September 10, 2019

Genetic "General Intelligence," Objectively Determined and Measured[§]

[§]The title adds the word *Genetic* to the start of Spearman's 1904 title that discovered phenotypic general intelligence, which he abbreviated as *g*

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Abstract

It has been known for 125 years that, in humans, diverse cognitive traits are positively intercorrelated; this forms the basis for the general factor of intelligence (*g*). We directly test for a genetic basis for *g* using data from seven different cognitive tests (N = 11,263 to N = 331,679) and genome-wide autosomal single nucleotide polymorphisms. A genetic *g* factor accounts for 58.4% (SE = 4.8%) of the genetic variance in the cognitive traits, with trait-specific genetic factors accounting for the remaining 41.6%. We distill genetic loci broadly relevant for many cognitive traits (*g*) from loci associated with only individual cognitive traits. These results elucidate the etiological basis for a long-known yet poorly-understood phenomenon, revealing a fundamental dimension of genetic sharing across diverse cognitive traits.

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Scores on psychometric tests of cognitive abilities (intelligence) robustly predict educational performance, socio-economic attainments, everyday functioning, health, and longevity (*1-3*). In 1904, Charles Spearman identified a positive manifold of intercorrelations among school test results and estimates of intelligence, leading him to propose that they arise from a single general dimension of variation, which he termed general intelligence (and which he denoted as *g*) (*4*). He theorized that most of the remaining variance in each cognitive test was accounted for by a factor specific to that test, which he called *s*. Thus, some variance in each cognitive test is shared with all other cognitive tests (*g*), and some is specific to that test (its *s*). Hundreds of studies have since replicated the finding that, when several or many diverse cognitive tests are administered to a sizeable sample of people, a *g* factor is found that accounts for about 40% of the total test variance (*5,6*). Considerable efforts over the past century have been placed on identifying the biological bases of *g*, spanning levels of analysis from molecular, to neuroanatomical, to cognitive (*7-11*).

Psychometrically, a hierarchical structure of cognitive abilities is commonly agreed, with cognitive tests' variance accounted for by three different strata of variation (Fig. S1), representing each test's specific variance (*s*), broad domains of cognitive function (e.g. reasoning, processing speed, memory), and *g* (*5*). Most twin studies that examine the heritability of human intelligence differences use test scores that mix *g* and *s*; relatively few have applied the twin method to the hierarchy of cognitive test score variance (*12*). The twin-based studies that have separated *g* variance from *s* variance indicate a strong heritable basis for *g,* suggesting that cognitive traits are positively correlated substantially because of strongly overlapping genetic architecture (*13-17*). These findings are consistent across studies, but draw inferences only indirectly, via comparisons of phenotypic correlations across monozygotic and dizygotic twins. To date, molecular genetic methods (GWAS) have been applied to phenotypic indices of *g* (*18-20*). However, the cognitive measures used have been scores derived from individual tests, principal components analysis of several tests, or composite scores from omnibus cognitive tests. They therefore have mixed *g* and *s* variance. On the other hand, GWASs of individual cognitive tests have not taken into account that all tests contain *g* variance, and so genetic loci for, say, verbal declarative memory or processing speed might either be related to *g* and/or to the named cognitive property (*21,22*). This is a common error in both phenotypic and genetic cognitive studies (*23*). Here we sought to test for a genetic *g* factor directly, using a multivariate molecular genetics approach that is applied to the hierarchy of cognitive variation. This investigation provides key insights into the shared genetic architecture across multiple cognitive traits and allows the explicit identification of genetic variants underlying *g*. It distinguishes

variants broadly relevant for many cognitive traits (via genetic *g*) from variants associated with only individual cognitive traits (via genetic *s* factors).

Results

Data for the present study came from the UK Biobank, a biomedical cohort study that collects a wide range of genetic and health-related measures from a population-based sample of community-dwelling participants from the UK. Participants were measured on up to seven cognitive traits using tests that show substantial concurrent validity with established psychometric tests of cognitive abilities, and good test-retest reliability (*24*): *Reaction Time* (RT; *n* = 330,024; perceptual motor speed), *Matrix Pattern Recognition* (*n* = 11,356; nonverbal reasoning), *Verbal Numerical Reasoning* (VNR; *n* = 171,304; verbal and numeric problem solving; the test is called 'Fluid intelligence' in UK Biobank), *Symbol Digit Substitution* (*n* = 87,741; information processing speed), *Pairs Matching Test* (*n* = 331,679; episodic memory), *Tower Rearranging* (*n* = 11,263; executive functioning), and *Trail Making Test – B* (Trails-B; *n* = 78,547; executive functioning). A positive manifold of phenotypic correlations was observed across the seven cognitive traits (Table S2).

We first aimed to determine the genetic contribution of *g* to the variation in each of the cognitive traits using molecular genetic data. We used a multivariable version of Linkage Disequilibrium Score Regression (LDSC) (*25*) implemented in Genomic SEM (*26*) to estimate genetic correlations among the cognitive traits from molecular genetic data. Prior to this formal modelling, we conducted exploratory analyses on the cognitive traits' genetic correlations, similar to those often conducted on cognitive phenotypes.

As was first reported at the phenotypic level by Spearman 125 years ago (*4*), we identified a positive manifold of *genetic* correlations among the UK Biobank cognitive traits, ranging from .14 to .87 (*M* = .53, *SD* = .22; Fig. S2; Tables S1-S2). The mean genetic correlation was .530, and the first principal component accounted for a total of 62.17% of the genetic variance. Using genomic-relatedness based restricted maximum-likelihood (GCTA-GREML) (*27,28*), a different estimator of the genetic correlations among the seven cognitive traits (Fig. S3), the mean genetic correlation was .502, and the first principal component accounted for 61.24% of the genetic variance. The correlation between LDSC- and GCTA-GREML- derived genetic correlations was r = .946, indicating very close correspondence between results of the two methods (Fig. S4).

We then proceeded with Genomic SEM to model the genetic covariance matrix formally; this allowed us to evaluate the fit of the genetic *g* factor model, estimate SEs for model parameters, estimate genetic correlations with collateral phenotypes, and incorporate genetic *g* explicitly into multivariate discovery. We applied Genomic SEM to fit a single common factor model to the LDSC-derived genetic covariance matrix among the seven cognitive traits. This model specified the genetic component of each cognitive trait to load on a single common factor, which we term genetic *g*. For

each trait, we additionally estimated residual, trait-specific genetic variance components (genetic *s*s). Thus, we formally distill the molecular genetic contributions of *g* and *s* to heritable variation in each of the cognitive traits, and test the fit of this model. Fig. 1 displays the standardized estimates for this model (top panel) and the standardized estimates from a phenotypic factor model (bottom panel) fitted to the phenotypic covariance matrix (Fig. S5; Table S3). Standardized genetic factor loadings were linearly associated with standardized phenotypic factor loadings and generally higher in magnitude (Fig. S6). Table 1 additionally reports both the proportion of genetic *g*:genetic *s* variance for each cognitive trait, and the respective absolute contributions. The genetic *g* factor accounted for 58.37% (SE = 4.84%) of the genetic variance in the seven cognitive traits. All of the traits' loadings were statistically significant, ranging from .31 to .98 (M = .74, SD = 0.22). Four of the cognitive traits have a genetic contribution to their variance that is principally from genetic *g* and much less from a genetic *s*; these are Trails-B (95.30% genetic *g*; 4.70% genetic *s*), Tower (72.80% genetic *g*; 27.20% genetic *s*), Symbol Digit (69.10% genetic *g*; 30.90% genetic *s*), and Matrices (68.20% genetic *g*; 31.80% genetic *s*). VNR (51.40% genetic *g*; 48.60% genetic *s*) and Memory (42.40% genetic *g*; 57.60% genetic *s*) are more evenly split. RT has the majority of its genetic influence from a genetic *s* (9.50% genetic *g*; 90.50% genetic *s*). We emphasize one important implication of these results, i.e. that genetic analyses of some of these individual traits will largely reveal results relevant to *g* rather than to the specific abilities thought to be required to perform the test (*23*). Fit indices ($\chi^2(14) = 117.019$, $p < .0001$; CFI = .970; SRMR = 0.088) indicated that the factor model closely approximated the observed genetic covariance matrix (Figs. S7-S8). As the pre-specified model was parsimonious and the fit was close, we chose to forego implementing data-driven exploratory steps to further improve fit. Tables S4-S5 report full parameter estimates for genetic and phenotypic factor models.

We next aimed to determine the contributions of individual genetic loci specifically to genetic *g*, and to distill those from loci associated with other levels of the cognitive hierarchy. We fit a multivariate GWAS of genetic *g* within Genomic SEM (*26*) to distinguish loci relevant to genetic *g* from loci whose patterns of association across the individual traits is inconsistent with their operation on genetic *g*, as indexed by the heterogeneity statistic, Q. We provide detailed explication of the Q statistic and how it can be appropriately interpreted in the *Interpreting the Heterogeneity Statistic* section of the Supplementary Materials. Genome-wide significant loci were defined using FUnctional Mapping and Annotation of genetic associations (FUMA) (*29*); see *Materials and Methods* section of the Supplementary Materials. The GWAS results for genetic *g* and Q are displayed in a Miami plot, Fig. 2. Our method distinguishes four types of significant loci. First, highlighted in red are genome-wide significant loci for genetic *g* that are not genome-wide significant loci for the univariate GWAS analyses of the individual traits. These are discoveries for

genetic contributions to differences in general intelligence made by leveraging the joint genetic architecture of the traits. Second, highlighted in blue are genome-wide significant loci for *g* that are also genome-wide significant loci in the univariate GWAS analyses for at least one individual cognitive trait. These hits might otherwise have been confused for loci relevant specifically to the individual trait, when in fact the multivariate results indicate that they are pleiotropic (*23*); i.e. they are relevant to genetic *g*. Third, highlighted in green are genome-wide significant loci for the univariate phenotypes that are not genome-wide significant loci for *g*. These may be loci that are specific to the individual traits, but not genetic *g*. Fourth, highlighted in yellow are loci that evince genome-wide significant heterogeneity (Q), indicating that they show patterns of associations with the cognitive traits that depart from the pattern that would be expected if they were to act on the traits via genetic *g*.

Q findings that exceed the genome-wide significance threshold for genetic *g* (yellow triangles) are false discoveries on genetic *g* that are likely driven by a strong signal in a subset of the cognitive traits or in a single cognitive trait. The Q statistic helps to safeguard against these false discoveries. The Q findings that do not surpass the genome-wide significance threshold for genetic *g* (yellow diamonds) are not significantly related to genetic *g* but are significantly heterogeneous in their patterns of associations with the cognitive traits. These loci may be relevant to specific cognitive traits, or to cognitive domains that are intermediate in specificity and generality between *g* and *s*, but not to general intelligence (see Fig. S1). We had coverage, here, of different hierarchically-intermediate traits (e.g. processing speed, memory, reasoning), but they were not measured by multiple tests of each. We were therefore unable formally to model effects on intermediate traits as separate from those on *s* factors specific to the individual cognitive traits.

Inspection of the univariate GWAS results for the individual traits may help to determine the sources of heterogeneity for the Q findings. For instance, a SNP (rs429358) within *APOE*, which is a known risk factor for Alzheimer's Disease (*30*), was a significant Q finding. With the exception of its association with VNR, this SNP displayed a pattern of associations with the traits that corresponded closely with the degree to which they represented genetic *g*. However, consistent with the inference that *APOE* is specifically relevant for cognitive aging, the SNP displayed a negligible null association with VNR (p=.142), which is a test that shows minimal age-related differences in the UK Biobank data (*31*). Another example of a Q finding is located on Chromosome 17 (chr17: 44021960- 44852612), which Davies et al. (*18*) reported to be significantly associated with both general cognitive ability and Reaction Time. From the univariate GWAS results, the largest association for this locus was with Reaction Time, a measure of psychomotor speed with a relatively low loading on genetic *g*. This locus may have a particularly pronounced association with speeded abilities, rather than a general association with genetic *g*. The third Q locus which is also significant

for genetic *g* is located on chromosome 3 (chr3:49120040-50234126). This locus has previously-reported associations with general cognitive ability, educational attainment, intelligence, and math ability (*18-20,32*). In the current study, this locus demonstrates significant heterogeneity and displays its largest associations with VNR, Tower, Matrices, and Trails-B, all measures of higher order cognition. It associations with measures of speed and episodic memory (more basic cognitive processes) are negligible.

Overall, we identified 30 genome-wide significant ($p < 5\times10^{-8}$) loci for genetic *g*, 23 of which were common with the univariate GWAS of the individual cognitive traits that served as the basis for our multivariate analysis. We identified, in total, 24 genome-wide significant loci for Q, 3 of which were significantly associated with genetic *g* (and therefore likely to be relevant to more specific cognitive traits, and false discoveries on *g*) and 15 of which were significantly associated with at least one individual cognitive trait in the test-specific GWASs.

The importance of these results may be seen by contrasting the results of Trails-B with Reaction Time. For Trails-B, all of the associated loci have already been reported in univariate GWASs of phenotypes that are essentially general cognitive ability (Table 2). On the other hand, most of the Reaction Time loci have not been found in such univariate GWASs of general cognitive ability. Therefore, when identifying loci associated with performance on an individual cognitive test, it is essential to know the extent to which its associations are broadly related to genetic *g* or specifically related to the phenotype under investigation. As we see in the case of Trails-B, none of its related loci associate exclusively to that test (Table 2); they all relate to the superordinate *g*. Failure to take the multivariate structure of the cognitive traits into account may lead to incorrect inferences (*23*)—either that discoveries made in a univariate GWAS of a cognitive trait are generalizable to the broader universe of cognitive traits when they are in fact specific to that trait, or that discoveries made in a univariate GWAS of a cognitive trait are specific to that trait when they are in fact broadly associated with all traits that load on genetic *g*. For instance, although it is not genome-wide significant for any of the univariate GWASs included in the current analysis, our multivariate analysis using Genomic SEM indicates that a locus on chromosome 7 (chr7:104558814-104588161) is associated with genetic *g*. Lee et al. (*32*) have previously reported this locus to be associated with math ability (Table S22), but there are no previously-reported associations with general cognitive function or intelligence. Similarly, we report an association of a locus on chromosome 8 (chr8:64496159-64842662) with Trails-B (an index of executive function, which is itself strongly genetically correlated with *g* (*13*) in the univariate GWAS, and our Genomic SEM analysis indicates that this locus is also related to genetic *g*. Lee et al. (*32*) have previously reported an association between this locus and math ability, but there are no published findings with general cognitive function or intelligence. In both cases, the current results indicate that the loci are broadly

relevant to many abilities via genetic *g*, not simply to math ability. Multivariate methods, such as that pioneered here, are necessary in order to distinguish whether a locus is narrowly relevant for an individual cognitive trait or broadly relevant to genetic *g*.

Whereas discovery of new genetic associations is not the focus of the current study, we present the largest GWAS to date of a memory phenotype (n = 331,679). From this GWAS, we report seven novel loci, defined as having no previously-reported associations in cognitive GWASs (Table S18). However, some of these loci have been associated with schizophrenia, (*33*) anti-saccade response, (*34*) developmental language disorder (linguistic errors), (*35*) hand grip strength, (*36*) and bone mineral density (*37*) (Table S25).

As expected, the genetic *g* factor identified here displayed strong genetic correlations with general cognitive function from Davies et al., (*18*) (r_g = .90, SE = 0.02), and Savage et al., (*20*) (2018) (r_g = .87, SE = 0.05), which were univariate GWASs of broad cognitive phenotypes, and that of Hill et al., (*19*) (r_g = .80, SE = 0.02), which was a GWAS of intelligence that incorporated educational attainment GWAS summary statistics to boost power via multi-trait analysis of GWAS (MTAG) (*38*). We emphasize, however, that it is not relevant to compare the numbers of genetic loci found to be related to cognitive traits in the present study with those previous studies. Rather, the focus here has been the novel contribution of distilling *g*-specific from non-*g*-related genetic loci. However, we have described particularly illustrative examples of loci found to be related to *g* and to specific traits, and all associations are comprehensively reported in the Supplementary Materials.

Negative genetic correlations were found between our genetic *g* and Alzheimer's disease (r_g = -.34, SE = 0.05), Schizophrenia (r_g = -.37, SE = 0.03), and ADHD (r_g = -.23, SE = 0.04). Additionally, genetic *g* had significant positive genetic associations with total Brain Volume (r_g = .20, SE = 0.04), and Longevity (r_g = .26, SE = 0.03). Genetic *g* had a positive genetic correlation with Educational Attainment (*32*) (r_g =.48, SE = 0.02) that is lower than those found between Education and previous GWASs of cognitive ability (all estimated at r > .69) (*18-20*). To determine whether this lower association was driven by the inclusion of speeded measures as indicators of genetic *g*, we re-estimated the genetic correlations using a genetic *g* factored formed from the cognitive traits that excluded speeded measures (RT, Trails-B, and Symbol Digit). This version of the genetic *g* factor accounted for 69.7% (SE = 11%) of the genetic variance in the four remaining cognitive traits. This version of genetic *g* produced a somewhat higher genetic correlation between genetic *g* and Educational Attainment (r_g =.60) that continued to be lower than those found between Educational Attainment and previous GWASs of general cognitive ability. We suspect that previous GWASs of general cognitive ability might have tapped more academic forms of cognitive function (i.e. crystallized abilities, such as verbal knowledge) than those tapped by the constellation to cognitive tests (even when excluding the speeded tests) used to form genetic *g* in the current

report. Table S6 reports genetic correlations of genetic *g* and other major intelligence GWASs with educational attainment, neural phenotypes, and longevity.

We next created polygenic scores (PGSs) for genetic *g* and the individual UK Biobank cognitive traits and used them to individually and simultaneously predict variance in cognitive performance and educational attainment in an independent study, Generation Scotland; N=6,950 unrelated individuals (Table S7). The cognitive measures were Wechsler Logical Memory (episodic memory), Mill Hill Vocabulary (crystallized knowledge), Wechsler Digit Symbol Substitution (processing speed), and Verbal Fluency (semantic fluency), as described previously (*39,40*). We also calculated the first unrotated principal component of the cognitive measures to index phenotypic *g*, and the first unrotated principal component of the cognitive measures excluding Mill Hill Vocabulary to index a more fluid *g*. Consistent with the Genomic SEM findings that individual cognitive outcomes are associated with a combination of genetic *g* and specific genetic factors, we observed a pattern in which many of the regression models that included both the polygenic score (PGS) from genetic *g* and test-specific PGSs were considerably more predictive of the cognitive phenotypes in Generation Scotland than regression models that included only either a genetic *g* PGS or a PGS for a single test. A particularly relevant exception involved the Digit Symbol Substitution test in Generation Scotland, which is a similar test to the Symbol Digit Substitution test in UK Biobank, for which we derived a PGS. We found that the proportional increase in R^2 in Digit Symbol by the Symbol Digit PGS beyond the genetic *g* PGS was <1%, whereas the genetic *g* PGS improved polygenic prediction beyond the Symbol Digit PGS by over 100%, reflecting the power advantage obtained from integrating GWAS data from multiple genetically correlated cognitive traits using a genetic *g* model. An interesting counterpoint is the PGS for the VNR test, which is unique in the UK Biobank cognitive test battery in indexing verbal knowledge (*24,31*). Highlighting the role of domain-specific factors, a regression model that included this PGS and the genetic *g* PGS provided substantial incremental prediction relative to the genetic *g* PGS alone for those Generation Scotland phenotypes most directly related to verbal knowledge: Mill Hill Vocabulary (62.45% increase) and Educational Attainment (72.59%).

Discussion

Until now, research on the positive manifold of correlations among cognitive traits has been phenotypic in nature, or has made inferences regarding the roles of genes only indirectly, using twin approaches. Therefore, we have previously not known to what extent genetic factors underlie the hierarchy of cognitive variation. Here, we have identified a genetic *g* factor using molecular genetic data, and we have discerned loci that operate on genetic *g* from those that operate on more specific cognitive traits. Harking back to Spearman's 1904 paper's title, the present study has contributed to understanding how measured "general intelligence" is "determined".

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Acknowledgements

This article benefited from valuable discussions with Michel Nivard. **Funding:** This work was supported by National Institutes of Health (NIH) grant R01AG054628. The Population Research Center at the University of Texas is supported by NIH grant P2CHD042849. I.J.D. and G.D are within the Lothian Birth Cohorts group, which is funded by Age UK (Disconnected Mind grant), the Medical Research Council (grant MR/R024065/1), and the University of Edinburgh's School of Philosophy, Psychology and Language Sciences. This research was conducted using the UK Biobank Resource (Application Nos. 10279 and 4844). We are grateful for the availability of data from Generation Scotland: Scottish Family Health Study. Generation Scotland received core support from the Chief Scientist Office of the Scottish Government Health Directorates [CZD/16/6] and the Scottish Funding Council [HR03006]. Genotyping of the GS:SFHS samples was carried out by the Genetics Core Laboratory at the Edinburgh Clinical Research Facility, University of Edinburgh, Scotland and was funded by the Medical Research Council UK and the Wellcome Trust (Wellcome Trust Strategic Award "STratifying Resilience and Depression Longitudinally" (STRADL) Reference 104036/Z/14/Z).

Author Contributions

I.J.D. and E.M.T-D. jointly conceived of the idea, designed the study, and formulated the analytic plan. J. F. and G. D. performed the analyses, with contributions from A.D.G. I.J.D. and E.M.T-D. wrote the paper, with contributions from J. F. and G. D. All authors contributed to editing the paper.

Competing Interests

I.J.D is a participant in UK Biobank.

Data Availability

Complete summary GWAS results from this paper will be made available at the time of publication at https://www.ccace.ed.ac.uk/node/335. Raw data for UK Biobank can be requested at https://www.ukbiobank.ac.uk/register-apply/. Raw data for Generation Scotland can be requested at https://www.ed.ac.uk/generation-scotland/using-resources/access-to-resources/access-process. Code to perform common factor modeling and multivariate GWAS within Genomic SEM can be found at https://github.com/MichelNivard/GenomicSEM/wiki.

Supplementary Material

Method

Interpreting the Heterogeneity Statistic

Figs. S1 – S12

Table S1 – S33

References (*42-66*)

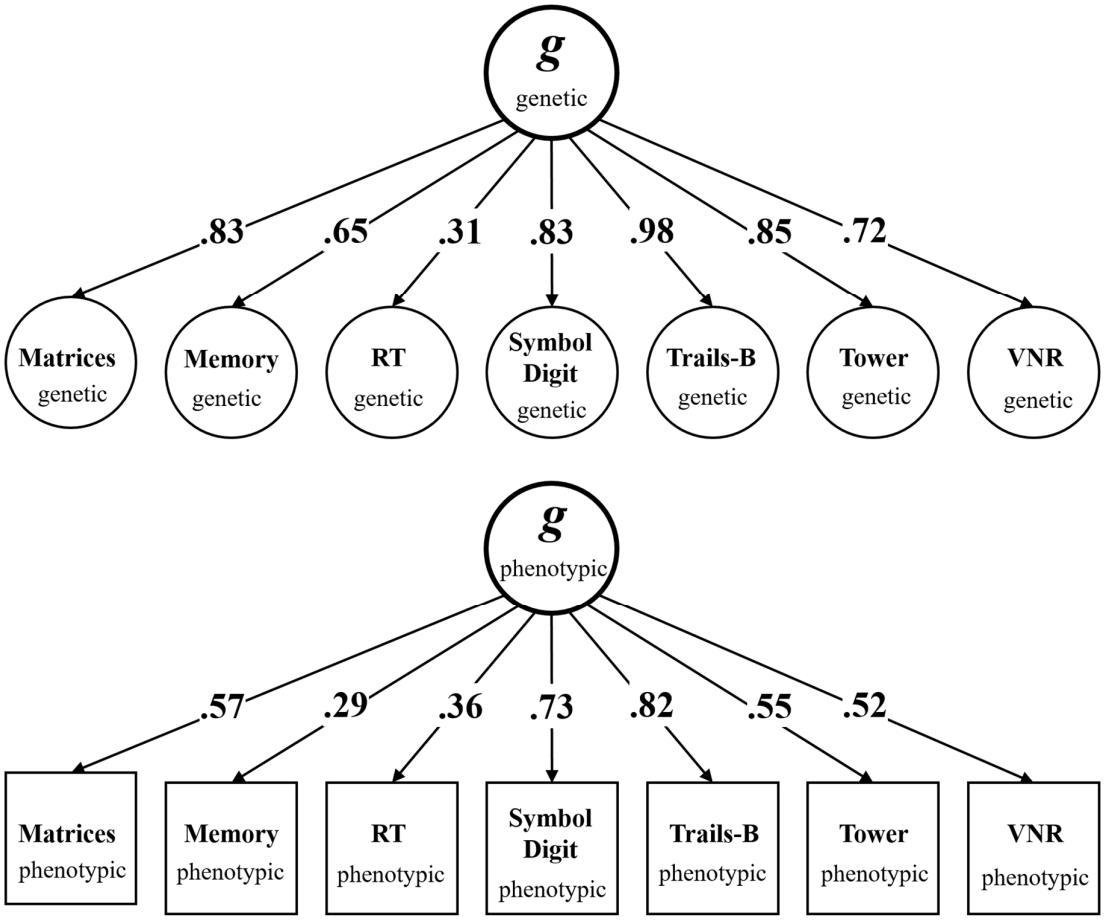

Fig. 1. Standardized genetic (top) and phenotypic (bottom) factor solutions for the covariance structure of seven UK Biobank cognitive traits used in the present study. Squares represent observed variables, i.e. the phenotypes that are directly measured. Circles represent latent variables that are statistically inferred from the data, i.e. the genetic and phenotypic *g* factors that are inferred through factor analysis, and the genetic components of the observed phenotypes that are inferred through LD Score Regression. Arrows are standardized factor loadings, which can be interpreted as standardized regression relations with the arrow pointing from the predictor variable to the outcome variable. Genetic factor models were estimated using Genomic SEM (*26*), and phenotypic models were estimated using the lavaan package for R (*41*). Matrix = Matrix Pattern Completion task; Memory = Memory – Pairs Matching Test; RT = Reaction Time; Symbol Digit = Symbol Digit Substitution Task; Trails-B = Trail Making Test – B; Tower = Tower Rearranging Task; VNR = Verbal Numerical Reasoning Test. All variables are scaled such that higher scores indicate better cognitive performance.

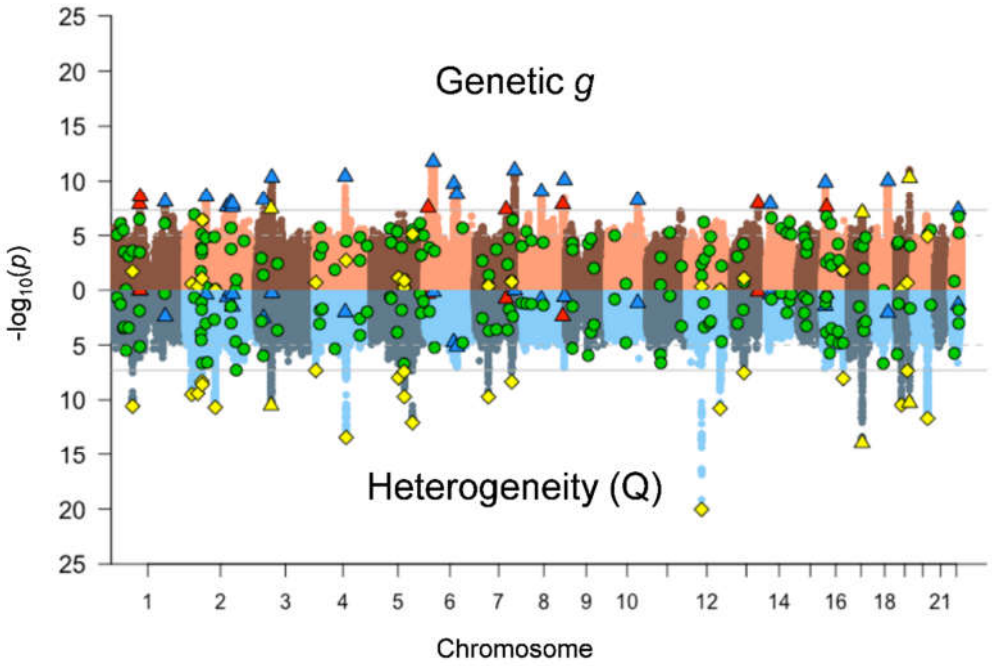

Fig. 2. Miami plot of unique, independent hits for genetic *g* (top) and Q (bottom). Q is a heterogeneity statistic that indexes whether a SNP evinces patterns of associations with the cognitive traits that departs from the pattern that would be expected if it were to act on the traits via genetic *g*. The solid grey horizontal lines are the genome-wide significance threshold ($p < 5\times10^{-8}$) and the dotted grey horizontal lines are the suggestive threshold ($p < 1 \times10^{-5}$). The following genome wide significant loci are highlighted:

Red triangles ▲*: g* loci unique of univariate loci.

Blue triangles ▲*: g* loci in common with univariate loci.

Green circles ●*:* univariate loci not in common with *g* loci.

Yellow triangles ▲*: g* loci in common with Q loci.

Yellow diamonds ◆*:* Q loci unique of *g* loci.

Table 1. Common factor solutions for the genetic (top section) and phenotypic (bottom section) covariance structure of seven UKB cognitive traits.

	Standardized Factor Loadings		Common (g) and specific (s) sources of genetic variation				
	Genetic *g*		Proportion of genetic variation explained by genetic *g* and genetic *s*		Proportion of phenotypic variation explained by genetic *g* and genetic *s* (HapMap3 Common Variants Only)		
Cognitive Trait	Estimate	SE	Common (g)	Specific (s)	Common (g)	Specific (s)	Total SNP h^2
Matrices	0.826	0.070	68.23%	31.77%	10.60%	4.90%	15.50%
Memory	0.651	0.031	42.38%	57.62%	1.70%	2.30%	4.00%
RT	0.308	0.026	9.49%	90.51%	0.70%	6.70%	7.40%
Symbol Digit	0.831	0.034	69.06%	30.94%	7.60%	3.40%	11.00%
Trails-B	0.976	0.035	95.26%	4.74%	14.20%	0.70%	14.90%
Tower	0.853	0.080	72.76%	27.24%	8.30%	3.10%	11.40%
VNR	0.717	0.024	51.41%	48.59%	10.90%	10.30%	21.20%
Mean %			58.37%	41.63%	7.71%	4.49%	12.20%
	Phenotypic *g*		Proportion of phenotypic variation explained by phenotypic *g* and phenotypic *s*				
Cognitive Trait	Estimate	SE	Common (g)	Specific (s)			
Matrices	0.566	0.010	32.04%	67.96%			
Memory	0.287	0.003	8.24%	91.76%			
RT	0.361	0.003	13.03%	86.97%			
Symbol Digit	0.727	0.003	52.85%	47.15%			
Trails-B	0.819	0.003	67.08%	32.92%			
Tower	0.545	0.010	29.70%	70.30%			
VNR	0.519	0.004	26.94%	73.06%			
Mean %			32.85%	67.15%			

Note. Matrices = Matrix Pattern Completion task; Memory = Memory – Pairs Matching Test; RT = Reaction Time; Symbol Digit = Symbol Digit Substitution Task; Trails-B = Trail Making Test - B; Tower = Tower Rearranging Task; VNR = Verbal Numerical Reasoning Test. All traits are scaled such that higher scores indicate higher cognitive performance. Common (*g*) R^2 = proportion of genetic variation accounted for genetic *g* or specific *s* factors. Specific (*s*) R^2 = proportion of genetic variance accounted for specific genetic factors associated with each cognitive test. Total SNP heritability = proportion of phenotypic variance accounted for the causal variants identified in each cognitive test univariate GWAS. *Note:* Standardized factor loadings indicate the standardized linear relationship between the factor and each of the cognitive outcomes. Models are fit to LDSC-derived genetic covariance matrices using Genomics SEM. As per best practices for LDSC, genetic covariance matrices were derived using HapMap3 SNPs with minor allele frequencies > 1%, excluding SNPs with INFO < .9 and those from the MHC region.

Table 2. Summary of Multivariate (Genetic *g*) and Univariate GWAS results.

Outcome	Significant loci (p < 5x10-8)	Unique of other published GWAS hits general cognitive ability[1]	Unique of other published GWAS hits other cognition[2]	Unique of other published GWAS hits educational attainment	Mean χ^2	Overlap with univariate hits	Overlap with Q_{SNP} hits
			Multivariate GWAS				
Genetic *g*	30	2	7	12	1.469	23	3
Q_{SNP}	24	10	12	15		15	-
			Univariate GWAS				
	Significant loci (p < 5x10-8)	Unique of other published GWAS hits specific to the named test	Unique of other published GWAS hits other cognition[3]	Unique of other published GWAS hits Educational attainment	Mean χ^2	Overlap with genetic *g* hits	Overlap with Q_{SNP} hits
Matrices	0	-	-	-	1.040	0	0
Memory	10	10	7	10	1.222	1	0
Reaction Time	39	0	23	31	1.418	5	10
Symbol Digit	1	1	0	1	1.187	1	1
Trails-B	7	7	0	4	1.202	6	2
Tower	0	-	-	-	1.022	0	0
VNR	89	4[4]	47	40	1.638	18	6

Note: The same 7,892,283 variants were used for univariate and multivariate GWAS. Genome-wide significant loci that were 250 kb or closer were merged into a single locus. Here we report loci that are independent from each other at $r^2 < 0.1$.
Matrices = Matrix Pattern Completion task; Memory = Memory – Pairs Matching Test; Symbol Digit = Symbol Digit Substitution Task; Trails-B = Trail Making Test – B; Tower = Tower Rearranging Task; VNR = Verbal Numerical Reasoning Test.

[1]*General cognitive ability includes entries from GWAS catalog for the following traits; cognitive ability, cognitive function, cognitive performance, extremely high intelligence, general cognitive ability, intelligence.*
[2]*Other cognition includes any entries for cognitive traits from GWAS catalog excluding those listed above* [1].
[3]*Other cognition includes all entries for cognitive traits from GWAS catalog except for the named test.*
[4]*For VNR the named test includes all traits listed in note 1, as this test has almost exclusively been published in meta-analyses of general cognitive ability.*
Tables S8-S28 report the individual SNPs, loci and, for those that have been reported in previous studies, the references for the studies, and the implicated phenotypes.