates of differences between children in what they take away from their education is important because their educational achievement directly determines admission to further education and employability and also predicts a wide range of health outcomes.[1–3] Pedigree-based methods, primarily twin studies comparing the similarity of identical and nonidentical twins, have consistently suggested substantial genetic influence on differences between children in their educational achievement.[4–10] It is now possible to use DNA-based methods to estimate genetic influence on variance in large samples of unrelated individuals.[11,12] No DNA-based estimates of genetic influence have as yet been reported for children's educational achievement, although evidence has been reported for the rough proxy of total number of years in education in adults.[13–16] This study used children's genotypes to estimate genetic influences on variance in educational achievement and its covariance with family socioeconomic status (SES).

Here we report the first investigation of genetic influence on the variance of children's educational achievement using DNA alone. The same DNA-based methods can also be used to estimate genetic influence on the covariance between traits.[17] This enabled us to investigate possible genetic mediation of the best predictor of children's educational achievement, their family's SES.[18,19] This correlation is often interpreted causally as family SES causing differences in children's educational achievement.[20] However, it remains unclear whether and to what extent the association between family SES and children's educational achievement is genetically mediated, because twin and family research is limited to studying phenotypes that can vary within a family. Key aspects of children's environment such as poverty, parental education and neighborhood cannot be investigated using the twin method because it is methodologically impossible to decompose variance in phenotypes shared within twin pairs.

The DNA-based technique, genome-wide complex trait analysis (GCTA),[11] fits the effects of genome-wide single-nucleotide polymorphisms (SNPs) as random effects in a mixed linear model to estimate variance or covariance captured by all SNPs simultaneously. Contrary to traditional family-based methods that estimate the genetic contribution to phenotypic variation or covariation by known kinship coefficients, GCTA relies on empirical genetic resemblance established from identity by state inferred from genome-wide SNP similarity of 'unrelated' individuals.

Because GCTA is based on unrelated individuals, it enables the decomposition of variance of phenotypes such as family SES that are the same for members of a family and therefore cannot be decomposed in analyses such as the twin method that rely on within-family differences. Another difference between the two methods is that, unlike the twin method, GCTA is limited to estimating additive genetic effects for the SNPs on the genome-wide DNA array or other DNA variants in linkage disequilibrium with the measured SNPs, which until recently have been common SNPs. Thus, GCTA will underestimate genetic influence to the extent that nonadditive effects or rare variants contribute importantly to heritability. This limitation of GCTA to additive effects of common SNPs is the same limitation of genome-wide association (GWA) studies that attempt to identify specific SNPs associated with a trait. GCTA is directly comparable to GWA results because both rely on the same experimental design using the same genetic signal;[21] GCTA provides an upper-limit estimate of the genetic effects that can be identified by GWA.

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GWA attempts aimed at identifying individually significant SNPs have generally captured only extremely small fractions of genetic variance of complex traits, the so-called *missing heritability* problem.[22] However, evidence has been accumulating that significant portions of phenotypic variation can be explained by the ensemble of markers not achieving genome-wide significance.[23] Markers are identified from GWAs using an initial discovery sample to construct a genome-wide polygenic score (GPS) in an independent replication sample by calculating the effect-size-weighted sum of trait-associated alleles for each individual. An aggregate GPS score can be used to assess genetic influence on trait variation.

As they are tapping into the same genetic signal, GPS based on GWA results and GCTA can be applied to the same data sets, with both estimating the polygenic contribution to trait variance or a shared polygenic covariance between traits captured by the additive effects of common SNPs. We therefore employ a two-method approach using GCTA and GPS to explore the genetic influence on the variance of children's educational achievement and on the covariance between family SES and children's educational achievement. Our study had four objectives:

(1) To estimate, for the first time using DNA data, genetic influences on children's educational achievement on an age-16 UK national examination of educational achievement using genome-wide genotypes from >3000 conventionally unrelated children. Specifically, we conduct GCTA[11] to quantify pairwise genomic similarity between each pair of individuals across millions of SNPs throughout the genome in order to estimate the proportion of phenotypic variation in children's educational achievement captured by all SNPs simultaneously.

(2) To investigate genetic mediation of the phenotypic correlation between family SES and children's educational achievement, we conduct bivariate GCTA to estimate the proportion of phenotypic covariation between children's family SES and children's educational achievement captured by children's genotypes.

(3) To create a GPS based on the results of a large GWA study on adults' total years of schooling[13] and investigate its association with variance in children's educational achievement and their family SES.

(4) To examine the role of general cognitive ability (intelligence) in the genetic nexus between children's educational achievement and their family SES. Molecular evidence as well as twin studies have shown that cognitive ability is heritable and accounts for substantial portion of genetic variance in educational achievement.[7,24–26] In addition, recent molecular evidence from the present sample of unrelated individuals showed high genetic correlation between family SES and children's intelligence at age 7 and 12 years.[27] Based on this evidence, it is important to address the question to what extent the genetic link between family SES and children's educational achievement is mediated by intelligence. For this reason, we perform GCTA mediation analyses to test for a direct genetic link between family SES and children's educational achievement independent of cognitive ability. Complementarily, we test whether the GPS of adults' total years of schooling explains variance in children's educational achievement independently of cognitive ability.

Our findings provide the first molecular evidence for substantial genetic influence on variation in children's educational achievement and its association with family SES. We further show that children's intelligence accounts for one third of this SNP link between family SES and children's educational achievement. In addition, we demonstrate that a GPS based on years of education in adulthood discovered in an independent large GWA meta-analysis[13] significantly explains variance in children's educational achievement in our sample, even after controlling for intelligence.

MATERIALS AND METHODS

Sample and genotyping
The sample was drawn from the Twins Early Development Study (TEDS), a multivariate longitudinal study that recruited over 11 000 twin pairs born in England and Wales in 1994, 1995 and 1996.[28,29] TEDS has been shown to be representative of the UK population.[30] Supplementary Table 2 shows that the genotyped subsample of TEDS is representative of UK census data from first contact through age 16 years.

The project received approval from the Institute of Psychiatry ethics committee (05/Q0706/228) and parental consent was obtained before data collection.

DNA data were available for 3747 children whose first language was English and had no major medical or psychiatric problems. From that sample, 3665 DNA samples were successfully hybridized to Affymetrix GeneChip 6.0 SNP genotyping arrays (Affymetrix, Santa Clara, CA, USA) using standard experimental protocols as part of the WTCCC2 project (for details see Trzaskowski et al.).[31] In addition to nearly 700 000 genotyped SNPs, more than one million other SNPs were imputed from HapMap 2, 3 and WTCCC controls using IMPUTE v.2 software.[32] A total of 3152 DNA samples (1446 males and 1706 females) survived quality control criteria for ancestry, heterozygosity, relatedness and hybridization intensity outliers. To control for ancestral stratification, we performed principal component analyses on a subset of 100 000 quality-controlled SNPs after removing SNPs in linkage disequilibrium ($r^2 > 0.2$).[33] Using the Tracy–Widom test,[34] we identified 8 axes with $P < 0.05$ that were used as covariates in GCTA and polygenic score analyses.

Measures
Educational achievement. Educational achievement was operationalized as performance on the standardized UK-wide examination, the General Certificate of Secondary Education (GCSE), taken by almost all (>99%) pupils at the end of compulsory education at typically at the age of 16 years. English, mathematics and science are compulsory subjects. Five or more GCSEs with grades A*–C are required for further education, including GCSE English and GCSE mathematics. The joint performance on these three compulsory subjects determines admission to further education and employability.

The data for the present study were collected by questionnaires sent by mail and by telephone interview of parents and twins themselves. After completed forms were received from the families, the grades were coded from 11 (the highest grade: A*) to 4 (the lowest pass grade: G); no information about failed results was available. For 1729 individuals, self- and parent-reported GCSE results were verified using data obtained from the UK National Pupil Database,[35] yielding correlations of 0.99 for mathematics, 0.98 for English and 0.96 for science.

The GCSE measure for the present analyses was the mean grade of the three compulsory core subjects, mathematics, English (mean grade of 'English Language' and 'English Literature'), and science (mean of any science subjects taken), requiring at least two measures to be nonmissing. Scores on the three compulsory core subjects were highly correlated (0.65–0.81).

Intelligence (IQ). Individuals were assessed at the ages of 2, 3, 4, 7, 9, 10, 12, 14, and 16 years on general cognitive ability using a battery of parent-administered and phone- and web-based tests. At ages 2, 3, and 4, tests were parent-administered and validated against standard tests administered by a trained tester. At age 7, tests were administered over the phone; at age 9, parents administered the tests; and at the ages 10–16, tests were web based. At each testing age, individuals completed at least two ability tests that assessed verbal and nonverbal intelligence. Psychometric properties of the tests have been described in detail elsewhere,[36] with the exception of the measurements used at age 16 years, where subjects completed a web-based adaptation of Raven's Standard and Advanced Progressive Matrices and the Mill-Hill Vocabulary Scale.[37–39]

For each composite measure at each of the nine ages, scores were regressed on sex and age, outliers above or below 3 s.d. from the mean were excluded and the standardized residuals were quantile normalized. Subsequently, a mean composite scale was created as the mean across the nine ages, performing mean-imputation for missing measurement occasions to avoid list-wise deletion.

Family SES. Converging evidence suggests that a composite of variables including parental education and occupation represents SES better than any single indicator.[18] To index family SES, we combined parental

education and occupation assessed when children were aged 2, 7 and 16 years. At age 2 years, SES was constructed as the mean of mother's and father's highest education level, mother's and father's occupation assessed by the Standard Occupational Classification 2000,[40,41] and maternal age at birth of eldest child. The SES composite when children were age 7 years was created similarly but without the variable of age of mother at birth of eldest child. At age 16 years, SES was composed as the mean of household income, maternal and paternal education level and maternal and paternal occupation. Mean composites were standardized and quantile normalized. The correlations between these three SES estimates ranged from 0.70 to 0.77. To increase reliability and maximize sample size, the final measure of family SES for this study was created as the mean composite score of parental SES reported when children were aged 2, 7, and 16 years, performing mean-imputation for missing data points.

Statistical analyses

GCTA. The GCTA model decomposes the trait variance into an additive genetic component ($_G$) captured by the available SNPs (and correlated markers in linkage disequilibrium with the genotyped SNPs) and a residual component containing all nonadditive genetic variance, interaction effects, environmental factors, error variance and additive genetic variance that is not tagged by the sampled SNPs. Hence, the GCTA model estimates lower-bound additive genetic variance for both phenotypes (V_G^{GCSE}, V_G^{SES}); and the correlation between the additive genetic components (ρ_G). The ρ_G is not biased in the same way V_G is. This is because the estimate of genetic correlation is a function of the ratio between SNP-tagged covariance and SNP-tagged variance that are biased to the same extent (that is, the estimates are subject to the same imperfect linkage disequilibrium between causal variants and genotyped SNPs) and hence cancel each other out.[42]

Using genome-wide SNP data, we estimate genetic variation and covariation from a representative sample of 3000 unrelated children. Our estimates were obtained by restricted maximum likelihood using the published algorithm for GCTA.[11] GCTA estimates the proportion of phenotypic variance of a trait tagged by sampled SNPs by fitting the polygenic effects of all SNPs simultaneously as random effects in a mixed linear model using a restricted maximum likelihood function. The so-called genetic relatedness matrix holds the mean pairwise genomic similarity (weighted by allele frequency) between all pairs of individuals in the sample across all SNPs. The variance tagged by all SNPs is estimated to be >0 when genetically more similar individuals are phenotypically more similar. The bivariate extension of the model relates the pairwise genetic similarity matrix to a phenotypic covariance matrix between traits (here family SES and educational achievement).[17] To prevent confounding of the SNP estimate by shared environment effects and the effects of causal variants that are not tagged by the SNPs, cryptic relatedness was removed from the analyses. This default procedure eliminates one individual from a pair whose genetic similarity is 0.025 or greater; a coefficient that approximates at least fifth-degree relatives. The removal of close relatives ensures that estimates reflect the tagging of causal variants through population linkage disequilibrium. This criterion removed seven individuals from the analyses. Analyses were executed using GCTA[11] and R software.[43]

The present sample size of ~3000 yields 80% power to detect a GCTA heritability estimate of 30% ($\alpha = 0.05$) and genetic correlation estimate of 0.6 ($\alpha = 0.05$; $V_G^1 = 0.20$; V_G^2: 0.30; $r_{Ph} = 0.50$).

Polygenic scores. We created polygenic scores from genome-wide data of over 3000 unrelated children using GWA results for total years of schooling from an independent discovery sample.[13] The same quality control criteria as for the GCTA analyses were applied to the data. Polygenic risk scores were constructed using the P-values and β-weights from the recent large ($N = 126\,559$) GWA based on years of education.[6] Quality-controlled SNPs were pruned for linkage disequilibrium based on P-value informed clumping in PLINK,[44] using $R^2 = 0.25$ cutoff within a 200-kb window. We removed the major histocompatibility complex region of the genome because of its complex linkage disequilibrium structure. 144 890 SNPs survived linkage disequilibrium pruning. For each individual, multiple polygenic scores were generated using the PLINK score option based on the top SNPs from the GWA analysis of educational attainment for varying significance thresholds (from 0.01 to 0.50). Numbers of SNPs per threshold are summarized in Supplementary Table 3. The scores were calculated as the sum across SNPs of

the number of reference alleles for each SNP multiplied by the effect size (β-coefficient) derived from the GWA analysis of years of education.

Polygenic scores were tested for association with the same quantitative measures used in the GCTA analyses (family SES, educational achievement (GCSE), intelligence and educational achievement controlled for intelligence) in linear regressions. These analyses were corrected for the first eight ancestry-informative principal components by entering them as covariates into the regression models. Analyses were performed in PLINK and R.

RESULTS

Phenotypically, children's educational achievement correlated 0.50 (0.02 s.e.) with their family SES. Both variables also correlated with intelligence: 0.55 (0.02 s.e.) for educational achievement and 0.38 (0.02 s.e.) for family SES (Supplementary Table 1).

Bivariate GCTA

Bivariate GCTA showed that the estimated proportion of variance tagged by the sampled SNPs was 0.31 (0.12 s.e.) in educational achievement, and 0.20 (0.11 s.e.) in family SES (Figure 1). The genetic correlation, indicating the extent to which the same SNPs are associated with family SES and children's educational achievement, was near unity ($r_G = 1.02$ (0.25 s.e.)).

Based on the genetic correlation between the two traits and the genetic contribution to variance of each trait respectively, GCTA estimates the genetic contribution to the phenotypic correlation between the two traits: $C_{(G)} = r_{1,2\ (G)} \sqrt{(V_1\ _{(G)} \times V_2\ _{(G)})}$, applied to the data: $0.25 = 1.02 \times \sqrt{(0.31 \times 0.20)}$. Hence, GCTA estimated the genetic contribution to the phenotypic correlation between family SES and children's educational achievement as 0.25 (0.09 s.e.), indicating that the proportion of the observed correlation tagged by the additive effects of available SNPs was 50% (that is, 0.25/0.50; Figure 1). This suggests approximately half of the phenotypic correlation between children's family SES and their educational achievement was mediated genetically.

Mediation analyses. To test whether intelligence mediates the observed association between family SES and children's educational achievement, we statistically controlled for intelligence by regressing GCSE on intelligence and entering the resulting standardized residuals into the bivariate GCTA model with family SES. When controlling for variance explained by children's intelligence, which yielded a univariate GCTA estimate of 0.38 (0.11 s.e.) (data not shown), the phenotypic correlation between family SES and children's educational achievement was reduced from 0.50 to 0.37 (0.02 s.e.). The GCTA estimate of the genetic covariation between family SES and children's educational achievement dropped from 0.25 (0.09 s.e.) to 0.17 (0.09 s.e.). Mirroring the mediation observed at the phenotypic level, this suggests that one-third of the SNPs tagging variation in family SES and children's educational achievement also captured individual differences in intelligence, implying two-thirds of the SNPs linking family SES and children's educational achievement were independent of intelligence.

Polygenic score analyses

Polygenic score analysis is designed to test whether SNPs that do not reach genome-wide significance in a discovery GWA are nonetheless significantly associated in aggregate with a trait in an independent sample. In the same sample of 3152 unrelated individuals, we created polygenic scores with varying numbers of SNPs (see Materials and methods) based on a large meta-analytic GWA study ($N = 126\,599$) of years of education.[13] Figure 2 displays the results of multiple linear regression analyses showing that the polygenic scores accounted for ~3.0% variance in educational
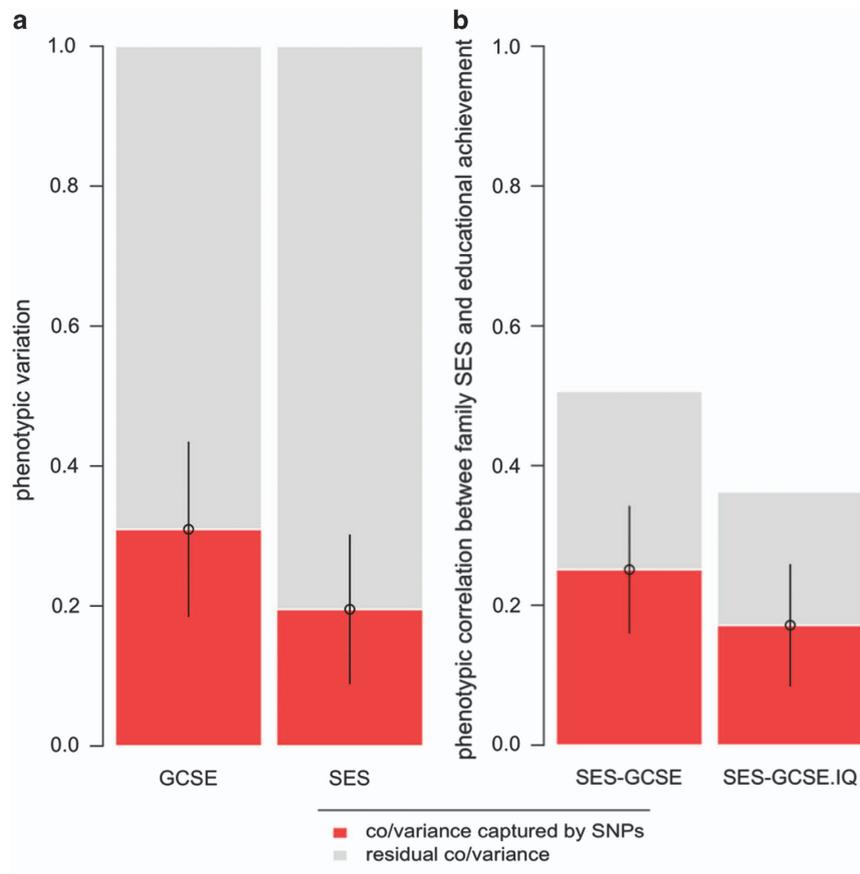
Figure 1. Bivariate genome-wide complex trait analysis (GCTA) of family socioeconomic status (SES) and children's educational achievement (General Certificate of Secondary Education (GCSE)). (**a**) Proportion of phenotypic trait variance tagged by the sampled SNPs in GCSE and family SES, respectively. (**b**) Covariance between family SES and GCSE captured by SNPs, without controlling for intelligence (left bar) and when controlling for intelligence (GCSE.IQ) (right bar). The length of the bar indicates the total phenotypic correlation between SES and GCSE. Solid black lines indicate standard errors.

achievement (GCSE), ~ 2.5% in family SES and ~ 1.0% in intelligence. All P-values were $\leq 3.79^{-07}$. Notably, the effect size for GCSE remained substantial (~ 2.0%) and significant ($P \leq 2.27^{-06}$) when statistically controlling for intelligence.

DISCUSSION
This study provides the first molecular evidence for substantial genetic influence on differences in children's educational achievement at the end of compulsory education in the United Kingdom and its association with family SES. Our GCTA results show that SNPs that are associated with both family SES and GCSE scores account for about half of the phenotypic correlation between SES and GCSE. Mediation analysis suggests that about one-third of this genetic effect also extends to children's intelligence, but two-thirds of the genetic association between family SES and GCSE scores is independent of intelligence. In GPS analysis, we show that SNPs associated with total years of education in adulthood discovered by an independent large GWA meta-analysis[13] explain up to 3% of the variance in children's educational achievement in our sample, and up to 2% of the variance after controlling for intelligence.

The GCTA heritability estimate of 31% for children's performance on a UK national examination at the end of compulsory education corroborates the vast literature of traditional family-based methods, mostly the twin method, showing that variation in children's educational achievement is under substantial genetic influence,[4,5,7–9,45,46] with heritability estimates converging at ~ 50%. This commonly observed discrepancy in phenotypic

variance explained by pedigree-based methods (that is, twin and family) and population-based methods (that is, GCTA) occurs because GCTA only captures genetic variance contributed by additive effects of common SNPs that are in sufficient linkage disequilibrium with the causal DNA variants.[47]

Our GCTA heritability estimate of 20% for family SES tagged by children's genotypes is very similar to GCTA heritability estimates of years of education in adulthood and socioeconomic measures tagged by adults' genotypes themselves in previous studies.[13–15] This is remarkable as children's genotypes are only a proxy for their parents' genotypes. In other words, GCTA effects on family SES estimated from children's DNA only reflect the extent to which children inherit parental characteristics associated with the family SES created by the parents. One such factor is intelligence, and we find that children's intelligence accounts for about one-third of the GCTA association between family SES and children's educational achievement. However, it is interesting that two-thirds of the GCTA association is *not* accounted for by children's intelligence. This finding of intelligence-independent shared genetic variance between family SES and children's educational achievement suggests that differences in educational achievement at the end of compulsory education and the level of education and occupation attained in adulthood are not merely the manifestation of differences in intelligence. This is in line with twin research that suggests that the heritability of educational achievement reflects many genetically influenced traits such as personality and self-efficacy, not just intelligence.[48]
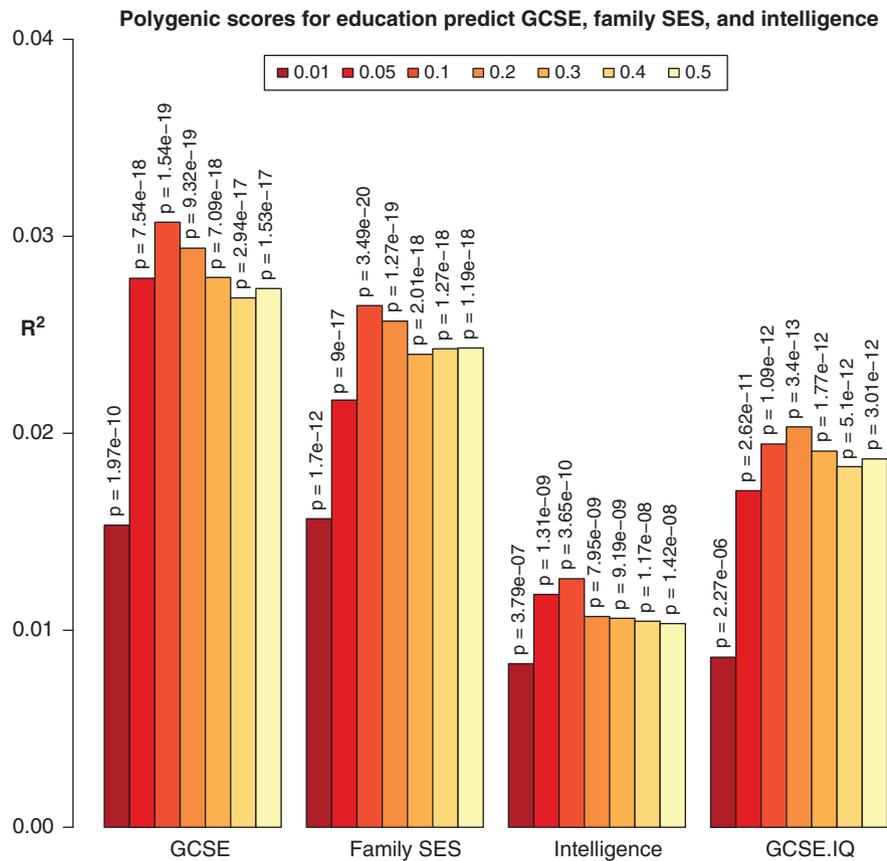
Polygenic scores for education predict GCSE, family SES, and intelligence

Figure 2. Genome-wide polygenic scores (GPS) for years of schooling in adults (Rietveld et al.[13]) predict variance (R^2) in children's educational achievement (General Certificate of Secondary Education (GCSE)), family socioeconomic status (SES), intelligence and educational achievement after controlling for intelligence (GCSE.IQ). GPS were created using different significance thresholds for inclusion of variants for years of education, ranging from $P = 0.01$ to 0.50, indicated by heat colors. The uncorrected P-values above each bar indicate the statistical significance of the observed association between the GPS and the respective trait.

The polygenic nature of behavioral traits poses a statistical challenge as enormous sample sizes are needed to identify genome-wide significant single DNA variants.[23] Therefore, genome-wide methods, such as GCTA and GPS analysis, that aggregate genetic effects across a multitude of markers have the assumption of polygenicity at their core and provide powerful approaches for exploring genetic influences on traits and shared between traits.

A GPS based on markers associated with years of education in adulthood in an independent discovery sample was significantly associated with children's educational achievement in our sample. Replicating results from polygenic score analyses of a recent Dutch study,[49] this shows that the shared polygenic link between children's educational achievement and adult measures of education even holds when limited to education-associated SNPs identified in an independent sample of adults. We further demonstrate that this polygenic link persists independently of children's cognitive ability, and that the educational attainment GPS of children's genotypes explains variance in their parents' socioeconomic status. The predictive power of GPS analysis in our independent sample illustrates that adequately powered GWA studies can identify replicable genetic associations with behavioral traits. Although the current GPS accounts for only a small amount of phenotypic variance, as prediction improves, GPS can identify profiles of genetic risk and protective factors for unrelated individuals, which will enable more powerful prediction models that combine genetic and nongenetic factors. Polygenic

predictors might also facilitate research on the causal pathways underlying these genetic predictors.[21,22,50]

The results need to be interpreted in the context of three main important methodological limitations. First, a specific limitation of this study is its modest statistical power in the GCTA analyses (see Materials and methods). The GPS analyses were sufficiently powered to identify trait-associated variance at high statistical significance, but were limited by the power of the discovery GWAS to detect the small effect sizes of single variants across the genome.[21,23] A second, general limitation is the allelic spectrum covered by the current DNA microarrays, such as the Affymetrix 6.0 GeneChip used in our study, that is restricted to common variants. Research has begun exploring the relative contribution of common and rare variants to variation of psychiatric traits (see, for example, Gaugler et al.[51] and Yang et al.[52]). Future studies with greater statistical power may explore the relative contribution of common and rare variants to trait variation of educational achievement and associated phenotypes. Third, both GCTA and GWAS, on which GPS analysis relies, are limited to detecting additive genetic variation that is captured by the sampled SNPs, which are typically common SNPs with minor allele frequencies > 0.05. Hence, GCTA heritability provides a lower-bound narrow-sense heritability estimate and represents the upper limit for detection of SNP associations in GWA studies and thus for GPS analysis. Generally, these limitations imply a substantial under-estimation of 'true heritability' in the present analyses.

The present analyses demonstrate the ability of DNA-based methods to explore the genetic architecture of extended

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phenotypes such as family SES that cannot be detected by traditional variance/covariance estimation methods that rely on known kinship relatedness. Quantitative DNA-based methods, which rely on empirically established pairwise genomic similarity among traditionally unrelated individuals, can supplement and extend family-based methods and thereby facilitate the move from behavioral genetics to behavioral genomics.

Importantly, no directionality or causality can be inferred from the present results. Heritability indexes the proportion of trait variance attributable to genetic effects in a particular population at a particular time.[53] Finding evidence for heritability of a trait or co-heritability of two traits does not imply resistance to environmental factors as genetic effects are dynamic and subject to developmental and environmental change.[54] Research on how the heritability of educational achievement differs across development and across context suggests that genetic influences on these phenotypes are maximized by environmental opportunity.[54–56] Differences in individuals' exposure to environments are not random. Genotype–environment correlation refers to the empirical observation that individuals experience different environments as a systematic function of their genotypes.[56–61] Genetic effects on phenotypes may be mediated through developmental or socio-contextual processes.

Our results also contribute to the extensive debate about meritocracy and social mobility[62] that has largely ignored the fact that parents and their offspring are genetically related. Usually a lower correlation between parental and offspring SES is seen as an index of social mobility.[63] However, considering genetics, we know that removing environmental sources of variation will not remove genetically driven resemblance between parents and offspring. To the contrary, as environmental differences diminish, individual differences that remain will to a larger proportion be due to genetic differences; that is, heritability would increase, which has also been demonstrated empirically.[55] That way, heritability could be seen as an index of social mobility.

No necessary policy implications arise from finding heritability of educational achievement and its link with family SES. However, consideration of empirical evidence will lead to better-informed policy decisions. Specifically, analogous to the long-established model of evidence-based medicine, we believe that evidence-based education facilitated by a dialog between scientists and policy makers will be beneficial to education of all children and can also benefit schools, teachers, and society at large.[64]

In summary, our GCTA results show a substantial contribution of common SNPs to variation in children's educational achievement and its association with family SES. This is further substantiated by the GPS analyses, revealing significant sharing of genetic variants between children's educational achievement and total years of education in adulthood. Together, these findings provide converging evidence for substantial genetic influence on differences in children's educational achievement and genetic links with family SES. Our findings add weight to the view that genetic variation plays an important, but not exclusive, role in educational inequalities and social mobility, which is at variance with views, that still prevail in some quarters, that these are solely the product of social forces and environmental inequalities.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGMENTS

AUTHOR CONTRIBUTIONS

RP directs and received funding for the Twins Early Development Study (TEDS). EK conceived of the present study and analyzed the data. EK and RP wrote the manuscript.

REFERENCES

1 OECD. *Education at a Glance 2013*. Organisation for Economic Co-operation and Development, 2013 Available at http://www.oecd-ilibrary.org/content/book/eag_highlights-2013-en.
2 Morris JN, Blane DB, White IR. Levels of mortality, education, and social conditions in the 107 local education authority areas of England. *J Epidemiol Community Health* 1996; **50**: 15–17.
3 White IR, Blane D, Morris JN, Mourouga P. Educational attainment, deprivation-affluence and self reported health in Britain: a cross sectional study. *J Epidemiol Community Health* 1999; **53**: 535–541.
4 Haworth CMA, Plomin R. Quantitative genetics in the era of molecular genetics: learning abilities and disabilities as an example. *J Am Acad Child Adolesc Psychiatry* 2010; **49**: 783–793.
5 Shakeshaft NG, Trzaskowski M, McMillan A, Rimfeld K, Krapohl E, Haworth CM *et al.* Strong genetic influence on a UK nationwide test of educational achievement at the end of compulsory education at age 16. *PLoS One* 2013; **8**: e80341.
6 Johnson W, Deary IJ, Iacono WG. Genetic and environmental transactions underlying educational attainment. *Intelligence* 2009; **37**: 466–478.
7 Calvin CM, Deary IJ, Webbink D, Smith P, Fernandes C, Lee SH *et al.* Multivariate genetic analyses of cognition and academic achievement from two population samples of 174,000 and 166,000 school children. *Behav Genet* 2012; **42**: 699–710.
8 Martin NG, Martin PG. The inheritance of scholastic abilities in a sample of twins I. Ascertainment of the sample and diagnosis of zygosity. *Ann Hum Genet* 1975; **39**: 213–218.
9 Gill CE, Jardine R, Martin NG. Further evidence for genetic influences on educational achievement. *Br J Educ Psychol* 1985; **55**: 240–250.
10 Haworth CMA, Plomin R. Genetics and education: Toward a genetically sensitive classroom. In: Harris KR, Graham S, Urdan T, McCormick CB, Sinatra GM, Sweller J (eds). *APA educational psychology handbook, Vol 1: Theories, constructs, and critical issues*. American Psychological Association: Washington, DC, USA, 2012, pp 529–559.
11 Yang J, Lee SH, Goddard ME, Visscher PM. GCTA: a tool for genome-wide complex trait analysis. *Am J Hum Genet* 2011; **88**: 76–82.
12 Yang J, Benyamin B, McEvoy BP, Gordon S, Henders AK, Nyholt DR *et al.* Common SNPs explain a large proportion of the heritability for human height. *Nat Genet* 2010; **42**: 565–569.
13 Rietveld CA, Medland SE, Derringer J, Yang J, Esko T, Martin NW *et al.* GWAS of 126,559 individuals identifies genetic variants associated with educational attainment. *Science* 2013; **340**: 1467–1471.
14 Marioni RE, Davies G, Hayward C, Liewald D, Kerr SM, Campbell A *et al.* Molecular genetic contributions to socioeconomic status and intelligence. *Intelligence* 2014; **44**: 26–32.
15 Benjamin DJ, Cesarini D, van der Loos MJ, Dawes CT, Koellinger PD, Magnusson PK *et al.* The genetic architecture of economic and political preferences. *Proc Natl Acad Sci USA* 2012; **109**: 8026–8031.
16 Rietveld CA, Conley D, Eriksson N, Esko T, Medland SE, Vinkhuyzen AA *et al.* Replicability and robustness of genome-wide-association studies for behavioral traits. *Psychol Sci* 2014; **25**: 1975–1986.
17 Lee SH, Yang J, Goddard ME, Visscher PM, Wray NR. Estimation of pleiotropy between complex diseases using single-nucleotide polymorphism-derived genomic relationships and restricted maximum likelihood. *Bioinforma Oxf Engl* 2012; **28**: 2540–2542.
18 White KR. The relation between socioeconomic status and academic achievement. *Psychol Bull* 1982; **91**: 461–481.
19 Sirin SR. Socioeconomic status and academic achievement: a meta-analytic review of research. *Rev Educ Res* 2005; **75**: 417–453.
20 Plomin R, Deary IJ. Genetics and intelligence differences: five special findings. *Mol Psychiatry* 2014. doi:10.1038/mp.2014.105.

21 Wray NR, Lee SH, Mehta D, Vinkhuyzen AA, Dudbridge F, Middeldorp CM. Polygenic methods and their application to psychiatric disorders and related traits. *J Child Psychol Psychiatry* 2014; **55**: 1068–1087.

22 Plomin R, Simpson MA. The future of genomics for developmentalists. *Dev Psychopathol* 2013; **25**: 1263–1278.

23 Dudbridge F. Power and predictive accuracy of polygenic risk scores. *PLoS Genet* 2013; **9**: e1003348.

24 Bartels M, Rietveld MJH, Van Baal GCM, Boomsma DI. Heritability of educational achievement in 12-year-olds and the overlap with cognitive ability. *Twin Res Hum Genet* 2002; **5**: 544–553.

25 Deary IJ, Strand S, Smith P, Fernandes C. Intelligence and educational achievement. *Intelligence* 2007; **35**: 13–21.

26 Benyamin B, Pourcain B, Davis OS, Davies G, Hansell NK, Brion MJ et al. Childhood intelligence is heritable, highly polygenic and associated with FNBP1L. *Mol Psychiatry* 2014; **19**: 253–258.

27 Trzaskowski M, Harlaar N, Arden R, Krapohl E, Rimfeld K, McMillan A et al. Genetic influence on family socioeconomic status and children's intelligence. *Intelligence* 2014; **42**: 83–88.

28 Haworth CMA, Davis OSP, Plomin R. Twins Early Development Study (TEDS): a genetically sensitive investigation of cognitive and behavioral development from childhood to young adulthood. *Twin Res Hum Genet* 2013; **16**: 117–125.

29 Oliver BR, Plomin R. Twins' Early Development Study (TEDS): a multivariate, longitudinal genetic investigation of language, cognition and behavior problems from childhood through adolescence. *Twin Res Hum Genet* 2007; **10**: 96–105.

30 Kovas Y, Haworth CMA, Dale PS, Plomin R. The genetic and environmental origins of learning abilities and disabilities in the early school years. *Monogr Soc Res Child Dev* 2007; **72**, vii, 1–144.

31 Trzaskowski M, Eley TC, Davis OS, Doherty SJ, Hanscombe KB, Meaburn EL et al. First genome-wide association study on anxiety-related behaviours in childhood. *PLoS One* 2013; **8**: e58676.

32 Howie BN, Donnelly P, Marchini J. A flexible and accurate genotype imputation method for the next generation of genome-wide association studies. *PLoS Genet* 2009; **5**: e1000529.

33 Fellay J, Shianna KV, Ge D, Colombo S, Ledergerber B, Weale M et al. A whole-genome association study of major determinants for host control of HIV-1. *Science* 2007; **317**: 944–947.

34 Patterson N, Price AL, Reich D. Population structure and eigenanalysis. *PLoS Genet* 2006; **2**: e190.

35 National pupil database - GOV.UK. Available at https://www.gov.uk/government/collections/national-pupil-database.

36 Hanscombe KB, Trzaskowski M, Haworth CM, Davis OS, Dale PS, Plomin R et al. Socioeconomic status (SES) and children's intelligence (IQ): in a UK-representative sample SES moderates the environmental, not genetic, effect on IQ. *PLoS One* 2012; **7**: e30320.

37 Raven J, Court J, Raven J. *Manual for Raven's Progressive Matrices and Vocabulary Scales*. Oxford University Press: Oxford, 1996.

38 Raven J, Court J, Raven J. *Manual for Raven's Progressive Matrices*. HK Lewis: London, 1998.

39 Raven J, Raven J, Court J. *Mill Hill Vocabulary Scale*. OPP, 1998.

40 Office for National Statistics, United Kingdom. *Standard occupational classification 2000: Structure and description of unit groups*. Stationery Office: London, UK, 2000.

41 Office for National Statistics, United Kingdom. *Standard Occupational Classification 2000: The coding index*. Stationery Office: London, UK, 2000.

42 Trzaskowski M, Yang J, Visscher PM, Plomin R. DNA evidence for strong genetic stability and increasing heritability of intelligence from age 7 to 12. *Mol Psychiatry* 2013; **19**: 380–384.

43 R Core Team. *R: A Language and Environment for Statistical Computing*. R Foundation for Statistical Computing, 2013 Available at http://www.R-project.org/.

44 Purcell S, Neale B, Todd-Brown K, Thomas L, Ferreira MA, Bender D et al. PLINK: a tool set for whole-genome association and population-based linkage analyses. *Am J Hum Genet* 2007; **81**: 559–575.

45 Plomin R, DeFries JC, Knopik VS, Neiderhiser JM. *Behavioral Genetics*. 6th ed. Worth Publishers: New York, 2013.

46 Johnson W, McGue M, Iacono WG. Genetic and environmental influences on academic achievement trajectories during adolescence. *Dev Psychol* 2006; **42**: 514–532.

47 Wray NR, Yang J, Hayes BJ, Price AL, Goddard ME, Visscher PM. Pitfalls of predicting complex traits from SNPs. *Nat Rev Genet* 2013; **14**: 507–515.

48 Krapohl E, Rimfeld K, Shakeshaft NG, Trzaskowski M, McMillan A, Pingault JB et al. The high heritability of educational achievement reflects many genetically influenced traits, not just intelligence. *Proc Natl Acad Sci USA* 2014; **111**: 15273–15278.

49 De Zeeuw EL, van Beijsterveldt CEM, Glasner TJ, Bartels M, Ehli EA, Davies GE et al. Polygenic scores associated with educational attainment in adults predict educational achievement and ADHD symptoms in children. *Am J Med Genet B Neuropsychiatr Genet* 2014; **165**: 510–520.

50 Kapur S, Phillips AG, Insel TR. Why has it taken so long for biological psychiatry to develop clinical tests and what to do about it? *Mol Psychiatry* 2012; **17**: 1174–1179.

51 Gaugler T, Klei L, Sanders SJ, Bodea CA, Goldberg AP, Lee AB et al. Most genetic risk for autism resides with common variation. *Nat Genet* 2014; **46**: 881–885.

52 Yang L, Neale BM, Liu L, Lee SH, Wray NR, Ji N et al. Polygenic transmission and complex neuro developmental network for attention deficit hyperactivity disorder: genome-wide association study of both common and rare variants. *Am J Med Genet B Neuropsychiatr Genet* 2013; **162B**: 419–430.

53 Falconer DS. *Introduction to Quantitative Genetics*. Ronald: New York, NY, USA, 1960.

54 Haworth CMA, Davis OSP. From observational to dynamic genetics. *Front Genet* 2014; **5**: 6.

55 Heath AC, Berg K, Eaves LJ, Solaas MH, Corey LA, Sundet J et al. Education policy and the heritability of educational attainment. *Nature* 1985; **314**: 734–736.

56 Tucker-Drob EM, Briley DA. Continuity of genetic and environmental influences on cognition across the life span: a meta-analysis of longitudinal twin and adoption studies. *Psychol Bull* 2014; **140**: 949–979.

57 Plomin R, DeFries JC, Loehlin JC. Genotype-environment interaction and correlation in the analysis of human behavior. *Psychol Bull* 1977; **84**: 309–322.

58 Kendler KS, Baker JH. Genetic influences on measures of the environment: a systematic review. *Psychol Med* 2007; **37**: 615–626.

59 Plomin R. *Genetics and Experience: The Interplay Between Nature and Nurture*. Sage Publications, Inc: Thousand Oaks, CA, USA, 1994.

60 Plomin R, Bergeman CS. The nature of nurture: genetic influence on 'environmental' measures. *Behav Brain Sci* 1991; **14**: 373–386.

61 Vinkhuyzen AAE, van der Sluis S, de Geus EJC, Boomsma DI, Posthuma D. Genetic influences on 'environmental' factors. *Genes Brain Behav* 2010; **9**: 276–287.

62 Young MD. *The Rise of the Meritocracy*. Thames and Hudson: London, UK, 1958.

63 Saunders P. *Social Mobility Delusions: Why So Much of What Politicians Say about Social Mobility in Britain Is Wrong, Misleading or Unreliable*. Civitas: London, UK, 2012.

64 Asbury K, Plomin R. *G is for Genes: The Impact of Genetics on Education and Achievement*. Wiley-Blackwell: Chichester, UK, 2013.

Supplementary Information accompanies the paper on the Molecular Psychiatry website (http://www.nature.com/mp)