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Intelligence indexes generalist genes for cognitive abilities ☆

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ABSTRACT

Twin research has supported the concept of intelligence (general cognitive ability, g) by showing that genetic correlations between diverse tests of verbal and nonverbal cognitive abilities are greater than 0.50. That is, most of the genes that affect cognitive abilities are highly pleiotropic in the sense that genes that affect one cognitive ability affect all cognitive abilities. The impact of this finding may have been blunted because it depends on the validity of the twin method. Although the assumptions of the twin method have survived indirect tests, it is now possible to test findings from the twin method directly using DNA alone in samples of unrelated individuals, without the assumptions of the twin method. We applied this DNA method, implemented in a software package called *Genome-wide Complex Trait Analysis* (GCTA), to estimate genetic variance and covariance for two verbal tests and two nonverbal tests using 1.7 million DNA markers genotyped on 2500 unrelated children at age 12; 1900 children also had cognitive data and DNA at age 7. Because each of these individuals is one member of a twin pair, we were able to compare GCTA estimates directly to twin study estimates using the same measures in the same sample. At age 12, GCTA confirmed the results of twin research in showing substantial genetic covariance between verbal and nonverbal composites. The GCTA genetic correlation at age 12 was 1.0 (SE = 0.32), not significantly different from the twin study estimate of 0.60 (SE = 0.09). At age 7, the genetic correlations were 0.31 (SE = 0.32) from GCTA and 0.71 (SE = 0.15).from twin analysis. The results from the larger sample and stronger measures at age 12 confirm the twin study results that the genetic architecture of intelligence is driven by pleiotropic effects on diverse cognitive abilities. However, the results at age 7 and the large standard errors of GCTA bivariate genetic correlations suggest the need for further research with larger samples.

1. Introduction

Because intelligence predicts educational attainment, income, health and longevity better than all other predictors combined, it is a key ingredient in the intellectual capital of knowledge-based societies (Deary, 2012). Intelligence is at the pinnacle of the hierarchical model of cognitive abilities that subsumes group factors and specific tests (Carroll, 1993, 1997), which is why it has been called general cognitive ability (g) (Jensen, 1998; Spearman, 1904). Genetic research, largely based on the twin method that compares resemblance for monozygotic and dizygotic twins, suggests that genes with pervasive effects across cognitive abilities are the genetic foundation for intelligence. In contrast to the average phenotypic correlations of about 0.30 between diverse cognitive abilities (Carroll, 1993), genetic correlations among cognitive abilities are consistently greater than 0.50 in more than a dozen studies in childhood, adolescence, and adulthood, with some evidence for increasing genetic correlations during childhood (Plomin, DeFries, Knopik, & Neiderhiser, 2013).

Genetic correlations indicate the extent to which the same genes affect different abilities; they are literally correlations between genetic effects on traits independent of heritability (Plomin, DeFries et al., 2013). This overlap in genetic effects is generally known as *pleiotropy* but has been dubbed *generalist genes* to highlight this finding in relation to cognitive abilities

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(Plomin & Kovas, 2005). Because genetic correlations are not 1.0, these same data also provide evidence for genetic specificity. However, given how diverse cognitive processes appear to be – such as verbal, spatial and memory – what is surprising is the extent of genetic overlap between these abilities. Although multivariate genetic research has drilled down beneath traditional tests of cognitive abilities to uncover similar results for elementary cognitive processes and brain structure and function (Deary, Penke, & Johnson, 2010), the present paper focuses on traditional tests of verbal and nonverbal cognitive function.

Because generalist genes would seem to be a major finding about the origins of individual differences in cognitive abilities – suggesting that g indexes general genes for cognitive abilities – it is surprising that this finding has had so little impact in related fields such as neuroscience or experimental cognitive psychology. We suggest that part of the reason for this neglect – in addition to the major reason that these fields generally ignore individual differences (Baddeley, 2012; Giedd & Rapoport, 2010) – is that the generalist gene finding rests largely on the twin design, although adoption research also supports the hypothesis. Even though the assumptions of the twin and adoption methods have been tested and generally pass these tests (Plomin, DeFries et al., 2013), these assumptions make it easier to ignore the results of twin and adoption studies.

The purpose of the present study is to investigate the genetic nature of cognitive abilities using a new method that is based solely on DNA, which avoids the assumptions of the twin and adoption methods. The method, implemented in a software package called Genome-wide Complex Trait Analysis (GCTA), correlates genetic similarity pair by pair with each pair's phenotypic similarity in a large sample of unrelated individuals. Specifically, the method partitions the phenotypic variance into additive genetic and residual components by fitting a genetic 'relatedness' matrix to a phenotypic matrix in a mixed linear model (MLM; Yang et al., 2010; Yang, Lee, Goddard & Visscher, 2011). Genetic similarity is assessed overall from hundreds of thousands of single-nucleotide polymorphisms (SNPs) in large samples of unrelated individuals; such data are widely available from genome-wide association (GWA) studies (Plomin, 2012). Crucially, unlike GWA studies, this MLM method does not rely on detecting associations with individual SNPs, but rather it calculates the overall effect of all SNPs as well as DNA variants correlated with the SNPs. Because the method does not have a consistent name, we refer to it as GCTA, which is the name of its software package. Univariate GCTA has found genetic influence for intelligence in adults (Chabris et al., 2012; Davies et al., 2011) and children (Plomin, Haworth, Meaburn, Price, & Davis, 2013), as well as for height (Yang et al., 2010) and weight (Yang, Manolio, et al., 2011), psychiatric and medical disorders (Lee, Wray, Goddard, & Visscher, 2011; Lee, DeCandia, et al., 2012; Lubke et al., 2012), and personality (Benjamin, Ebstein, & Belmaker, 2002; Vinkhuyzen et al., 2012).

Bivariate GCTA has recently been developed to estimate genetic correlations between traits (Lee, Yang, Goddard, Visscher, & Wray, 2012). It was first applied to the longitudinal correlation between intelligence in childhood and old age (Deary, Yang, Davies, Harris, Tenesa, Liewald, et al., 2012) and subsequently to childhood intelligence from age 7 to age 12 (Trzaskowski, Yang, Visscher, & Plomin, in press). We have also applied bivariate GCTA to confirm twin study estimates of high genetic correlations between g and academic performance in reading, mathematics and language (Trzaskowski et al., 2013). The present study uses bivariate GCTA to address the fundamental issue of the genetic nature of intelligence itself. We compare GCTA estimates of genetic variance and covariance to estimates from the twin method using the same sample assessed longitudinally at ages 7 and 12 and the same measures of verbal and nonverbal cognitive abilities. Such direct comparisons between GCTA and twin study estimates go beyond merely testing the methodological validity of the twin method: As explained later, they reveal important information about the genetic architecture of intelligence.

2. Method

2.1. Participants

The sample was drawn from the Twins Early Development Study (TEDS), which is a multivariate longitudinal twin study that recruited more than 11,000 twin pairs born in England and Wales in 1994, 1995 and 1996 (Haworth, Davis, & Plomin, 2013; Oliver & Plomin, 2007). TEDS has been shown to be the representative of the UK population (Kovas, Haworth, Dale, & Plomin, 2007). The project received approval from the Institute of Psychiatry ethics committee (05/Q0706/228) and parental consent was obtained prior to data collection. Individuals were included if their first language was English and they had no major medical or psychiatric problems. Using data collected at ages 7 and 12, respectively, GCTA was conducted on approximately 1900 and 2500 unrelated individuals (only one member of each twin pair) with DNA and cognitive data. Twin model-fitting analyses were conducted on around 1900 twin pairs at age 7 and around 2350 pairs at age 12. As expected for representative twin studies, the twins included similar numbers of MZ twins, same-sex DZ twins, and opposite-sex DZ twins (see Table 1 for sample size details.)

2.2. Genotyping

Although DNA is available for more than 12,000 TEDS participants, funds were available to genotype 3665 individuals (one member only per twin pair) on Affymetrix GeneChip 6.0

Table 1
Twin and GCTA parameter estimates for verbal and nonverbal abilities at ages 7 and 12.

	Twin			GCTA	
	A	C	E	A (SE)	E (SE)
Age 7					
Verbal	.29 (.06)	.34 (.05)	.36 (.02)	.47 (.18)	.52 (.17)
Nonverbal	.21 (.07)	.28 (.05)	.50 (.03)	.26 (.17)	.74 (.17)
Age 12					
Verbal	.36 (.06)	.21 (.05)	.43 (.02)	.23 (.13)	.76 (.13)
Nonverbal	.42 (.06)	.16 (.05)	.42 (.02)	.15 (.14)	.84 (.14)

Standard error (SE) is shown in parentheses. Twin analyses were restricted to twin pairs for whom one member of the twin pair was included in GCTA. The twin analyses at age 7 were based on 734 MZ and 1146 DZ twin pairs for verbal and 742 MZ and 1164 DZ twin pairs for nonverbal; twin analyses at age 12 were based on 920 MZ and 1432 DZ twin pairs for verbal and 894 MZ and 1402 DZ twin pairs for nonverbal. The numbers of unrelated individuals in GCTA analyses were 1900 for verbal and 1917 for nonverbal at age 7 and 2496 for verbal and 2428 for nonverbal at age 12.