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Childhood obesity risk increased by newly-discovered genetic mutations

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Health professionals could intervene to help children before they develop weight problems.

(PhysOrg.com) -- Three new genetic variations that increase the risk of obesity are revealed in a new study, published today in the journal *Nature Genetics*. The authors suggest that if each acted independently, these variants could be responsible for up to 50% of cases of severe obesity.

Together with existing research, the new findings should ultimately provide the tools to predict which young children are at risk of becoming obese. Health professionals could then intervene to help such children before they develop weight problems, say the researchers from Imperial College London, the French National Research Institute CNRS and other international institutions.

In the UK, one in ten children under the age of six is obese, according to the Department of Health's National Child Measurement Programme 2007/08.

For today's ten-year study, scientists looked at the genetic makeup of obese children under six and morbidly obese adults, most of whom had been obese since childhood or adolescence, and compared this with age matched people of normal weight. The study reveals three previously unidentified genetic variations that increase the risk of severe obesity significantly, giving new insight into the reasons why some people become obese and others do not.

The gene variant most strongly associated with childhood obesity and adult morbid obesity in the study is located near the PTER gene, the function of which is not known. This variant is estimated to account for up to a third of all childhood obesity, and a fifth of all cases of adult obesity.

The second variant associated with child and adult obesity is found in the NPC1 gene. Previous studies in mice have suggested that this gene has a role in controlling appetite, as mice with a non-functioning NPC1 gene suffer late-onset weight loss and have poor food intake. This gene variant accounts for around 10 per cent of all childhood obesity and about 14 per cent of adult morbid obesity cases.

The final variant is found near the MAF gene, which controls the production of the hormones insulin and glucagon, as well as chains of amino acids called glucagon-like peptides. These hormones and peptides are known to play key roles in people's metabolisms by metabolising glucose and carbohydrates in the body. In addition, glucagon and glucagon-like peptides appear to have a strong effect on people's ability to feel 'full' or satiated after eating. This variant accounts for about 6 per cent of early-onset obesity in children, and 16 per cent of adult morbid

obesity.

Further research is needed to determine whether the gene variants are acting independently, but if they are, then together these three new variations may account for up to half of all cases of severe adult and child obesity.

Professor Philippe Froguel, one of the authors of the study from the Department of Genomic Medicine at Imperial College London said: "When young children become obese, their lives can be affected in a very negative way. Sadly, obese children are often unfairly stigmatised and they can suffer heart and lung problems, painful joints, diabetes and cancer as they grow up.

"Understanding the genetic basis of obesity is the first step towards helping these children. Once we identify the genes responsible, we can develop ways to screen children to find out who is most at risk of becoming obese. Hopefully we can then intervene with measures such as behavioural therapy, to make sure a child forms healthy eating habits and does not develop a weight problem," added Professor Froguel.

The researchers reached their conclusions by conducting a genome-wide association study of 1,380 Europeans with early-onset childhood obesity and adult morbid obesity, and 1,416 age-matched normal weight controls. The study revealed 38 genetic markers with a strong association to a higher than normal body mass index, which the researchers evaluated in 14,186 Europeans, identifying three mutations that are significantly linked to obesity.

Source: Imperial College London