The genetic correlation between educational attainment, intracranial volume and IQ is due to recent polygenic selection on general cognitive ability. Evidence for opposite directional selection on stature.

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Synopsis

This is the first paper to report evidence of a cross-population genetic correlation between educational attainment and IQ. Principal component analysis (PCA) was used to identify the underlying genetic structure resulting from recent directional selection. Converging evidence from two different genetic databases (1000 Genomes and ALFRED, comprising 14 populations and 8 racial groups, respectively) and two independent sets of genes (14 in total)found by GWAS to have a significant association with IQ and Educational Attainment, reveals a high correlation (around 0.9) between these two social science constructs across populations and ethnic groups. This correlation in turn provided convergent validity for the genetic measures identified with PCA. Two alleles associated with higher intracranial volume were positively correlated to the two PCs.

A separate analysis carried out on an independent set of alleles related to human stature suggests that this trait was subject to different directional selective pressures and provided evidence for the discriminant validity of alleles supposedly related to IQ and educational attainment.One-way ANOVA showed that the average frequencies of height increasing alleles for three racial groups (East Asian, Sub-Saharan African and European) differed significantly and that Africans had significantly higher frequencies than East Asians.

A significant negative genetic correlation (r around 0.9) between height and intelligence was found at a cross-population level, contrasting the generally positive correlation found within populations. Evolutionary explanations in terms of Allen's rule and the theory of cold winters are attempted. The GWAS hits for height were from studies carried out on different ethnic groups, and the converging results suggests that the same genes have similar effects across racial groups.

This paper provides evidence that Principal Component Analysis and ANOVA can be used to detect deviations from random drift and detect directional selection on polygenic traits in recent human evolutionary history.

Keywords : Intelligence; Educational attainment; Evolution; Polygenic adaptation

Introduction

A recent study (Piffer, 2013) provided evidence for recent selection on cognitive abilities in human populations. The author showed that human populations have different frequencies of alleles increasing educational attainment and IQ and that these frequencies are positively correlated with national IQs and national scores on standardized educational attainment tests. After principal component analysis (PCA) of 10 variants associated with educational attainment, a single component emerged that explained 45% of the variance. This component can be interpreted as indicating the strength of natural selection (Piffer, 2014).

That study relied on the assumption that educational attainment can be considered a proxy for intelligence or IQ. Indeed, selection for intelligence (as opposed to selection for educational attainment) is more likely to have occurred, because education is a recent cultural phenomenon, which was not accessible to the vast majority of the population until the modern era. Thus, the goal of this paper is to test the assumption that the principal component that emerged from population frequencies of educational attainment alleles reflects a genuine genetic background for higher intelligence.

In fact,general intelligence (*g*) is a good predictor of performance in educational achievement tests, particularly in subjects such as math and English, where it explained, respectively, 58.6% and 48% of the variance in a longitudinal study based on >70,000 English children (Deary et al, 2006). Kaufman et al (2012) found high correlations between measures of academic *g* and cognitive *g*.

There is a great deal of evidence that the same genes contribute to the heritability of IQ and educational attainment. A twin study by Tambs et al. (1989) found that genetic variance for educational attainment explained half of the genetic variance for IQ. A recent study based on a large sample of twins revealed a strong bivariate correlation (0.76- 0.94) between heritabilities of educational attainment and general intelligence (Calvin et al., 2012).

Thus, the hypothesis of this study is that genes influencing educational attainment were subject to the same selective pressures as the genes influencing IQ. This in turn would support the hypothesis that there was recent selection on general intelligence across human populations.

A prediction of this hypothesis is that the frequencies of IQ increasing alleles are correlated across populations to the principal component extracted from the Rietveld et al.'s 10 SNPs by Piffer (2013). Moreover, principal component analysis should reveal a signal of positive selection for the SNPs associated with IQ, and this signal (principal component) should be correlated to the component found by Piffer (2013) for 10 SNPs. This prediction is supported by the association between general cognitive ability (*g*) and the top 3 signals in a subsample from Rietveld's et al. meta-analysis (2013). In turn, a significant relationship between these two components constitutes a test of convergent validity of the two measures.

The method of principal components analysis has been employed by Piffer (2013, 2014) to detect signals of recent polygenic selection, that is, the evolution of phenotypes governed by many common genetic variants with small effects (Pritchard & Di Rienzo, 2010; Pritchard, Pickrell, & Coop, 2010). Piffer (2013) showed that frequencies of SNPs associated with general intelligence were not randomly distributed and found a very high correlation between a principal component extracted from 10 alleles and national IQs. In a subsequent study, the same author showed that the distribution of these alleles plus two alleles associated with IQ, significantly deviated from chance expectation across three continental groups (East Asians, Europeans and Africans) (Piffer, 2014). This study will deploy principal component analysis to study the relationship between genes regulating IQ and educational attainment at a cross-ethnic level.

Two recently published studies have discovered new genetic variants significantly associated with increased intelligence (*g*). Desrivières et al. (2014) have found evidence for an effect of a mutation within the NPTN gene on cortical thickness and intelligence, using a relatively large sample of adolescents (N=1584). NPTN is involved in neurite outgrowth and synaptic plasticity, and the minor allele (A) of rs7171755 is associated with lower expression of NPTN in the human prefrontal cortex, an area responsible for higher cognition (Passingham and Wise, 2012). The number of minor alleles at rs7171755 was inversely correlated with average cortical thickness. In the left hemisphere, a decrease of 0.0189 mm (that is, 0.7% of the average left cortical thickness) per risk allele was observed, explaining 2% of variance.

Rs7171755 A is associated with verbal IQ (β=−1.5048; *p*= 0.0076), a correlation that was not mediated by indirect effects on mean or temporal thickness. An association with noverbal IQ was also found, although this was mediated by indirect effects of this allele on cortical thickness.

Another recent study (Benyamin et al., 2014) has reported an association between rs236330, located within gene *FNBP1L*, and general intelligence, replicating the results from a previous study (Davies et al, 2011). This gene is strongly expressed in neurons, including hippocampal neurons and developing brains, where it regulates neuronal morphology (Davies et al, 2011). Two other SNPs seem to be related to general cognitive ability:

1) rs324650, whose association with IQ has been replicated in four association studies (Comings et al, 2003; Dick et al, 2007; Gosso et al, 2006, 2007). This SNP is located in the gene *CHRM2* (cholinergic receptor, muscarinic #2), which is involved in neuronal excitability, synaptic plasticity and feedback regulation of acetylcholine release.

2) APOE (Apoliprotein E) is the most extensively studied polymorphism in the context of cognitive aging (Laukka et al, 2013). Apolipoprotein E (ApoE) is a class of apolipoprotein found in the chylomicron and Intermediate-density lipoprotein (IDLs) that is essential for the normal catabolism of triglyceride-rich lipoprotein constituents.

This gene has three common alleles: ε2, ε3, and ε4. The ε4 variant is the largest known genetic risk factor for late-onset sporadic Alzheimer disease (AD) in a variety of ethnic groups (Sadigh-Eteghad et al., 2012).

A recent meta-analysis, which comprised 77 studies representing over 40,000 people (Wisdom et al, 2011) found that *APOE*4* (rs429358 C) carriers performed worse than noncarriers in all eight cognitive domains examined including episodic memory, global cognitive functioning, executive functioning and perceptual speed. Although an interaction with age was manifest, so that the effects of this allele were stronger in older people, age was not a significant predictor of effect size changes for perceptual speed. Small et al. (2004) found that possession of APOE 4 is associated with poorer performance on tests of global

cognitive function, episodic memory, and executive function. It has also been shown that young healthy adults who carry the Apoe ε4 allele demonstrate altered patterns of brain activity both at rest and during cognitive challenges (Scarmeas & Stern, 2006).

Height SNPs were used as a comparison to test the discriminant validity of the method applied to the IQ and educational attainment genes, because human stature is a highly polygenic trait whose phenotypic values differ across human populations. That is, if the genes associated with height show a signal of recent selection, this genetic component should be less correlated to either the IQ or educational attainment genetic components than these two are among each other.

Another anthropometric variable, intracranial volume, because it represents maximally attained brain size (Ikram et al, 2012) which in turn is correlated to intelligence.

Results and Discussion

Intelligence

A principal component analysis was carried out with Oblimin rotation with the 1000 Genomes data-set. Two components were extracted that explained 62.5% and 30.6% of the variance, respectively. Kaiser-Meyer-Olkin was not satisfactory (0.472). Chi-squared (Bartlett's test of sphericity)=35.04, df=6, $p< .001$. Inspection of the structure matrix revealed that 3 of 4 SNPs loaded highly on the first component (Table 3a) but one SNP (rs7171755) did not load significantly on it (r=-.051).

Thus, the "offending" variable was removed and another PCA was carried out, using the other 3 SNPs. One component was extracted that explained 82.73% of the variance. This produced a more satisfactory solution (KMO=.741). Chi-squared (Bartlett's test of sphericity)=20.4, df=3, $p<0.001$. The structure matrix revealed that this component is clearly interpretable as a "meta-gene" for higher intelligence (Table 3b). The correlation between the component scores extracted from the first PCA with 4 SNPs and the second PCA with only 3 SNPs revealed that they were almost identical (r=0.998, $p<0.01$). Component scores are reported in Table 4.

This component was correlated with the PC extracted by Piffer (2013) from the 10 SNPs associated with educational attainment. The two components were highly correlated (r=0.85, p<0.01), even though they were extracted from frequencies of different genetic variants.

Another analysis was carried out on the ALFRED dataset. Frequencies for the 8 continental groups, or races were used, because populations reported in ALFRED for APOE*4 did not match exactly those for the other three genes.

A single component was extracted that explained 66.8% of the variance. Kaiser-Meyer-Olkin was satisfactory (0.629). Chi-squared (Bartlett's test of sphericity)=14.8, df= 6, p=.022. The structure matrix (Table 5) was clearly interpretable as a meta-gene for higher intelligence, as the 4 alleles loaded highly on the component and in the expected direction, as all had positive loadings but the only intelligence decreasing allele (rs429358 C) which loaded negatively on this component.

Component scores are reported in Table 6, along with PC scores from educational attainment factor found by Piffer (2013). The correlation between the two components is r=0.93 (p<0.01).

Height

Six polygenic scores were created from the 52 SNPs with p< 10^-7 belonging to the six published studies. These are reported in table 7.

In order to test the hypothesis that they represent the same underlying genetic structure, due to recent polygenic selection, a principal component analysis was carried out. A single component was extracted that explained 86.9 % of the variance. Kaiser-Meyer-Olkin was satisfactory (0.741). Chi-squared (Bartlett's test of sphericity)=122.629, df= 15, p=.000. The component matrix (table 8) shows that the component is clearly interpretable as a genetic background for higher stature.

Table 9 reports the component scores.

A correlation between Height PC, IQ and Educational Attainment PCs were computed and these were both strongly negative (r= -0.923; r= - 0.929), p<0.05.

The SNPs with the highest factor loadings (0.9) were searched on ALFRED, to better assess the worldwide pattern of allele frequencies. These are reported in table 10. A principal component analysis was carried out. A single component was extracted that explained 80.45% of the variance. Kaiser-Meyer-Olkin was satisfactory (0.600). Chi-squared (Bartlett's test of sphericity)= 21.96, df=6, p=0.01. The component matrix (table 11) shows that the component is clearly interpretable as a genetic background for higher stature. Component scores are reported in table 10 (last column).

This PC was correlated with the Educational Attainment and IQ PCs (reported in Table 6). The correlations were strongly negative and significant (r= -0.89; -0.92), $p<0.05$.

ANOVA

Given the strong signal of recent selection found on height increasing alleles, ANOVA was carried out to determine whether allele frequencies differed significantly between races. The null hypothesis that there are no significant differences corresponds to the neutral model of genetic evolution. Refutation of the null hypothesis suggests a mechanism of non-random evolution, or natural selection.

A one-way ANOVA was performed to test for different frequencies of height increasing alleles across the three human races (African, East Asian, European).The SNP hits that were the same across studies (N=6) were deleted, resulting in a total of 46 SNPs. Allele frequencies significantly differed between the three races, F (2, 137)= 3.196, p= 0.044. Tukey post-hoc comparisons of the three groups indicated that the African group (M= 65.86%, had significantly higher allele frequencies than the East Asian group (M= 49.67%), 95% CI [0.62, 29.76], p= 0.039.
Comparisons between the European group (M= 54.43%) and the other two groups were not statistically significant at $p<.05$.

Intracranial Volume

Two SNPs related to intracranial volume were found using the NHGRI GWAS Catalog.

These were rs9303525 and rs4273712, with a GWAS significance of 8x10^-15 and 2x10^-13, respectively (Ikram et al., 2012). Their frequencies (1000 Genomes) are reported in table 12.

Their polygenic score (Average frequency) was positively correlated to the IQ and the Educational Attainment PCs (r=0.85 and 0.91, respectively), $p<0.05$.

Another search was performed on ALFRED, but frequencies were found only for rs rs4273712. These are reported in table 13 The correlation between frequency of the allele increasing intracrainal volume and the two cognitive PCs (IQ and Educational attainment) among the nine ALFRED's racial groups were r=0.67 and 0.56, respectively and the former was significant(p= 0.045).

Discussion

This study provides evidence that mental abilities were subject to recent selection in a polygenic fashion, bolstering the hypothesis presented in two recent studies (Piffer, 2013, 2014). The hypothesis that the same kind of directional selection acted on alleles associated with educational attainment and alleles associated with IQ or general cognitive ability (*g*) was supported by the strong association between the principal components extracted from ten SNPs taken from Rietveld et al's meta-analysis and the four SNPs associated with IQ across independent samples and studies. Thus, this study provides converging evidence for recent selection from two different genetic data bases (1000 Genomes and ALFRED) and two different sets of genes.

Principal component analysis revealed a signal of positive selection for the four SNPs associated with IQ, and this signal (principal component) was highly correlated to the component found by Piffer (2013) for 10 SNPs associated with educational attainment in Rietveld et al's (2013) meta-analysis.

Indeed, the components extracted from the 1000 Genomes database for two independent sets of SNPs (10 educational attainment SNPs and 4 IQ SNPs) were strongly correlated at a cross population level (r=0.85). The components that emerged from the analysis of the ALFRED dataset, which comprised eight distinct racial groups, had an even higher correlation (r=0.93).

Thus, the genotypic correlations between intelligence and educational attainment at a cross-population level (around 0.9) are strikingly similar to those found within

populations (0.76-0.94; Calvin et al, 2012). In turn, this correlation provided convergent validity for the genetic measures of cognitive ability identified with PCA.

All four alleles loaded highly on the principal component (0.75-0.87) and in the expected direction (positive and negative for intelligence increasing and decreasing alleles, respectively) in the ALFRED dataset. This reveals that they load robustly and consistently on an underlying factor, making the case for random drift much weaker. A similar picture can be obtained from the 1000 Genomes dataset, although one SNP (rs7171755) failed to load significantly on the principal component. This is likely due to the lower representativeness in terms of racial groups (only three) and coverage of genetic diversity compared to the ALFRED database, which comprises more genetically heterogeneous populations from distant parts of the world, corresponding to eight distinct racial groups. This strengthens the results obtained by Piffer (2014) which showed that allele frequencies for Educational Attainment and IQ were significantly different between Europeans, East Asians and Sub-Saharan Africans.

An analysis was carried out on another polygenic trait, height, whose average phenotypic values vary across ethnic groups. This produced a signal of recent polygenic selection, showing higher values for Africa, lower for Europe and lower still for East Asia. ANOVA confirmed that the three races differed significantly in terms of allele frequencies and Tukey's post-hoc test revealed a significant difference favouring Africans vs East Asians. The genetic results are in line with the widely known physical difference between ethnic groups within the US, where East Asians on average have shorter stature.

This finding in turns provided converging evidence that principal component analysis can detect signals of polygenic selection, confirming the validity of the factor analytic method, as was already shown by Piffer (2014) with regards to educational attainment and IQ alleles.

It must be highlighted that, although the GWAS hits adopted in this study came from different human populations, representative of the major human races (Japanese, Han Chinese, European), the results did not differ significantly across studies, as shown by the strikingly similar factor loadings of the six polygenic scores on the principal component. This suggests that GWAS hits are not significantly influenced by the

sampled population, possibly because most SNPs have the same phenotypic effects across all human ethnic groups.

It can be speculated that selection for the IQ and educational attainment genes was due to selective pressure for higher intelligence, rather than educational attainment. First, because most of these mutations are present at respectable frequencies among sub-Saharan Africans; thus they emerged before the human diaspora 60kya, which greatly predates the invention of writing and formal education. Second, intelligence has had more time to evolve than educational attainment skills and thus create population differentiation in terms of allele frequencies.

The alleles associated with a phenotype reflecting adult brain size, namely intracranial volume, were positively correlated to the IQ and Educational Attainment PCs. This suggests that brain size increases following the out of Africa migration, partially account for cognitive differences between human groups.

No specific predictions regarding the relationship between height and intelligence were made, other than the general prediction that the two sets of genes related to intelligence (educational attainment and IQ) would be more strongly correlated to each other than either is to height, thus providing a test of discriminant validity. In fact, a strong and significant negative correlation between the principal components for genetic height and intelligence was found. This contrasts the (very weak) positive correlation found within populations, where taller people have a small IQ advantage over shorter people (Pearce et al., 2005; Humphreys, Davey & Park, 1985). This correlation is in part due to common genetic factors (Marioni et al., 2014) and assortative mating (Beauchamp et al., 2011). The results of the present study indicate that, although within populations some genes may have pleiotropic effects on stature and intelligence, the selective pressure on stature and intelligence, had opposite directions across human populations. This suggests that the environments that selected for higher intelligence were also more advantageous for shorter people. A possible explanation of this phenomenon can be inferred from Allen's rule, which posits that endotherms from colder climates usually have shorter limbs than the equivalent animals from warmer climates. This is based on the principle that in cold climates, the greater the exposed surface area, the greater the loss of heat and therefore energy. Animals in cold climates need to conserve as much

energy as possible. A low surface area to volume ratio helps to conserve heat as there is a smaller surface area for the heat to pass through. Probably also human populations follow Allen's rule (Katzmarzyk & Leonard, 1998).

The Arctic Mongoloid physical type has been proposed as an example of an adaptation to cold climates, following Allen's rule (Steegman & Platner, 1968). In fact, East Asians have also the shortest stature and the low values found in the present study for their stature's genetic principal components, lend support to this assumption. This evolutionary scenario is in accord with the "cold winters theory", which posits that survival in colder climates poses two evolutionarily novel problems that would have required high intelligence to solve: finding food and keeping warm (Templer & Arikawa, 2012). Thus, the negative link between intelligence and stature across populations could be the result of cold climates providing a fitness advantage for shorter stature (via Allen's rule) and higher intelligence (via "cold winters theory"). The present study only provides suggestive evidence for this hypothesis, although an accurate analysis of the evolutionary link between intelligence and stature goes beyond the scope of this paper.

Conclusion and Prospects

This is the first study to provide evidence that height increasing alleles were subject to different selective pressures across races and shows that the methodology first applied by Piffer (2013) to cognition genes, can be fruitfully extended to any polygenic traits whose underlying genetic variation has been extensively studied.

Materials and Methods

Frequencies for the four alleles were obtained from 1000 Genomes. These are reported in Table 1. All alleles are regarded as having a beneficial effect on intelligence, with the exception of APOE*4 (rs429358 C), which has a detrimental effect. Their frequencies are reported in Table 1

A separate search was carried out on ALFRED. Two SNPs in high linkage disequilibrium ($r^2 \geq 0.8$ were found instead of rs324650 and rs236330 (respectively,

rs420817 and rs2363322). Linkage disequilibrium was calculated with SNAP (SNP Annotation and Proxy Search, https://www.broadinstitute.org/mpg/snap/), using the 1000 Genomes pilot 1 dataset, CEU as population panel and a distance limit of 500 kB. The frequencies for 3 SNPs are reported in Table 2a whereas the frequencies for rs429358 are reported separately in Table 2b because they were available for different populations.

Table 2c reports frequencies for racial groups, as averages of the populations composing them.

Height and Intracranial volume SNPs were found using the NHGRI GWAS catalog (www.genome.gov/gwastudies).

The SNPs that met the following criteria were selected: a) study published since 2010; b) a p value <10^-7.c) In case a study had more than 10 SNPs that met the first two criteria, only the first 10 SNPs (with the lowest p value) were chosen.

In order to assess the bias due to ethnicity, different GWAS carried out on the three major races (East Asian, Sub-Saharan African, European) were included.

Frequencies of height increasing alleles were obtained from 1000 Genomes. For each study, a polygenic score (average frequency across all SNPs) was calculated.

The following 6 studies met criteria for inclusion, resulting in a total of 52 SNPs (Berndt et al., 2013; Hao, 2013; Carty, 2011; N'Diaye, 2011; Allen, 2010; Okada, 2010).

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Tables

Table 1. IQ increasing alleles. Frequencies from 1000 Genomes

	rs236330 C (rs236322 G)	rs324650 T (rs420817 C)	rs429358 C (APOE 4)	rs7171755 G
AFR	32	26	26	49
AMR	80	61	11	54
ASN	87	91	9	46
EUR	77	46	14	56
ASW	40	32	16	60
LWK	31	25	37	42
YRI	28	24	21	50
CLM	84	58	15	48
MXL	85	65	8	53
PUR	68	57	10	62
CHB	92	92	10	46
CHS	89	92	8	46
JPT	79	88	8	46
CEU	81	45	16	56
FIN	75	52	18	55
GBR	71	46	15	55
IBS	61	21	18	64
TSI	82	46	9	57

Table 2a. IQ increasing alleles. Frequencies from ALFRED.

	rs7171755 G	rs236330 C (rs236322 G)	rs324650 T (rs420817 C)
Afr.H-G			
San	0.08	0.42	0.17
Biaka	0.48	0.45	0.32
Mbuti	0.27	0.43	0.47
Afr. Farmers			
Bantu	0.365	0.18	0.44
Yoruba	0.52	0.13	0.42
Mandenka	0.46	0.17	0.56
Middle East			
Mozabite	0.57	0.38	0.45
Bedouin	0.66	0.63	0.45
Druze	0.67	0.8	0.67
Palestinian	0.43	0.78	0.47
Europe			
Adygei	0.62	0.85	0.56
Basque	0.65	0.71	0.42
French	0.66	0.71	0.59
Italians	0.48	0.75	0.49
Orcadian	0.66	0.81	0.66
Russian	0.64	0.7	0.46
Sardinian	0.57	0.61	0.66
Central Asia			
Burusho	0.48	0.9	0.78
Kalash	0.76	1	0.78
Pashtun	0.63	0.93	0.76
Balochi	0.54	0.88	0.67
Brahui	0.54	0.86	0.76
Hazara	0.58	0.85	0.71
Sindhi	0.72	0.86	0.72
East Asia			
Dai	0.45	0.65	1
Mongolia	0.5	0.95	1
Daur	0.61	0.89	0.94
Han	0.38	0.9	0.99
Hezhe	0.72	1	0.94

Japanese	0.41	0.715	0.96
Koreans	0.519	0.923	0.935
Lahu	0.4	0.8	0.95
Miao	0.5	0.55	0.9
Naxi	0.5	0.89	1
Oroquen	0.55	1	1
She	0.7	0.75	1
Tu	0.5	0.8	0.95
Tujia	0.5	0.95	1
Uyghur	0.7	0.95	0.95
Xibe	0.39	0.83	0.83
Yi	0.45	0.95	0.95
Yakut	0.58	0.835	0.94
Southeast Asia			
Cambodians.Khmer	0.68	0.825	0.95
Oceania			
Papuan New Guinean	0.59	0.515	0.79
Melanesian. Nasioi	0.34	0.985	0.97
Native American			
Pima. Mexico	0.42	0.88	1
Maya. Yucatan	0.36	0.82	0.9
Amerindians	0.5	0.5	1
Karitiana	0.1	0.99	0.83
Surui	0.21	1	1

Table 2b. APOE*4 (IQ decreasing allele). Frequencies from ALFRED.

	Apoe E4 (rs429358 C)
Afr.H-G	
San	0.37
Biaka	0.407
Mbuti	0.29
Afr. Farmers	
South African	0.285
Zulu	0.27
Bamileke	0.222
Bariba	0.14
Beninese	0.252
Berba	0.17
Chadians	0.273
Congolese	0.333
Ewe	0.21
Fang	0.2
Fon	0.294
Fulani	0.244
Hausa	0.189
Hutu	0.238
Malinke	0.167
Merina	0.182
Mossi	0.125
Songhai	0.059
Toucouleur	0.176
Tutsi	0.385
Wolof	0.03
Afars and Issas	0.118
Kenyan	0.37
Sudanese	0.291
Tanzanian	0.178
Ugandans	0.25
Bambara	0.219
Nigerians	0.31
Middle East	
Arabs	0.1
Lebanese	0.088
Saudi	0.12
European	
Austrian	0.114
Azorian	0.095

Basque	0.072
Belarusian	0.091
Belgian	0.163
British	0.141
Catalans	0.126
Cypriot. Greek	0.07
Czech	0.107
Danes	0.174
Dutch	0.166
English	0.123
Finns	0.219
French	0.118
Germans	0.139
Greeks	0.065
Hungarian	0.114
Icelander	0.165
Irish	0.14
Italians	0.088
Mari	0.149
Norwegian	0.177
Poles	0.108
Portuguese	0.082
Russia	0.104
Sardinian	0.064
Scot	0.149
Spaniards	0.107
Swedes	0.181
Swiss	0.11
Ukrainian	0.094
Central Asia	
Komi-Zyrian	0.13
Pamirian	0.044
Baiga	0.033
Brahmin	0.0815
Gond	0.03
Gujarati	0.109
Kathris	0.057
Koch	0
Kshatriya	0.096
Mala	0.039
Marathas	0.133
Punjabi	0.135
Rajput	0.059

Sikh	0.074
East Asia	
Dai	0.047
Han	0.069
Japanese	0.097
Korean	0.118
Uyghur	0.127
Southeast Asia	
Taiwanese	0.079
Thai	0.009
Malaysians	0.119
Oceania	
Australian Aborigines	0.278
Javanese	0.17
Papuan New Guinean	0.374
Samoans	0.238
Melanesian. Nasioi	0.32
Native American	
Alaskan Natives	0.193
Greenlander	0.231
Huicholes	0.264
Inuit. Canadian	0.23
Inuit. Greenalnd	0.209
Mazatecan	0.1
Mexican	0.073
Nahuas	0.05
Maya	0.11
Ache	0
Cayapa	0.28
Gaviao	0.33
Guarani	0.17
Kaingang	0.13
Pilaga	0.16
Surui	0.12
Toba	0.145
Wai-Wai	0.47
Wichi	0.045
Yanomami	0.156
Zoro	0.3

Table 2c. Three IQ increasing alleles + one IQ decreasing allele (APOE*4) for continental groups. Frequencies from ALFRED.

	rs7171755 G	rs236330 C	rs324650 T	APOE E4
Afr.H-G	0.277	0.433	0.32	0.355
Afr. Farmers	0.448	0.16	0.397	0.22
Middle East	0.582	0.6475	0.51	0.102
European	0.611	0.734	0.549	0.123
Central Asia	0.6	0.897	0.74	0.07
East Asia	0.519	0.851	0.957	0.08275
Southeast Asia	0.68	0.852	0.95	0.0835
Oceania	0.465	0.75	0.88	0.276
Native American	0.318	0.838	0.946	0.179

Table 3a. Structure matrix, PCA 1000 Genomes

	PC1
Rs236330 C	0.929
Rs324650 T	0.881
Rs429358 C	-0.915
Rs7171755 G	-0.051

Table 3b. Structure matrix, PCA 1000 Genomes.

	PC1
Rs236330 C	0.928
Rs324650 T	0.903
Rs429358 C	-0.897

Table 4. Principal components, 1000 Genomes dataset.

	PC1a (4)	PC1b (3)
ASW	-0.87462	-0.82125
LWK	-2.12144	-2.2304
YRI	-1.4393	-1.44863
CLM	0.33382	0.30497
MXL	0.78406	0.79823
PUR	0.27212	0.33265
CHB	1.21692	1.1567
CHS	1.25794	1.20436
JPT	1.02249	0.97191
CEU	0.03992	0.0641
FIN	-0.05455	-0.05205
GBR	-0.07393	-0.0543
IBS	-0.76389	-0.68019
TSI	0.40046	0.45388

Table 5. Structure matrix, ALFRED.

	PC1
Rs7171755 G	0.752
Rs236330 C	0.866
Rs324650 T	0.769
Rs429358 C	-0.875

Table 6. Principal component from ALFRED for 4 IQ alleles (IQ PC) and for Educational Attainment (Piffer, 2013).

	IQ PC	Ed. Att. PC
Afr.H-G	-1.84	-2.1
Afr. Farmers	-1.32	-1.71
Middle East	0.12	-0.19
European	0.27	0
Central Asia	0.85	0.1
East Asia	0.83	0.97
Southeast Asia	1.15	0.32
Oceania	-0.14	-0.685
Native American	0.07	-0.9

Table 7. Polyenic scores from 6 Height GWAS.

	Berndt et al. 2013	Hao et al. 2013	Carty et al. 2011	N'Diaye et al., 2011	Okada et al., 2010	Allen et al., 2010
ASW	60.6	53	51.5	60.888	69.6	70
LWK	61.1	52	56.5	61.667	69.7	71.5
YRI	61.8	50.6	59.625	63.444	72.5	72
CLM	51.7	59.4	37.125	53.444	63.6	55.8
MXL	52.7	61	33.875	53.666	61.7	58.7
PUR	52.7	54.6	37.375	56	64.4	57.6
CHB	44.2	70.2	33.375	46.888	47.9	43.8
CHS	45.1	71.8	35.25	48.888	48.8	43.3
JPT	42.3	69.4	34.625	49.444	52.3	43.9
CEU	58.8	57.4	35	55	62.6	60.8
FIN	55.5	59.2	32.5	55.77777778	61	60
GBR	58.6	56.4	34.625	57.333	62.6	60.3
IBS	56	48.6	37.875	56.777	64.9	57
TSI	58.7	57.8	32.875	54.111	62.9	60.5

Table 8. Component matrix.

Publication	PC1
Berndt et al.	0.939
Hao et al.	-0.928
Carty et al.	0.763
N'Diaye et al.	0.986
Okada et al.	0.977
Allen et al.	0.979

Table 9. Component scores (Height increasing alleles).

	PC1
ASW	1.161
LWK	1.342
YRI	1.596
CLM	-0.198
MXL	-0.242
PUR	0.107
CHB	-1.623
CHS	-1.515
JPT	-1.422
CEU	0.149
FIN	-0.051
GBR	0.244
IBS	0.384
TSI	0.069

Table 10. Frequencies for top height increasing alleles.ALFRED.

	rs1991431-A (rs9846369 T)	rs42235 T (rs2282978 C)	rs11658329 C (rs9901507 A)	rs3791679 A	Average	PC1
Afr.H-G	0.846666667	0.536666667	0.866	0.976	0.8066	1.681
Afr. Farmers	0.78	0.47	0.885	0.953	0.772	1.462
Middle East	0.3125	0.425	0.375	0.668	0.445	0.062
Europe	0.36	0.438571429	0.251	0.738	0.447	0.113
Central Asia	0.27	0.25	0.162857143	0.708	0.347	-0.465
East Asia	0.263777778	0.141944444	0.0665	0.293	0.191	-1.178
Southeast Asia	0.24	0.24	0.24	0.24	0.24	-0.928
Oceania	0.3275	0.13	0	0.727	0.296	-0.740
Native American	0.522	0.304	0.082	0.814	0.430	-0.00714

Table 11. Component matrix. Top 10 height increasing alleles.Frequencies from ALFRED

SNPs	PC loadings.
rs1991431-A (rs9846369 T)	0.935
rs42235 T (rs2282978 C)	0.901
rs11658329 C (rs9901507 A)	0.914
rs3791679 A	0.835

Tabl2 12. Alleles associated with higher intracranial volume. Frequencies from 1000 Genomes.

		rs9303525-A	rs4273712-G
AFR		70	7
AMR		77	40
ASN		100	48
EUR		76	28
ASW		63	15
LWK		75	2
YRI		70	6
CLM		73	33
MXL		79	53
PUR		79	33
CHB		100	49
CHS		100	46

JPT		99	50
CEU		79	25
FIN		89	23
GBR		75	29
IBS		79	36
TSI		63	33

Table 13. Frequencies of rs4273712, associated with intracranial volume. ALFRED.

	rs4273712 G
Afr.H-G	0,033333333
San	0
Biaka	0,03
Mbuti	0,07
Afr. Farmers	0,063333333
Bantu	0,07
Yoruba	0,06
Mandenka	0,06
Middle East	0,355
Mozabite	0,38
Bedouin	0,4
Druze	0,37
Palestinian	0,27
Europe	0,244285714
Adygei	0,38

Basque	0,25
French	0,28
Italians	0,2
Orcadian	0,19
Russian	0,18
Sardinian	0,23
Central Asia	0,385714286
Burusho	0,42
Kalash	0,28
Pashtun	0,52
Balochi	0,28
Brahui	0,46
Hazara	0,38
Sindhi	0,36
East Asia	0,431388889
Dai	0,25
Mongolia	0,5
Daur	0,33
Han	0,47
Hezhe	0,5
Japanese	0,45
Koreans	0,585
Lahu	0,15
Miao	0,45

Naxi	0,56
Oroquen	0,45
She	0,45
Tu	0,45
Tujia	0,5
Uyghur	0,35
Xibe	0,44
Yi	0,4
Yakut	0,48
Southeast Asia	0,41
Cambodians,Khmer	0,41
Oceania	0,015
Papuan New Guinean	0
Melanesian, Nasioi	0,03
Native American	0,65
Pima, Mexico	0,86
Maya, Yucatan	0,6
Amerindians	0,42
Karitiana	0,73
Surui	0,64