Educational attainment polygenic scores in Hungary: evidence for validity and a historical gene-environment interaction

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Abstract

Educational attainment is a substantially heritable trait, and it has recently been linked to specific genetic variants by genome-wide association studies (GWASs). However, some variants may index social stratification, and polygenic score (PGS) heritability may differ across cohorts reflecting the changing relative influence of genetic and environmental influences on educational attainment over time. We used a Hungarian (N=829) sample of healthy volunteers to assess the validity of the most recent educational attainment polygenic score in a population culturally and genetically different from the one used in GWAS discovery, as well as changes in PGS heritability over time. We used an English (N=976) sample with identical measurement protocols as comparison.

We found that the PGS is valid in Hungary, accounting for 2-6.5% of the variance in educational attainment. We also replicated previous Estonian findings about generally increased PGS heritability in those attaining higher education after the fall of Communism, with PGS heritability up to 6.5% in the youngest cohort. In a comparable English sample the same PGS

accounted for 9-11% of educational attainment variance. Our results provide evidence that polygenic scores for educational attainment are valid in diverse European populations. Our findings also provide further evidence that the fall of Communism, possibly along with other historical changes in education policy, was the source of a gene-environment interaction through which genetic factors became more important for higher educational attainment in those who graduated high school after this event.

Key words: educational attainment, polygenic score, heritability, gene-environment interaction

Introduction

Educational attainment is a key psychological and sociological variable, which comprises an important part of socioeconomic status and it is positively correlated with income and health, but negatively with crime and welfare dependency (Behrman et al., 1997). Educational attaiment is moderately heritable, with a substantial shared environmental component (Branigan et al., 2013) and it shares substantial, but not all genetic variance with cognitive abilities (Krapohl et al., 2014).

Early reports on the heritability of educational attainment were derived from family pedigree studies, most notably twin studies (Cesarini and Visscher, 2017). Recently, however, the heritability of educational attainment was confirmed with molecular genetic methods. Single nucleotide polymorphism (SNP) heritability studies (Davies et al., 2016; Hill et al., 2016) confirmed that genetic similarity between non-related people is positively associated with the phenotypic similarity of educational attainment, with common genotyped SNPs accounting for up to 20% of the total variance. Large-scale genome-wide association (GWA) studies linked specific genetic variants to educational attainment (Rietveld et al., 2013; Okbay et al., 2016; Lee et al., 2018). Polygenic scores based on GWAS results confirmed the predictive value of these genetic variants (also termed polygenic score [PGS] heritability), typically accounting for up to 10% of the phenotypic variance in educational attainment itself (Domingue et al., 2015; Allegrini et al., 2018), cognitive abilities (de Zeeuw et al., 2014; Selzam et al., 2016; Allegrini et al., 2018), social mobility (Ayorech et al., 2017) and overall socioeconomic success (Belsky et al., 2016; Belsky et al., 2018) in independent samples.

However, the association between genetic variants identified by GWAS and phenotypes may be mediated or moderated by environmental variables in at least two ways.

First, SNP or PGS heritability may partially or fully reflect shared environmental rather than true genetic effects through passive gene-environment correlation (Young, 2019), with the genetic variants identified by GWAS or used to calculate the relatedness matrix reflecting social stratification (that is, belonging to certain extended families or social classes which exert the true causal effect). Within-family comparisons usually reveal a weaker but still significant effect

of PGSs between siblings than in the general population (Belsky et al., 2018; Selzam et al., 2019), consistent with some social stratification but also with substantial true genetic effects. Another possible test of social stratification-free PGS heritability estimation is the use of populations in which the genetic signal of social class is presumably different than in the GWAS discovery population. The validity of education attaiment PGSs has been demonstrated among others in samples of Icelanders (Kong et al., 2018), Estonians (Rimfeld et al., 2018) and African Americans (Domingue et al., 2015; Lee et al., 2018; Rabinowitz et al., 2019), usually with significant but lower validity than in cohorts similar to GWAS discovery samples (Allegrini et al., 2018).
Second, neither the pedigree-based or SNP heritability of educational attainment nor the external validity of polygenic scores is a biological constant. There is evidence that between-country differences (Lee et al., 2018) and within-country changes in education policy (Heath et al., 1985) as well as the attendance of different types of schools (Trejo et al., 2018) may affect the heritability of educational attainment (gene-environment interaction). In other words, the relative importance of genetic and environmental effects on individual differences in educational attainment is affected by the characteristics of the environment. It has been argued (Hauser et al., 2002; Nielsen, 2008; Conley et al., 2015) that a high heritability of educational attainment is a sign of a meritocratic educational system, because attainment is determined by innate abilities and preferences instead of shared environmental effects such as social class or parental income. The social changes due to the fall of Communism (FoC) in the former Eastern Block may have had a particular effect on educational meritocracy. In line with this hypothesis, a recent Estonian study (Rimfeld et al., 2018) found that the SNP and PGS heritability of educational attainment was higher in Estonians who attended school after FoC, suggesting that the educational system in Estonia has become more meritocratic.
We estimated the external validity of an educational attainment polygenic score based on a GWAS of American and British individuals (except for 36631 Estonians) (Lee et al., 2018) in a sample of over 800 Hungarians with both genetic and educational attainment data. Hungary is similar to Estonia in the sense that it was part of the Warsaw Pact until 1989, where access to higher education was limited and in part regulated according to political considerations instead of meritocratic principles (Ladányi, 1995; Hrubos et al., 2016). In this sample, we were able to demonstrate significant external validity of the Lee et al. (EA3) educational ability PGS. This PGS accounted for only ~2% of the variance in educational attainment, as opposed to 10-12% in Anglo-Saxon replication samples in the literature and over 9% in an English sample with similar characteristics to ours. However, the PGS explained 6.5% of educational attainment variance in the subpopulation of participants who finished high school after FoC and since then reached a high enough age to graduate from college before 2004-2005 at the time of the data collection.

Methods

We used genetic data and self-reported level of education collected in the NewMood study (New Molecules in Mood Disorders, Sixth Framework Program of the European Union, LSHM-CT-2004-503474) to validate the EA3 polygenic score in Hungarian participants (Budapest sample, N=829). We used data from English participants from NewMood (Manchester sample, N=976) to provide a comparison group with an identical phenotypic and genotypic data collection regimen. Participants of 18-60 years of age were recruited through advertisements, general practices and a website. Full details of the recruitment strategy and criteria have been published previously (Lazary et al., 2008; Juhasz et al., 2009; Juhasz et al., 2011). For this study the experimental cohort was limited to unrelated individuals of self-reported European white ancestry as this was the largest ethnic group.

The study was approved by the local Ethics Committees (Scientific and Research Ethics Committee of the Medical Research Council, Budapest, Hungary; and North Manchester Local Research Ethics Committee, Manchester, UK) and was carried out in accordance with the Declaration of Helsinki and all relevant rules and regulations as part of the NewMood study. All participants provided written informed consent.

Educational attainment

Participants filled out close-ended questions about whether they attained certain educational levels. These levels were „No qualification", „O-levels", „A-levels", „Degree" „Professional qualification" and „Other (please specify)". In the Hungarian version of the questionnaire, British educational levels were translated as their Hungarian counterparts (O-levels as „szakmunkásképző", vocational education; A-levels as „érettségi", high school diploma; Professional qualification as „szakvizsga", a vocational or specialist qualification). If a participant gave a response about an „Other" qualification, it was decided individually which of the other educational levels this corresponds to based on the participant's comments. The educational level of each participant was coded as a nominal variable.

Age groups

For ethical reasons, we did not store data about the birth year of our participants or exactly when they were interviewed. However, given that data collection was performed in 2004 and 2005, we can estimate the birth year of each participant within a one year margin based on self-reported age at data collection. We divided our participants in three age groups based on their age at FoC and whether they were old enough to have realized their potential for educational attainment by the time data was collected: 1) YPostC (young participants attending high school after FoC): age <24 at data collection (earliest possible birth year in 1981, possibly not old enough to have attained a university education); 2) PostC (participants attending high school mostly after FoC): age 24-31 years at data collection (birth year 1973-1981, at most 16 years old

at FoC in Hungary and old enough to have attained a university education); 3) PreC (participants attending high school mostly before FoC): age at least 32 years at data collection (latest possible birth year in 1973, at least 16 years old at FoC in Hungary). We provide detailed statistics about the sample sizes, ages and educational attainments of these groups in Table 1. We hypothesized that the validity of the EA3 polygenic score will be different in these age groups in Hungary, but not in England, due to a gene-environment interaction induced by the historical political changes in Hungary and their effects on the educational system (Rimfeld et al., 2018).

	Budapest				**Manchester**			
	YPostC	PostC	PreC	All participants	YPostC	PostC	PreC	All participants
EDUCATION								
No qualification	1	1	4	6	2	5	24	31
Professional qualification	1	1	1	4	5	14	70	89
O-levels or equivalent	0	10	20	36	16	50	144	211
A-levels or equivalent	259	114	109	512	70	32	89	192
University degree	14	95	145	271	107	121	225	453
All participants	275	221	279	829	200	222	552	976
AGE								
18	5	0	0	5	23	0	0	23
19	25	0	0	25	45	0	0	45
20	65	0	0	65	36	0	0	36
21	86	0	0	86	33	0	0	33
22	61	0	0	61	30	0	0	30
23	33	0	0	33	33	0	0	33
24	0	25	0	25	0	32	0	32
25	0	19	0	19	0	25	0	25
26	0	31	0	31	0	35	0	35
27	0	19	0	19	0	27	0	27
28	0	36	0	36	0	29	0	29
29	0	22	0	22	0	22	0	22
30	0	22	0	22	0	33	0	33
31	0	26	0	26	0	19	0	19
32	0	21	0	21	0	36	0	36
33-35	0	0	52	52	0	0	79	79
35-40	0	0	78	78	0	0	151	151
40-45	0	0	53	53	0	0	145	145
45-50	0	0	45	45	0	0	95	95
50-55	0	0	36	36	0	0	18	18
55-60	0	0	15	15	0	0	28	28
All participants	275	221	279	775	200	258	516	974

Table 1. The distribution of age and educational level across age groups. Note that the 'All participants' columns under 'Education' also contain participants with no age data, who were consequently not assigned to either age group ($N_{Budapest}$=54, $N_{Manchester}$=2). For the same reason, counts in these columns are not equal to the sum of the age group columns and the total count of 'All participants' is different for the 'Education' and 'Age' panels.

Genotyping and polygenic score extraction

Genomic DNA was extracted from buccal swabs collected by cytology brush (Cytobrush plus C0012; Durbin PLC). Genotyping was carried out using Illumina's CoreExom PsychChip, genomic positions were defined according to the build GRCh37/hg19. Further details of imputation and quality control were published elsewhere (Eszlari et al., 2019).

Polygenic scores were constructed using PRSice-2 and publicly available summary SNP effect size data (Lee et al., 2018), downloaded from https://www.thessgac.org/data. We used the effect sizes which were constructed without 23andMe data but released for all SNPs, not only the top 10000. We used the stable 1.26.0 Genome-wide Complex Trait Analysis (GCTA) version for the calculation of SNP heritability with the 10 first principal components calculated from genomic data. A minor allele frequency (MAF) cutoff of 0.05 was used.

Results

Genomic-relationship-matrix restricted maximum likelihood method (GREML-GCTA) SNP heritabilities indicated that all common SNPs accounted for 30.5% of educational attainment variance in the total Budapest sample (SE=25%, p=0.09) and 58% in the Manchester sample (SE=20%, p=0.01). When we excluded participants younger than 24 years old and consequently possibly still in education, SNP heritability was 72% (SE=40%, p=0.03) and 40% (SE=27%, p=0.05) in the Budapest and Manchester sample, respectively. We note, however, that our sample sizes were below the several thousand individuals usually considered necessary for this type of analysis (Knopik et al., 2016). GCTA models failed to properly converge when we further restricted samples to single age groups due to very low sample sizes, and therefore we did not perform SNP heritability analyses within these separately.

The EA3 PGS was significantly associated with highest education level attained, but with much higher validity in the Manchester sample (Budapest: R^2=2%, p=0.0009; Manchester: R^2=9.2%, p= $10*10^{-5}$; all p-values based on random permutations in PRSice) (Figure 1).

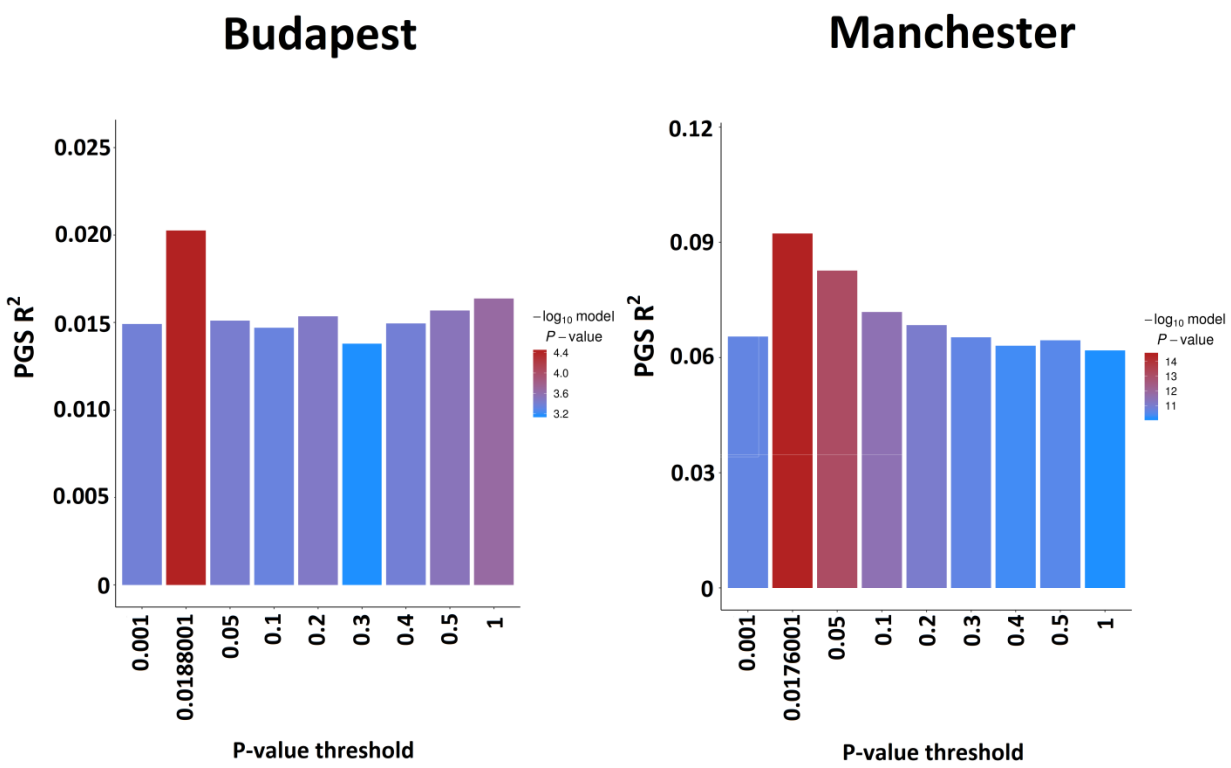

Figure 1. Educational attainment variance explained by PGSs at various GWAS p-value thresholds in the Budapest (left) and Manchester (right) samples.

The PGS heritability of educational attainment was subject to both age group and country effects (Figure 2). The EA3 polygenic score accounted for 3.7% of the variance of educational attainment in Hungarians who were at least 16 years old in 1989, but 6.5% among those who were at most 16 years old at that time, but at least 24 years old during data collection, sufficient for the attainment of a college degree. Among English participants at least 24 years old during data collection, PGS heritability was 11% among those at least 16 years old in 1989, and 9.3% among those at most 16 years old. PGS heritability among those under 24 years old at data collection was substantially different across countries (1.2% in the Budapest sample and 6.1% in the Manchester sample), but educational attainment at this age had minimal variance in Hungarians (over 90% completed A-level equivalents, see Table 1).

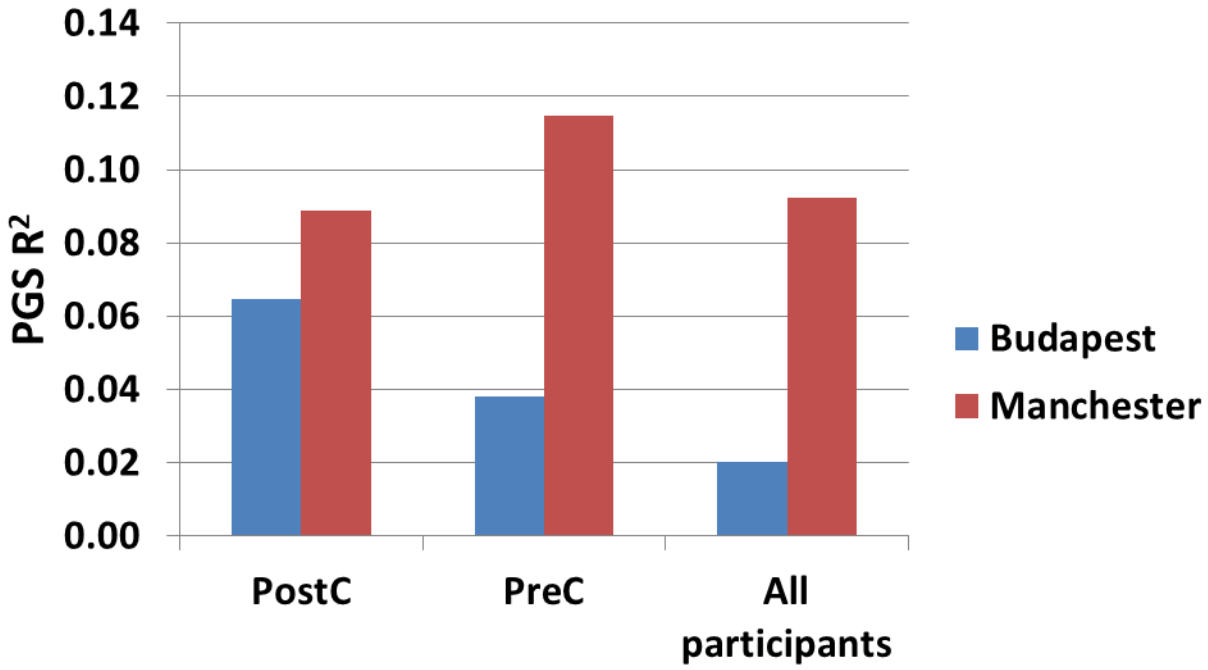

Figure 2. Educational attainment variance explained by the best-fit EA3 polygenic score in Hungary and England among participants of different ages at the time of the fall of Communism in Hungary. PostC and PreC refers to participants at most and at least 16 years old at FoC, respectively (see Table 1). „All participants" also includes participants with no available age data.

The significance of country and age group differences in the PGS heritability of educational attainment was assessed by taking the square root of R^2 values to obtain correlation coefficients, and comparing these using Fisher's r-to-z method (Rimfeld et al., 2018). PGS heritability was significantly higher in both the full Manchester sample and in its either age group than the full-sample Budapest PGS heritability. The PGS heritability was also significantly higher in Manchester than in Budapest among those at least 16 years old in 1989, but there was no difference in the younger age group. The full set of comparisons is shown in Table 2 (note the differences in statistical power resulting from different sample sizes, see Table 1).

	BP_PostC	BP_PreC	BP_All	MAN_ PostC	MAN-PreC	MAN_All
BP_ PostC		0.69	1.54	0.51	1.14	0.71
BP_PreC	0.4902		0.4354	1.27	**2.08**	1.71
BP_All	0.1236	0.78		**2.29**	**3.72**	**3.61**
MAN_PostC	0.6101	0.2041	**0.022**		0.59	0.09
MAN-PreC	0.2543	**0.0375**	**0.0002**	0.5552		0.6
MAN_All	0.4777	0.0873	**0.0003**	0.9283	0.4777	

Table 2. Age and country differences in the PGS heritability of educational attainment. The upper diagonals contains z-values and the lower diagonal contains p-values for the relevant comparisons (bold denotes significance at p-value<*0.05*). BP: Budapest sample, MAN: Manchester sample. PostC and PreC indicate age groups, see Table 1. „All" indicates all participants, including those with no age data.

Figure 3 shows group means and the dispersion of PGSs by country, age group and educational attainment level. The highest mean values were always found in university-educated participants. High school-educated participants had lower means, followed by individuals with vocational educations (O-levels in the Manchester sample). Individuals with professional educations had somewhat higher means. We note, however, that the low number of participants with low educational attainments led to less precision in estimating mean PGSs. Note especially the limited educational attainment variability in the Budapest sample, with most participants having either high school or university educations.

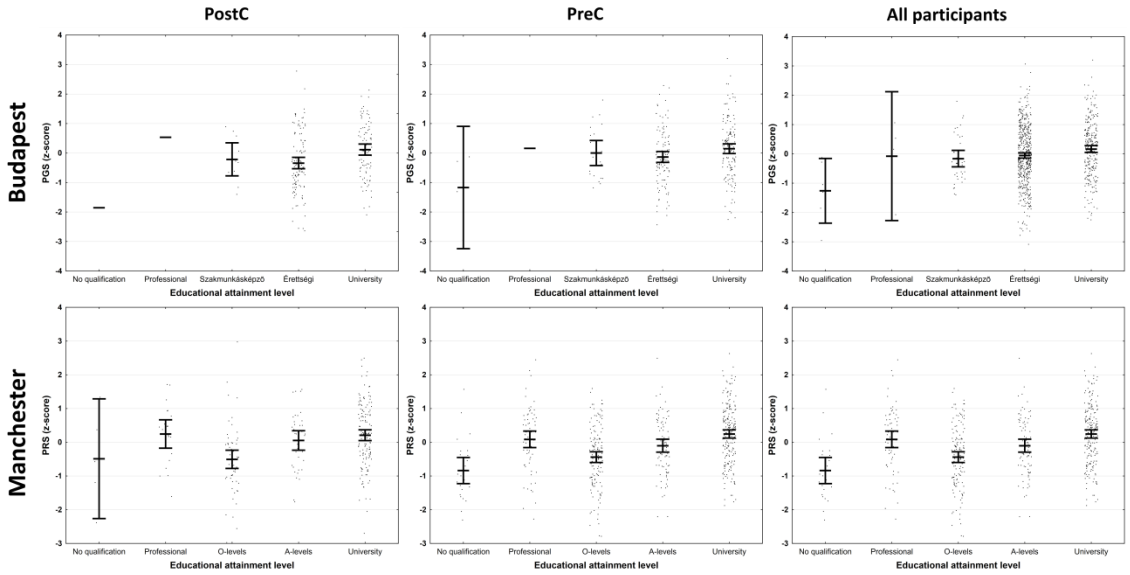

Figure 3. PGSs by country and educational attainment levels. PostC and PreC indicate age groups, see Table 1. „All participants" includes partipants with no age data. Educational attainment categories are equivalent, but indicated with the original questionnaire terms for authenticity. In the Budapest sample, „Szakmunkásképző" refers to a vocationally-oriented high school education, while „Érettségi" refers to high school education with a successful final standardized examination. Central horizontal lines show group means and whiskers indicate 95% confidence intervals (CIs), overplotted with raw data. Note that some Hungarian groups were represented by a single participant which did not permit the estimation of CIs.

We set the age cutoff between PreC and PostC groups at 32 years in 2004-2005 (16-17 years old at FoC) following Rimfeld et al, but still somewhat arbitrarily. In order to test the effect of different age cutoffs on the results, we calculated PGS heritability by 5-year age bins and also performed a specification curve analysis using all possible PreC/PostC age cutoffs between 26-45 years in 2004-2005 (Figure 4, Table 3). In line with previous analyses, we never included those under 24 years old in either the PreC or the PostC groups.

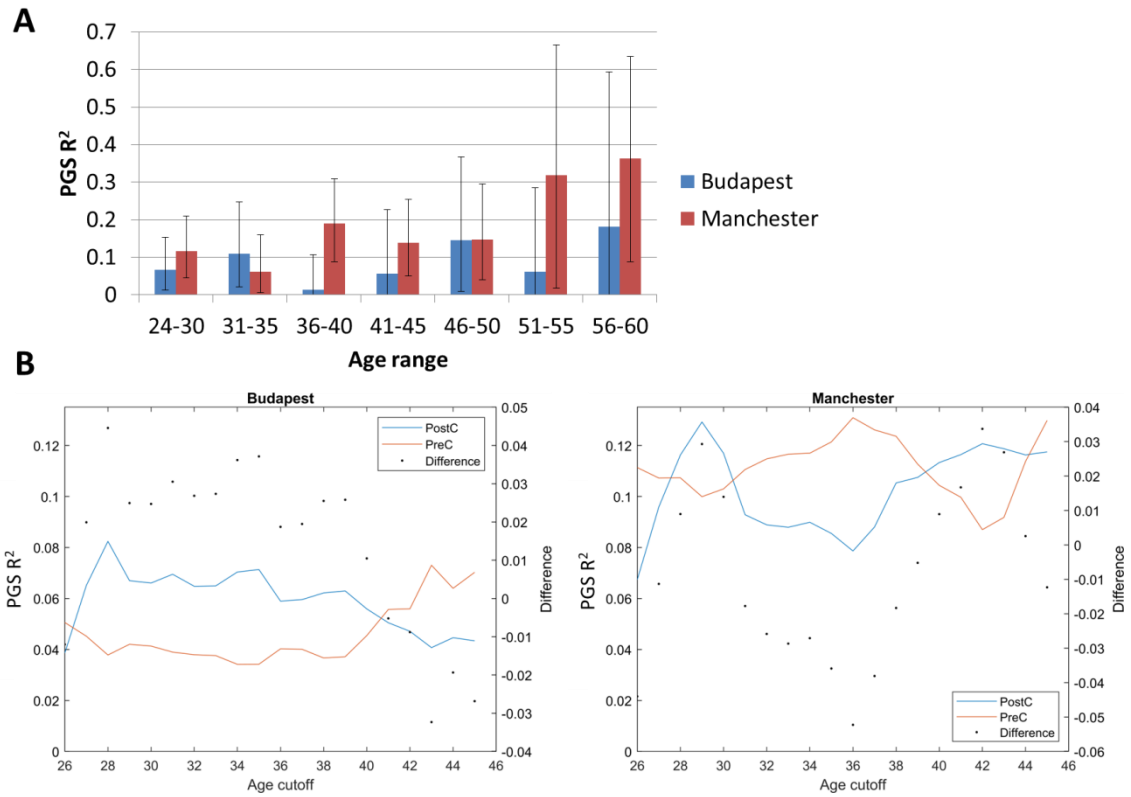

Figure 4. Panel A: The PGS heritability of educational attainment within 5-year age bins in both subsamples. Confidence intervals were determined by taking the positive square root of the R^2 values, calculating the 95% confidence intervals of the resulting correlation coefficient and squaring the values at its limits. Because negative R^2 values are not defined, the lower confidence intervals of non-significant values was set to 0. Detailed data about subsample composition is given in Table 3. Panel B: Specification curve analysis of the effects of PreC/PostC age cutoffs on PGS heritability in the Budapest and Manchester samples. Axis Y shows PGS heritability in the PreC and PostC groups if the age cutoff (age in 2004 or 2005 at data collection) indicated on axis X was used. A secondary Y axis and dots show the PostC-PreC difference.

	Age group	24-30	31-35	36-40	41-45	46-50	51-55	56-60
Budapest	N	174	99	78	53	45	36	15
	R2	0.066	0.110	0.013	0.056	0.145	0.062	0.181
	Upper CI	0.153	0.247	0.108	0.227	0.368	0.284	0.593
	Lower CI	0.013	0.021	0.000	0.000	0.010	0.000	0.000
	No education (%)	0.57	0.00	0.00	3.77	4.44	0.00	0.00
	Professional (%)	0.00	1.01	0.00	1.89	0.00	0.00	0.00
	O-level or equivalent (%)	2.30	7.07	3.85	1.89	11.11	19.44	20.00
	A-level or equivalent (%)	52.87	44.44	42.31	39.62	35.56	38.89	20.00
	University (%)	44.25	47.47	53.85	52.83	48.89	41.67	60.00
Manchester	N	203	134	151	145	95	18	28
	R2	0.117	0.061	0.189	0.139	0.148	0.318	0.363
	Upper CI	0.210	0.160	0.309	0.255	0.296	0.666	0.635
	Lower CI	0.046	0.007	0.088	0.050	0.039	0.017	0.088
	No education (%)	2.46	0.75	0.66	6.21	7.37	5.56	17.86
	Professional (%)	6.40	11.94	7.95	15.17	17.89	0.00	14.29
	O-level or equivalent (%)	22.17	23.13	30.46	24.14	26.32	22.22	28.57
	A-level or equivalent (%)	15.76	13.43	15.89	17.93	15.79	22.22	7.14
	University (%)	53.20	50.75	45.03	36.55	32.63	50.00	32.14

Table 3. Sample sizes, educational attainment frequencies, PGS heritabilities and their 95% confidence intervals by country and 5-year age cohort.

We found trend level age subgroup differences in the PGS heritability of educational attainment (Figure 4, Panel A). In Hungary, the lowest PGS heritability was found in the relatively numerous 36-45 year old cohort (born between 1959/1960 and 1968/1969), and it was higher in the oldest cohorts of the sample. In England, PGS heritability was consistently higher in older cohorts, with a similar maximum in the oldest cohorts. It must be noted, however, that many age subgroups had small sample sizes and participants with different educational attainment levels were not equally represented in each subgroup, leading to range restriction effects (Table 3).

The differences in PreC/PostC PGS heritabilities were not very sensitive to where exactly the cutoff was placed in wide ranges. In the Budapest sample, variance explained remained in the 6-7.5% range for the PostC group and 3.5-4.5% in the PreC group if age cutoffs of 28-39 years (birth years 1965-1977, 12-24 years old at FoC) instead of 32 years (birth years: 1972-1973, 16-17 years old at FoC) were used. However, the inclusion of even older participants in the PostC group resulted in the reversal of the gap. In the Manchester sample, no systematic effects were seen in PostC-PreC PGS heritability differences as a function of age cutoff.

Discussion

Ours is the first study to estimate the external validity of educational attainment PGSs in Hungary, and the second to do so in a former Warsaw Pact country. We are also unaware of any other behavior genetic study about educational attainment in Hungarians. We found that 1) genetic variants from a recent GWAS that predict educational attainment in Western European and American validation samples also do so in Hungary, but with reduced effect sizes 2) similar to a previous Estonian study (Rimfeld et al., 2018), we found evidence for a higher PGS heritability in Hungary among those who were at most 16 years old at the time of FoC could consequently already apply to and attend university in a democratic political system.
PGS heritabilities were similar in Hungary to what was reported in Estonia (full sample R^2=2% in our study and 2.3% in Rimfeld et al; among those graduating high school after FoC 6.5% in our study and 6.1% in Rimfeld et al). In our English control group, however, PGS heritability was higher (9-11%) than even in young Hungarians. In this Discussion, we hypothesize that 1) reduced PGS heritability in Hungary and Estonia may in part reflect the lack of social stratification effects compared to the Anglo-Saxon replication samples more frequently used in the literature 2) increased within-country PGS validity after FoC, present in both an earlier Estonian and the current Hungarian study but absent in our English comparison sample, may be the result of increased educational meritocracy in the investigated period.
Educational attainment is affected by the shared environment (Branigan et al., 2013). Polygenic scores may reflect both truly genetic and shared environmental influence (Kong et al., 2018; Young et al., 2018). This is because higher educational attainment in children with higher polygenic scores may be because the PGS is comprised of genetic variants causing better abilities in the child, but also because it indexes the child's belonging to families with higher socioeconomic status, which are the direct cause of higher educational attainment through environmental effects – that is, PGS may reflect social stratification. While the between-sibling validity of polygenic scores (Domingue et al., 2015; Belsky et al., 2018; Selzam et al., 2019) excludes the possibility that educational attainment polygenic scores purely reflect population stratification, the reduction of effect sizes in this design has been consistent with an up to 50% contribution of such effects to PGS validity in the general population (Selzam et al., 2019; Young, 2019). While we are unaware of any study which quantifies between-country variations in the genetic signal of social class or other vectors of shared environmental effects on educational achievement, due to the highly divergent histories of these countries we find it unlikely that social stratification-driven effects on educational attainment are associated with similar genetic variants in Hungarian, Estonian and English samples. The degree of reduction in the PGS heritability in former Warsaw Pact countries relative to Anglo-Saxon samples (9-11% in the current sample, over 10% in a larger British sample (Allegrini et al., 2019; Selzam et al., 2019)

versus 6-6.5% in young Hungarians and Estonians) is consistent with the roughly 50% reduction seen in recent within-family studies (Young et al., 2018; Selzam et al., 2019) which by design exclude social stratification, and the remaining proportion may index true genetic effects. We note, however, that genetic nurture (a true genetic effect on the parents causing a behavioral phenotype which increases offspring educational attainment) may still contribute to PGS heritability in the latter countries (Kong et al., 2018).

While social stratification effects can inflate PGS heritability estimates, a truly higher heritability of educational attainment can be the sign of educational meritocracy (Hauser et al., 2002; Nielsen, 2008; Conley et al., 2015), that is, a system in which higher education levels are attained by those with better innate ability, not by those with, for instance, better-off families or better political connections. While we are unable to quantitatively compare educational meritocracy in the current British, Hungarian and Estonian educational systems, we note that just like in Estonia, increased educational meritocracy in the investigated period after FoC may account for increased PGS heritability (Rimfeld et al., 2018). Before FoC, the Hungarian higher education system consisted exclusively of state-operated institutions (Hrubos et al., 2016). Universities belonged to eight different ministries until the 1993 law on education which unified their control in a new Ministry of Education. Entrance was based on central, written examinations which also served as high school graduation examinations, in addition to a personal, oral entrance examination with the university's committee. These committees were staffed by university professors, but often also by a representative of the Communist Party and university students were represented by a member of the Communist Youth Association (KISZ) before 1985. Explicit quotas of over 50% were in place for the children of workers and peasants until 1962 (Ladányi, 1995). After 1962 , such affirmative action policies were eliminated but the children of workers and peasants were still preferred over other applicants with equal qualifications, and the children of „martyrs of the workers' movement" and the recipients of certain awards could automatically gain university admission.

A series of changes took place in the years immediately preceding and following FoC. Private and religious institutions became legal in 1991, and by 1998 there were 55 state-operated and 34 other institutions (including 28 religious ones) in Hungary (Hrubos et al., 2016). A distinction between two levels of higher education was made: a 3-year degree („főiskola") and a 5-year degree („egyetem", literally „university"). Oral entrance examinations could now in some cases be substituted entirely by the results of central written examinations. This became the dominant policy in engineering and agricultural faculties in the early '90s (Ladányi, 1995). Even if universities still chose to organize oral entrance examinations, the enrollment policy was designed to be more open, and political representatives were no longer present in committees. Student enrollment steadily grew, by 40% between 1989 and 2005 (Hrubos et al., 2016). Higher education remained free, except for a brief suspension due to austerity measures in 1996-1998.

In sum, the selection of university students underwent both qualitative and quantitive changes after FoC. The previous Estonian study on the same effects (Rimfeld et al., 2018) invokes increases in educational meritocracy – first of all, the abandonment of political considerations in university admissions – as the chief driver of increased PGS heritability after FoC. Because similar changes took place in Hungary, this can plausibily explain at least some of the increased PGS heritability.

Our work suffers from a number of limitations. The largest of these is the modest size of our sample, which allowed limited statistical power to detect subgroup effects and SNP heritability (Table 2). This was especially pronounced when studying differences of PGS heritability across 5-year age bins, and we emphasize that our results about within-PreC age subgroup differences in PGS heritability is a finding that requires replication. The sufficiently powered study by Rimfeld et al did not find a similar effect for socioeconomic status, the PGS heritability of which was consistently low in older Estonian cohorts. We note, however, that large, approximately population-representative genetic databases like the Estonian Biobank are rare in Central and Eastern Europe, and therefore ours is probably the best Hungarian dataset currently available to test our hypotheses. Second, our database was not nationally representative and most educational attainment differences existed between completion and non-completion of college. This may have exerted a downward bias on our PGS validity estimates due to range restriction, especially in the Hungarian sample. We are unaware of any statistical method which can correct for restriction of range in a nominal variable, and therefore did not attempt such a correction. Third, the validity of the EA3 polygenic score in both countries was lower than average in participants with no age data and among those too young to have obtained a 5-year university degree. These differences were especially stark in the Budapest subsample. This suggests lower education and/or genetic data quality in those with missing age data, which may have also exerted a downward bias on our total Hungarian PGS validity estimate. Finally, the investigated after-FoC period ends in 2004-2005 at the time of data collection and our study does not investigate educational attainment after this time.

In sum, our works demonstrate that genetic variants discovered in mostly Anglo-Saxon GWAS samples also predict educational attainment in Hungary, where social stratification effects can likely be circumvented. While PGS heritability is lower, its effect size in young participants is consistent with the effects seen in within-family studies which also exclude social stratification. In line with Estonian data, individual genetic differences played a larger role shaping educational attainment in those graduating after the fall of Communism.

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Conflict of interest

Bill Deakin has share options in P1vital. He has also performed speaking engagements, research and consultancy for AstraZeneca, Autifony, Bristol-Myers Squibb, Eli Lilly, Janssen-Cilag, P1vital, Schering Plough, and Servier (all fees are paid to the University of Manchester to reimburse them for the time taken). All the other authors declare no conflict of interest.

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