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Genetic studies reveal new causes of severe obesity in childhood

Scientists in Cambridge have discovered that the loss of a key segment of DNA can lead to severe childhood obesity. This is the first study to show that this kind of genetic alteration can cause obesity. The results are published today in Nature.

The study, led by Dr Sadaf Farooqi from the University of Cambridge and Dr Matt Hurles from the Wellcome Trust Sanger Institute, looked at 300 children with severe obesity.

The team scanned each child's entire genome looking for types of mutation known as copy number variants (CNVs). CNVs are large chunks of DNA either duplicated or deleted from our genes. Scientists believe this type of mutation may play an important role in genetic diseases.

By looking for CNVs that were unique in children with severe obesity, compared with over 7,000 controls (apparently healthy volunteers from the Wellcome Trust Case Control Consortium 2), they found that certain parts of the genome were missing in some patients with severe obesity.

According to Dr Farooqi: "We found that part of chromosome 16 can be deleted in some families, and that people with this deletion have severe obesity from a young age.

"Our results suggest that one particular gene on chromosome 16 called SH2B1 plays a key role in regulating weight and also in handling blood sugar levels. People with deletions involving this gene had a strong drive to eat and gained weight very easily."

Dr Matt Hurles adds: "This is the first evidence that copy number variants have been linked to a metabolic condition such as obesity. They are already known to cause other disorders such as autism and learning difficulties."

The findings also have implications for diagnosing severe childhood obesity, which has on occasion been misattributed to abuse. Some of the children in the study had been formally

placed on the Social Services 'at risk' register on the assumption that the parents were deliberately overfeeding their children and causing their severe obesity. They have now been removed from the register.

"This study shows that severe obesity is a serious medical issue that deserves scientific investigation," says Dr Farooqi. "It adds to the growing weight of evidence that a wide range of genetic variants can produce a strong drive to eat. We hope that this will alter attitudes and practices amongst those with professional responsibility for the health and well-being of children."

Obesity is increasing throughout the world and is now recognised as a major global public health concern. Although the increased prevalence of obesity over the past 30 years is undoubtedly driven by environmental factors, genetic factors play a major role in determining why some people are more likely to gain weight than others.

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Notes to editors:

1. The paper, Elena G. Bochukova et al, 'Large, rare chromosomal deletions associated with severe early-onset obesity' is published in Nature on 6 December 2009.

2. The study was funded by the Wellcome Trust, the largest charity in the UK. It funds innovative biomedical research, in the UK and internationally, spending over £600 million each year to support the brightest scientists with the best ideas. The Wellcome Trust supports public debate about biomedical research and its impact on health and wellbeing.

3. The study represented a collaboration between Dr Farooqi's team at the University of Cambridge Metabolic Research Laboratories (MRL), part of the Institute of Metabolic Science (IMS) and Dr Hurles's team at the Wellcome Trust Sanger Institute.

4. The mission of the MRL is to undertake basic and translational research relevant to the understanding, prevention and treatment of diabetes, obesity and other related endocrine and metabolic disorders.

5. The Wellcome Trust Sanger Institute, which receives the majority of its funding from the Wellcome Trust, was founded in 1992 as the focus for UK sequencing efforts. The Institute is responsible for the completion of the sequence of approximately one-third of the human genome as well as genomes of model organisms such as mouse and zebrafish, and more than 90 pathogen genomes. In October 2005, new funding was awarded by the Wellcome Trust to enable the Institute to build on its world-class scientific achievements and exploit the wealth of genome data now available to answer important questions about health and disease. These programmes are built around a Faculty of more than 30 senior researchers. The Wellcome Trust Sanger Institute is based in Hinxton, Cambridge, UK.