Single change in genetic sequence can significantly impact BMI variability

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(Medical Xpress)—One small change to the DNA sequence can cause more weighty changes to the human body, according to a new study released today.

The discovery comes thanks to a worldwide consortium of researchers that includes Professor and Chair of Quantitative Genetics at The University of Queensland (UQ), Peter Visscher, from the Queensland Brain Institute (QBI) and Diamantina Institute (DI) at UQ.

He and his team have found a single change in genetic sequence at the gene FTO had a significant effect on the variability of body mass index (BMI).

BMI is a commonly used measure of obesity. It measures someone's weight adjusted for his or her height.

Professor Visscher said that the genetic change, called a single nucleotide polymorphism (SNP), was the replacement of one nucleotide – the units that make up our DNA – with another.

"They are the most abundant type of variation in the human genome," he said.

"SNPs occur normally throughout our DNA and most have no effect on our health, however, we've found one that does have a small but significant effect on variation in BMI."

After analysing data from almost 170,000 people, he and his team established that those with a sequence variant in the FTO gene not only weighed more on average, but the measured weights varied more than in the group without the variant.

The variability of BMI within the group with two copies of the variant was, in fact, 7 per cent larger than the group without the variant.

Professor Visscher said this equated to around half a kilogram difference in the standard deviation of weight.

"So as a group, people with two copies of the weight increasing variant are a few kilograms heavier and vary more," he said.

Genetic differences in variability of specific traits have been seen in many plant and animal species but specific genes or mechanisms to explain the phenomenon had not been identified.

Professor Visscher's study is the first to look systematically at genetic effects on variation of a complex trait in humans using a very large sample size.

"The study is important because it demonstrates that genes can be found that affect trait variability.

"This is a first step towards understanding how genes control variation," Professor Visscher said.

This study is also the first to offer researchers an indirect method to measure genotype by environment interactions without having a measure of specific environmental factors.

"If a gene interacts with specific environmental factors then this can be

observed with our method," Professor Visscher said.

"For example, if the effect of a gene on weight is smaller in people who physically exercise than in people who do not, then this will lead to less variation among people with two copies of the weight decreasing variant.

"In our study we did not measure specific environmental effects such as physical exercise so we can't say for sure whether our results are due to a genotype-environment interaction."

This is the second study Professor Visscher has published in the prestigious journal Nature this year.

Earlier this year he identified that genetic differences also affect how intelligence changes across a lifetime.

The work also suggested these changes in intelligence were largely influenced by environmental factors.

More information: This research, entitled "FTO genotype is associated with phenotypic variability of body mass index" had Advanced Online Publication in the journal *Nature* on September 17.

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