MedicalXpress

Obesity starts in the head? 6 newly discovered genes for obesity have a neural effect

January 8 2009

The international GIANT (Genetic Investigation of Anthropometric Parameters) consortium works on the discovery of obesity genes. So far, the scientists have analyzed two million DNA variations in 15 genome-wide association studies with a total of more than 32,000 participants. The hereby identified candidate genes were validated in 14 further studies including 59,000 participants. In addition to the FTO and MC4R genes already known, it was now possible for six more obesity genes to be identified: TMEM18, KCTD15, GNPDA2, SH2B1, MTCH2, and NEGR1.

Gene expression analyses have shown that all six genes are active in brain cells. Also the previously known two obesity genes, FTO and MC4R, show a similar expression pattern; in case of the MC4R gene, a genotype-dependant influence on the behavior of appetite is already established.

Scientists of the German National Genome Research Network (NGFN), Prof. H.-Erich Wichmann and Dr. Iris Heid from the Helmholtz Zentrum München, Institute of Epidemiology, who lead the German participation of this consortium, emphasize: "Definitely, the two main causes for obesity are poor nutrition and lack of physical activity. But the biology of these genes suggests genetic factors underlying the different reaction of people to lifestyle and environmental conditions."

With the exception of the SH2B1 gene, which plays a role in the leptin signalling and thus in the regulation of appetite, none of the other five genes was hitherto discussed as obesity genes. Iris Heid and her collegue Claudia Lamina from the Ludwigs-Maximilians-Universität München are enthused: "The purely statistical approach of the genome-wide association analysis can depict new aspects of the biology of weight regulation, which were previously unanticipated."

As a next step, the scientists evaluate other anthropometric measures, in order to shed light on different aspects of obesity. In addition, they will expand and include further studies into their analysis as they have realized that the individual studies are all too small, and only by means of collaboration, is it possible to achieve further success here.

Publication: Willer et al.: Six New Loci Associated with Body Mass Index Highlight a Neuronal Influence on Body Weight Regulation. *Nature Genetics* 2008 (DOI 10.1038/ng.287)
www.nature.com/ng/journal/v41/n1/abs/ng.287.html

Source: Helmholtz Zentrum München - German Research Center for Environmental Health