

## **Couch potato? It could be genetic**

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Scientists in China and Aberdeen have made a key discovery which could explain why some people are 'couch potatoes'.

(Medical Xpress)—Scientists in China and Aberdeen have made a key discovery which could explain why some people are 'couch potatoes'.

They have found that a mutation in a gene, which has a critical role in the brain, may explain why some people are less inclined to exercise and are more likely to put on weight and develop health problems.

Their study - published in *PLOS Genetics* - also raises the prospect that in the future there could be a personalised pill that could reverse the



problem.

Scientists from the Chinese Academy of Sciences, Institute of Genetics and Developmental Biology (IGDB) in Beijing and the University of Aberdeen, compared 'normal' <u>mice</u> with mice that had a mutation in a gene called SLC35D3.

The researchers discovered that SLC35D3 produces a protein which plays a key signalling role in the brain's dopamine system – this system is involved in a range of functions including regulation of <u>physical activity</u> <u>levels</u>.

Specifically they found that SLC35D3 seems to be important for transporting a type of dopamine receptor, from where they are made inside the cell, to the cell surface, where they can bind with dopamine.

However mice with this gene mutated had far fewer of this type of dopamine receptor on their brain cell surfaces. Instead, the <u>dopamine</u> <u>receptors</u> were stuck within the cell. This meant that their signalling process was not functioning properly.

Professor Wei Li, of the IGDB, where all the work was carried out, led the study. He said: "We discovered that mice with this gene mutation were typical couch potatoes. They walked only about a third as much as a normal mouse, and when they did move they walked more slowly. The mice became fat and they also developed other symptoms similar to a condition in people called 'metabolic syndrome' - a medical term for those with a combination of risk factors related to diabetes, <u>high blood</u> <u>pressure</u> and obesity."

Professor John Speakman, who works between the University of Aberdeen and the IGDB, and was a co-author on the paper, said: "We discovered that SLC35D3 plays a critical role in transporting the



dopamine 1 receptor from where it is made inside the cell, to the <u>cell</u> <u>surface</u>. Hence dopamine signalling in the mutant mice was significantly impaired."

Professor Li added: "What was of particular interest, was that what that when we gave the mice a drug that acted on the dopamine signalling system, the genetic defect could be overcome and the mice became more active and thinner."

The researchers then screened 400 overweight and obese Chinese patients with metabolic syndrome and found mutations in the SLC35D3 gene in two of them.

As the mice could be treated using a drug that acted on the dopamine receptor, the scientists suggest that in the future people with metabolic syndrome could possibly be screened to see if they have the relevant mutations. If so, perhaps drugs could be offered as a treatment.

Professor Li said: "We are really excited about these findings. A longstanding prescription in combating obesity is to mind your mouth and move your legs. However, genetics contributes to the reluctance to move in some obese people. Medical treatments will in the future be tailored to fit a person's individual genetic make-up."

Professor Speakman added: "Although only about one in about 200 people may have these 'rare' mutations, there are a very large number of people worldwide that have <u>metabolic syndrome</u>. Consequently the population of sufferers that may benefit from being treated with dopamine receptor drugs runs into many millions of patients. The work is a perfect example of successful translational work – from great basic science to an important potential clinical application."

More information: Zhang Z, Hao C-J, Li C-G, Zang D-J, Zhao J, et



al. (2014) "Mutation of SLC35D3 Causes Metabolic Syndrome by Impairing Dopamine Signaling in Striatal D1 Neurons." *PLoS Genet* 10(2): e1004124. <u>DOI: 10.1371/journal.pgen.1004124</u>

## Provided by University of Aberdeen

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