Science & Society

EMBO reports

GWAS and cognitive abilities: Why correlations are inevitable and meaningless

GWA studies to identify genetic factors for educational achievements largely ignore underlying social structures and dynamics

Ken Richardson

Genomewide association studies (GWAS) are a relatively new and powerful tool to identify gene variants involved in human variation. The method scans the whole genome for small genetic variations—single nucleotide polymorphisms or SNPs—that correlate with differences in a particular trait, such as disease susceptibility or behavioral differences. GWAS have also looked for genetic variation related to cognitive ability test scores (CA) or educational attainments (EA). These aspirations have been thwarted by finding only small and usually non-significant associations and failure to replicate the results. Recent studies claim to have overcome this problem by summating across large numbers, usually thousands, of the most promising weak effects identified from strength of association statistics into "polygenic scores" (PGS). Based on various tiers of statistical adjustments, some studies reported significant correlations between PGS and cognitive abilities [1,2].

> *"... such portents of social engineering based on genetic differences are conceptually simplistic and potentially misleading."*

These publications have prompted proposals to address complex social and cognitive problems such as school performance or cognitive abilities based on genetic variation. Typical of the exuberance surrounding these GWAS/PGS findings is the suggestion that "recent results are a harbinger of future widespread use of PGS to predict genetic risk and resilience in the social and behavioral sciences" and even as a future basis for "personalized learning" in schools [2].

Here, I argue that such portents of social engineering based on genetic differences are conceptually simplistic and potentially misleading. First, there is already some cryptic but functionally irrelevant genetic stratification in human populations, which, quite likely, will covary with social stratification or social class. Second, this genetic stratification will correlate, adventitiously, with cognitive variation. Thirdly, the "dependent" variables (CA and EA) are themselves used to perpetuate social structure—and thereby the genetic structure—through social policy. This invalidates statistical assumptions of independence used in GWAS/PGS analyses. Generally, it raises questions about cause and effects: Are the observed genetic variations the cause of differences in CA and EA or are they a mere side effect of social stratification and underlying genetic stratification?

Societies are genetically stratified

Even within freely breeding species, genetic population structure is widespread. Its causes are, among other things, migration and "genetic drift", or the uneven dispersal of gene variants. These result in different frequencies of (usually functionally benign) variants, or alleles, among subgroups.

> *"... are the observed genetic variations the cause of differences in CA and EA or are they a mere side effect of social stratification and underlying genetic stratification?"*

In humans, genetic population structures have also emerged in response to social forces. Throughout human history, migrants with different genetic backgrounds have not always dispersed evenly within a specific society, but clustered both "horizontally" (geographically) and "vertically" (in different social strata or classes). Let us take the example of Great Britain, the source of much of the contemporary GWAS data, to illustrate the effects of migration, gene flow and stratification.

Invasions by Anglo-Saxons and their domination over native Romano-British from the 5th–7th centuries AD were followed by geographically more confined Viking incursions, apparently with limited interbreeding [3]. From 1066 on, invading Normans became a distinctive ruling class in Britain, forming a landed, military and

Berwick upon Tweed, UK. E-mail: k.richardson@mac.com
DOI 10.15252/embr.201744140 | Published online 4 July 2017

ecclesiastical aristocracy with a distinctive language. Many from today's upper class can trace their ancestry back to this immigration. In the late 17th century, tens of thousands of Huguenots—French protestants escaping religious oppression—settled in, largely as artisans and manufacturers, especially around London and East Anglia. According to some estimates, one in every six Britons today has some Huguenot ancestry. Roma people originating from north India arrived in Britain at various times. Currently estimated to number around two hundred thousand, they exist mainly as travelers and largely work as hawkers, basket weavers, and ostlers. A large Jewish influx following bitter persecution in Russia and elsewhere in Europe increased the Jewish population of England to about 250,000. Though many were initially very poor, they tended to settle in middle-class occupations such as law, finance, tailoring, and commerce mainly in the large industrialized cities. Thousands of German immigrants came during the mid-19th century to London and some northern cities. They initially worked largely as waiters and clerks, but many went on to become middle-class restaurant owners and businesspeople. During the mid-1800s and 1930s, immigrants from Ireland escaped famine and poverty to work in construction and domestic labor. As many as six million people in the UK today are estimated to have at least one Irish grandparent. In the 2011 Census of England and Wales, over a million people specified themselves as either African, Caribbean, or "White and Black Caribbean" [4]. Their dispersal has generally been both geographically and "vertically" confined a systematic stratification that has entailed considerable ethnic prejudice and overt racism. The most recent migrants to the UK come from Eastern Europe and India and tend to be better-educated and over-represented in both high-skilled and low-skilled occupations.

> *"In humans, genetic population structures have also emerged in response to social forces."*

This is, of course, only one example of a complex population structure; countries with history of large immigration waves, such as the USA, are probably even more diverse. The point is that migration history creates correlations between social class and genetic variation, albeit functionally irrelevant to CA or EA.

Social stratification has maintained genetic stratification

Generally, immigrants have dispersed in their host countries, but not randomly. In the UK, a conspicuous "horizontal" structure, even from Anglo-Saxon and Norman migration, is still apparent today by way of regional genetic clustering described in the *People of the British Isles* project [3]. It is also evident in the uneven distribution of specific allele frequencies in some data sets such as the UK10 Consortium.

An uneven distribution of gene frequencies is also manifested "vertically", that is, across social classes. As the immigrants dispersed across social strata so did their genes. In spite of intermingling, these social and genetic clines have persisted over many generations maintained by social power structures. As Foster and Sharp [5] commented, "The lines that exist between social categories can constitute partial barriers to interaction, reproduction, and migration. Consequently, some members of a particular social population may share similar SNPs, similar conserved or ancestral haplotypes, or similar variants of disease susceptibility, drug metabolism, and environmental-response genes in frequencies and patterns that are not found in other social populations".

This would explain why GWAS find stratification in polygenic scores that correlate with even simple measures of socioeconomic status, or SES [2]. Other interesting evidence lies in the way that genetic variation across the UK correlates with surname distribution. Under a quantitative polygenic model, the status of most advantaged and disadvantaged families should converge within a few generations. This should also apply to English surnames, which are inherited along with genes. Using educational status in England from 1170 to 2012 as an index of class structure, Clark and Cummins [6] found that status differences have persisted to some extent over as many as 20 to 30 generations. For example, individuals bearing elite surnames from medieval times remain over-represented in the wealthier and better-educated classes in Britain today.

In sum, it seems highly likely that genetic differences—albeit ones irrelevant to CA/EA differences—will correlate with social class. This is why contemporary GWAS/PGS find direct (but weak) correlations with SES [2], although interpreted as an effect of genetic variation *on* SES, rather than *vice versa* as argued here. Of course, all the correlations account for only small amounts of variance in the respective traits and in a context in which the vast majority of genetic variation is within, rather than between, local groups. But that is all that is needed to account for the tiny correlations found in GWAS/PGS.

> *"An uneven distribution of gene frequencies is also manifested "vertically", that is, across social classes."*

The authors argue that they have taken account of these correlations linked to SES. However, the latter is only defined in shallow terms, usually as some composite of parents' education and level of employment. Such indices are only weak reflections of the deeper psychological and cultural differences characterizing social classes as alluded to by the American Psychological Association [7]. Furthermore, lifetime SES changes are quite common.

Social stratification creates cognitive differentiation

We can now see how the association between genetic and social stratification also becomes associated with CA/EA. It is well established that the different occupations and social roles of different social classes lead to disparate knowledge and cognitive and affective processes. The American Psychological Association therefore emphasizes the need "to attend more fully to the impact of socioeconomic position on psychological processes and outcomes, the subjective experiences of social class status, and psychosocial processes related to the social and political implications of class inequities" [7]. The report also indicates how just being low status "gets into the body" to

affect the immune system, reduces resistance to infection and affects health and general vitality, including that needed for school and test performance.

The problem is that cognitive tests are designed on the assumption that all cognitive differences can be assessed against a singular set of criteria. In other words, cognitive tests, instead of describing cognitive differences in relation to their contexts, merely "screen" for degrees of match/mismatch with a set of "ideal" criteria. It is not difficult to show that those criteria are closely related to social class.

Cognitive tests reflect prior social stratification

Genomewide association studies for cognitive abilities involve some form of testing for IQ or "intelligence". However, IQ tests have never had what is called objective "construct" validity in a way that is mandatory in physical and biomedical sciences and that would be expected of genetic research accordingly. This is because there is no agreed theoretical model of the internal function—that is, intelligence—supposedly being tested. Instead, tests are constructed in such a way that scores correlate with a social structure that is assumed to be one of "intelligence".

> *"... either directly or indirectly, IQ and related tests are calibrated against social class background..."*

Such "criterion" validity was adopted by the original test designers. Sir Francis Galton tried to use quasi-physiological tests such as reaction time, sensory acuity, and perceptual judgment to design a composite test of intelligence. Its "validity" was inferred by comparing the scores with participants' social status. There was little association, and, failing to correlate even with educational attainments, the tests were rejected as valid measures [8].

In Paris, Alfred Binet wanted to identify, for remedial purposes, children who might have difficulties learning in school. He used classroom observation and teachers' judgments to identify knowledge and cognitive skills that children should have learned at different ages: general knowledge, defining common words, constructing sentences, describing similarities, and such like. These observations were then used to devise test items. However, since such competencies are also more likely to be pre-learned or primed in literate middle-class families, rather than working class homes [8], Binet's test scores adventitiously correlated with social class.

> *"... surveys going back to the 1960s have routinely shown that neither school nor university grades are good predictors of occupational performance."*

Today, the underlying logic of IQ tests remains much the same and is largely based, directly or indirectly, on social class background. Even the so-called culture-free tests, such as the Raven's Matrices, reflect the—only slightly veiled—degree of familiarity with certain problem structures that distinguish cultural backgrounds [8]. In effect, we are presumed to know who is intelligent and to accept a test as a measure of intelligence if it identifies such persons.

In summary, either directly or indirectly, IQ and related tests are calibrated against social class background, and score differences are inevitably consequences of that social stratification to some extent. Through that calibration, they will also correlate with any genetic cline within the social strata. Whether or not, and to what degree, the tests also measure "intelligence" remains debatable because test validity has always been indirect and circular.

For example, IQ tests are so constructed as to predict school performance by testing for specific knowledge or text-like rules—like those learned in school. But then, a circularity of logic makes the case that a correlation between IQ and school performance proves test validity. From the very way in which the tests are assembled, however, this is inevitable. Such circularity is also reflected in correlations between IQ and adult occupational levels, income, wealth, and so on. As education largely determines the entry level to the job market, correlations between IQ and occupation are, again, at least partly, self-fulfilling.

IQ poorly predicts educational success

More telling is the degree to which IQ scores predict the more independent measures of job performance: Raw correlations are surprisingly small, usually around 0.2 [8]. More usually cited, however, are "corrections" (such as that for measurement error) that double correlations to around 0.5. But these entail much socio-psychological idealism. For example, variation in a test score may not be owing to measurement errors so much as natural variation in testee performance. Again, correction becomes, to some extent, guesswork, yet the adjusted correlations depend upon it. Moreover, job performance is very difficult to rate. The usual ratings—those of supervisors—both show very poor agreement with each other and with other ratings of performance (for discussion see [8]). Finally, there is considerable evidence that correlations may be attributable to non-cognitive factors, such as self-confidence, which again reflect social background [9].

> *"The dynamics of human variation, group differences and measurement reside [...] in far more complex, multi-level systems."*

In sum, CA, as measured by IQ-type tests, is intrinsically inter-twined with social stratification and its associated genetic background, by the very nature of the tests. Some of the best evidence for that point lies in what is called the "Flynn effect": the striking rise in average IQ scores in developed and developing countries. It closely corresponds with the demographic swelling of the middle classes over the same period. It is also well known that children adopted into middle-class homes exhibit massive leaps in IQ compared with peers left in institutions.

Much of this argument about poor predictability of CA is equally applicable to EA. Performance scores, such as Scholastic Attainment Tests, are poor predictors of later attainments in higher education or occupations. A review of thirteen years of previous research in the USA found only moderate associations between school and university performance [9]. The same study found that "in U.K. data, a small correlation was

observed between A level points [High School grades] and university GPA ($r = 0.25$), again reflecting previous findings" (and thus explaining less than ten percent of variation in outcome). Similarly, surveys going back to the 1960s have routinely shown that neither school nor university grades are good predictors of occupational performance. One review put the correlations, six or more years after graduation, as low as 0.05 (see [8] for review).

In sum, the cognitive abilities and educational differences that GWAS/PGS are being used to predict are not the objective, stable or precisely measured variables we would expect in genetic research. Instead, they are labile and, at least in part, reflections of social class background. Finally, it is also important to realize that scores on these variables have been actively used through selection policies and mating choice to perpetuate that stratification.

Sidebar A: Further reading

On immigration stratification:
Panayi P (1996) German immigrants in Britain. In *Germans in Britain since 1500*, P Panayi (ed.), 1815–1914. London: Hambledon Press
Cottrel B (2009) *The Huguenots in England: immigration and settlement c. 1550–1700*. Cambridge: Cambridge University Press

On class and genetic associations:
Tyrrell J, Jones SE, Beaumont R, Astley CM, Lovell R, Yaghootkar H, Tuke M, Ruth KS, Freathy RM, Hirschhorn JN *et al* (2016) Height, body mass index, and socioeconomic status: mendelian randomisation study in UK Biobank. *BMJ* **352**: i582

On the poor definition and validity of CA and EA:
Richardson K, Norgate SH (2015) Does IQ really predict job performance? *App Dev Sci* **19**: 153–169
Armstrong JS (2012) Natural learning in higher education. *Encyclopedia of the sciences of learning*. London: Springer
Flynn JC (1987) Massive IQ gains in 14 nations: what IQ tests really measure. *Psych Bull* **101**: 171–191

On population structure and inappropriate genetic models:
Dandine-Roulland C, Bellenguez C, Debette S, Amouyel, P, Génin E, Perdry H (2016) Accuracy of heritability estimations in presence of hidden population stratification. *Sci Rep* **6**: 26471
Nelson RM, Pettersson ME, Carlborg O (2013) A century after Fisher: time for a new paradigm in quantitative genetics. *Trends Genet* **29**: 669–676
Génin E, Clerget-Darpoux F (2015) The missing heritability paradigm: a dramatic resurgence of the GIGO syndrome in genetics. *Hum Hered* **79**: 1–4

Attempts to correct for population structure

Of course, most researchers have been aware of the possibility of spurious correlations from population structure and attempted to correct for it statistically. The correction method mostly used until recently has been to eliminate the most closely genetically related individuals from current samples, usually by principal components analysis (PCA). But that only detects genetic structures to the level of third or fourth cousins and does not correct for deeper population structure even when it is known to be present [10]. As described above, there are many reasons for thinking that stratification goes much deeper than what is evident in PCA, reflecting genealogies maintained over many generations.

In addition, all attempts for correction involve many assumptions and raise many difficulties of interpretation. One is the assumption that the contribution of SNPs is additive/independent when variation in complex traits is by definition due to combinatorial, non-additive/interactive effects of multiple environmental and genetic factors [8]. Another serious problem is that population structure has been actively created and maintained by social policy, *using* IQ testing and schooling, the very variables assumed, in GWAS, to be independent of such structure. Those social dynamics, of course, play havoc with statistical assumptions.

Domingue *et al* [1] claim that their analysis, in which PGS correlate with EA and CA among siblings, controls for both population structure and environmental sources of variation. However, the assumption that siblings share the same environment is a misunderstanding of human development. It ignores, for example, how differences in physiognomy, height, and self-presentation—all possibly associated with SNP differences—influence judgments of intelligence and educability by teachers and others, thereby influencing test performances and achievements [8].

Conclusion

A superficial reading of papers on GWAS and CA/EA can seem quite convincing: "hard" genetic data, neat scores, and simple correlations. However, they skim over the social, historical, and psychological complexities of human populations and the nature of cognition and education. Associations between SNPs and CA or EA are an inevitable result of the class structure of developed societies, unevenly dispersed immigration, and the "systemic stratification" created by the use of the measures themselves. Such deliberate perpetuation of stratification, and non-independence of variables, also confounds attempts to correct for population structure in GWAS/PGS.

This questions at least part of the motivation of GWAS for cognitive functions: to foster a targeted genetic approach to improve human cognitive development and education. That, of course, is a daunting prospect. Some investigators are rightly cautious about such aspirations, if only about the technical feasibilities. However, their concerns should be dispelled by the realization that the aspiration is not merely technically daunting, but conceptually unrealistic. The dynamics of human variation, group differences, and measurement reside—as argued here—in far more complex, multi-level systems.

Finally, it is worth emphasizing that there are many other assumptions underlying this research program, not least about the nature of the gene itself, and of human development. Others warn that the simple, hundred-year-old models of genetic variation underlying GWAS are now known to be far from genetic realities and have led to an upsurge in GIGO (Garbage-In Garbage-Out) genetics. It may be time to give those critiques some closer attention.

Acknowledgements
The author is grateful to Mike Jones for helpful comments on a previous draft.

Conflict of interest
The author declares that he has no conflict of interest.

References

1. Domingue BW, Belsky DW, Conley D, Harris KM, Boardman JD (2013) Polygenic influence on educational attainment: new evidence from the National Longitudinal Study of Adolescent to Adult Health. *Open* 1: 1 – 13
2. Selzam S, Krapohl E, von Stumm S, O'Reilly PF, Rimfeld K, Kovas Y, Dale PS, Lee JJ, Plomin R (2016) Predicting educational achievement from DNA. *Mol Psychiat* 22: 267 – 272
3. Leslie S, Winney B, Hellenthal G, Davison D, Boumertit A, Day T, Hutnik K, Royrvik EL, Cunliffe B, Lawson D *et al* (2016) The fine-scale genetic structure of the British population. *Nature* 519: 309 – 314
4. National Statistical Office (2011) *2011 Census*. London: HMSO
5. Foster MW, Sharp RR (2017) Race, ethnicity, and genomics: social classifications as proxies of biological heterogeneity. *Genome Res* 12: 844 – 850
6. Clark G, Cummins N (2014) Surnames and social mobility in England, 1170–2012. *Hum Nat* 25: 517 – 537
7. American Psychological Association (2006) *Report of the APA task force on socioeconomic status*. Washington, DC http://www.apa.org/pi/ses/resources/publications/task-force-2006.pdf.
8. Richardson K (2017) *Genes, brains, and human potential: the science and ideology of intelligence*. New York, NY: Columbia University Press
9. Richardson M, Abraham C, Bond R (2013) Psychological correlates of university students' academic performance: a systematic review and meta-analysis. *Psychol Bull* 138: 353 – 387
10. Dandine-Roulland C, Bellenguez C, Debette S, Amouyel P, Génin E, Perdry H (2016) Accuracy of heritability estimations in presence of hidden population stratification. *Sci Rep* 6: 26471