



Asian Journal of
Cell Biology

ISSN 1814-0068



Academic
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New Discovery Explains Weight Problems in Huntington's Disease

Huntington's disease has long been linked to jerky movements. Now, researchers in Lund, Sweden, have shown that the metabolism can also be seriously affected by the hereditary disease. The new laboratory findings provide hope of entirely new treatment methods.

The study, which has been published in the scientific journal *Cell Metabolism*, shows significant changes in the brain's hormone control centre, the hypothalamus. In a series of experiments on mice, which had the mutated Huntington's protein injected into this area of their brains, the animals soon demonstrated a reduced ability to regulate their metabolism.

"With the selectively produced mutated protein, we saw immediate changes; the mice started to eat more and became very fat. We have now been able to prove that there is a causal relationship between this mutated protein in the hypothalamus and weight gain. The changes we see in the mice's brains are similar to those we have previously observed in the brains of Huntington's patients," says doctor and researcher Åsa Petersén at Lund University.

The effects of the mutated Huntington's protein disable the normal control of blood sugar levels in the body. It is probable that a resistance to insulin is developed, which makes some nerve cells deaf to important signals. This stops the complex metabolic system working.

The research group has previously shown that the pathological changes in the hypothalamus begin up to ten years before the movement problems are seen. This means that new treatments targeted at the small communications

control centre, the hypothalamus, could provide relief to Huntington's patients at a much earlier stage.

One of the most promising treatments that are currently being researched aims to 'turn off' the mutated Huntington's gene. The research group in Lund has successfully tested the method on mice, with the result that they stopped developing irregularities in their metabolism.

"Our idea is to turn off the mutated gene in the hypothalamus. The problem is that we don't want to turn off the normal Huntingtin gene, which still has an important function. We now hope to be able to refine our method and focus specifically on the mutated Huntingtin," says Åsa Petersén.

The newly discovered changes in the hypothalamus in Huntington's disease are a growing research field. The targets for new treatments are non-motor symptoms such as weight problems, sleeping problems and depression.

Journal Reference: 1. Sofia Hult, Rana Soylu, Tomas Björklund, Bengt F. Belgardt, Jan Mauer, Jens C. Brüning, Deniz Kirik, Åsa Petersén. Mutant Huntingtin Causes Metabolic Imbalance by Disruption of Hypothalamic Neurocircuits. *Cell Metabolism*, Volume 13, Issue 4, 428-439, 6 April 2011 DOI: 10.1016/j.cmet.2011.02.013