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Intelligence inheritance – three genes that add to your IQ score

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Intelligence, cognitive ability or cognitive performance is usually measured by a battery of tests that aim to quantify skills such as memory and analytical ability. There is loads of variation between people in how they perform on such tests, and these differences can be due to genetic and environment factors, and their interplay.

In research published in the *Proceedings of the National Academy of Science* (*PNAS*) today, we show three genetic variants in humans that can account for a couple of IQ points – but before you get excited, these are only three variants out of likely thousands.

The genetics of cognitive performance

While a measure of "intelligence" can be controversial, cognitive performance scores are widely used because of their predictive ability. Educational attainment, income, job performance and health are all correlated with cognitive performance.

By comparing the cognitive performance between family members, including comparisons between identical and non-identical twins, scientists are able to quantify the contribution of genetic and environmental causes of individual differences.

Decades of research have shown that genetic factors account for about half of the causes of individual difference in cognitive performance, and recent studies using unrelated people have confirmed that a substantial proportion of individual difference is due to genetic factors.

So, we know now that cognitive performance is heritable, but where are the genes? Despite considerable attempts to find genes for cognitive performance, no specific genes had been found and replicated.

One reason for this puzzle is that there are a lot of genes involved – thousands, even – and their individual gene effect sizes are tiny. Past studies couldn't find them because sample sizes were not large enough to detect genes with statistical significance.

So how did we overcome this problem?

Last year, a huge international collaborative study of more than 126,000 people correlated millions of genetic variants with educational attainment and discovered three genetic variants associated with it.

Education attainment is correlated with cognitive performance, so given

these two observations, we tested the genetic variants for education attainment with their associations with cognitive performance, which we report in *PNAS* today.

We tested 69 genetic variants from the educational attainment study (of almost 107,000 people) in independent samples of 24,000 people who had a cognitive performance score. This two-stage strategy is called a "proxy-phenotype method" since educational attainment is a proxy phenotype (an observable characteristic or trait) for cognitive performance.

The essence of this design was to piggy-back on a much larger study from a correlated trait (educational attainment) to pre-select a small number of genetic variants. These were then tested for association with cognitive performance – a bit like leveraging a large study on the genetics of weight to find genes for diabetes.

Three genetic variants (out of thousands)

Previously, using a genome-wide study in a sample of 18,000 individuals , we could not identify a single genetic variant associated with cognitive performance. Using the new proxy strategy, though, we identified three genetic variants associated with cognitive performance. As expected from the calculation, the effects of these variants on cognitive performance are tiny.

A copy of each variant accounts for only 0.3 points on a standard IQ test (with a mean of 100 and standard deviation of 15). A person who inherits all six copies (note: one genetic variant has two copies) of increasing variants differs by 1.8 points compared to individual who inherits none. That's a small difference.

Another interesting finding from our study is related to the potential

relevance to our health. A combination of genetic effect calculated from 60 education attainment-associated variants is correlated with memory and absence of dementia in an independent sample of almost 9,000 individuals.

While it is premature to suggest the biological function of the genes identified, our additional analysis suggests that the genes are related to synaptic plasticity – the main mechanism in the brain for learning and memory.

The take-away message

This study of normal variation in cognitive performance confirms that there is no gene with a large effect on this trait. There is no "gene for intelligence" – instead, cognitive performance is likely to be influenced by thousands of genes, each having a small effect.

While the individual effect of the genetic variants are extremely small, their identification may lead to knowledge of the biological pathways involved in cognitive performance and cognitive ageing. This insight may eventually lead us into a better understanding of the mechanism involves in memory loss and dementia.

Finally, because individual gene effects are small, an implication of the study is that even larger studies, for example on millions of people, will lead to the discovery of many more gene variants.

More information: Cornelius A. Rietveld, et al. "Common genetic variants associated with cognitive performance identified using the proxy-phenotype method." *PNAS* 2014 ; published ahead of print September 8, 2014, DOI: 10.1073/pnas.1404623111

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