Genome analysis shows the combined effect of many genes on cognitive traits

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Individual differences in cognitive abilities in children and adolescents are partly reflected in variations in their DNA sequence, according to a study published in *Molecular Psychiatry*. These tiny differences in the human genome can be used together to create so-called polygenic scores; the sum of a number of genetic variants an individual carries reflecting

the genetic predisposition to a particular trait. This includes differences in educational achievement (how well pupils do in English, maths, and science), how many years of education they complete, and their IQ at age 16.

Researchers at King's College London, UK analysed genetic information from 7,026 UK children at ages 12 and 16 included in the Twins Early Development Study, a longitudinal study of twins born in England and Wales between 1994 and 1996. Intelligence and educational achievement at ages 12 and 16, and their associated genetic variants, were analysed. Intelligence was assessed via verbal and non-verbal web-based IQ tests. Educational achievement was assessed by how well pupils did in English, maths, and science, which are compulsory in the UK.

The researchers showed that polygenic scores, which reflect the combined effect of multiple genetic variants, may predict up to 11% of the difference in intelligence and 16% of the difference in educational achievement between individuals.

Andrea Allegrini, the corresponding author said: "The effects of single variants on a given trait are often extremely small, and difficult to capture accurately. However, most behavioural traits share a substantial proportion of genetic variation that is a proportion of genetic variants affect multiple traits at the same time. The degree to which shared genetic influences account for similarities between traits is known as genetic correlation.

Multivariate (so-called multi-trait) genomic approaches make use of genetic correlations between traits to more accurately estimate the effect of genetic variants on a given trait. These can be used to increase the predictive power of polygenic scores. We compared several novel, state of the art, multi-trait genomic methods to maximise polygenic score prediction."

The authors found that when analysing genetic variants associated with intelligence, they were able to predict 5.3% of the difference in intelligence between individuals at age 12 and 6.7% of the difference at age 16. For educational achievement, analysing genetic variants associated with educational attainment (years of schooling), they predicted a maximum of 6.6% of the difference at age 12 and 14.8% at age 16. The authors also showed that analysing variants associated with educational attainment allowed them to predict 7.2% of the variance in intelligence at age 12 and 9.9% at age 16, because of the genetic correlation between the two traits.

When taking a multivariate/multi-trait approach, and adding three other, genetically correlated traits and their associated genes to the analysis, prediction accuracy improved to 10% of the difference in intelligence at age 16 and 15.9% of the difference in educational achievement. The authors also tested three different genomic methods to show that their predictive accuracy was similar.

Andrea Allegrini said: "Our findings indicate that there are no notable differences between the multi-trait prediction methods we tested. Even though these methods employ different mathematical models, they arrive at similar conclusions. This is extremely encouraging as it indicates that our estimates are robust, in that they are generally stable across methods tested."

He added: "However, it is also important to understand that these are average differences, which means that many people with a low genetic predisposition to educational attainment can still do very well in school, and vice versa. As such, these scores are probabilistic; they do not show that education or intelligence are determined by a person's genes."

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