Identical twins with significant weight differences shed light on the phenomenon of metabolically healthy obesity

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A unique study of 16 pairs of identical twins in which one twin is obese and the other lean has yielded some surprising results. In 8 of the pairs of twins, the obese twin was as 'metabolically healthy' as his or her lean co-twin, while in the other 8 pairs, the obese twin had a poorer blood fat profile, higher liver fat and increased insulin production and resistance, and higher blood pressure—all hallmarks of unhealthy obesity that can lead to diabetes, heart problems and other complications. The study is by Dr Kirsi Pietiläinen, Dr Jussi Naukkarinen and colleagues from the Obesity Research Unit, University of Helsinki, Helsinki, Finland, and is published in *Diabetologia*, the journal of the European Association for the Study of Diabetes (EASD).

Not all obese individuals display the metabolic disturbances commonly associated with excess fat accumulation. Mechanisms maintaining this 'metabolically healthy obesity' (MHO) are as yet unknown. In this new research, the authors studied different fat depots and transcriptional pathways in subcutaneous adipose tissue (SAT) of participants to analyse their relationship to the MHO phenomenon.

The sixteen rare young adult obesity-discordant identical (monozygotic) twin pairs (intra-pair difference in BMI ?3kg/m2 and BMI range 20-40 and aged 23-36 years, were examined for detailed characteristics of metabolic health (subcutaneous-, intra-abdominal- and liver fat [magnetic resonance imaging (MRI)/ spectroscopy]), an oral glucose

tolerance test (OGTT-to determine how quickly glucose is cleared from the blood), lipids, and certain markers of inflammation such as adipokines and C-reactive protein (CRP). The function of the mitochondria (part of the cell machinery) and inflammation in the SAT were also studied.

In all 16 pairs, the average weight difference between the obese co-twin and the lean-co-twin was 17kg. In half (8/16) of the pairs the obese co-twin had significantly higher liver fat (around 7 times higher), a 78% increase in insulin production during OGTT, increased CRP, significantly more disturbance in the blood fat profile and greater tendency for high blood pressure compared with the lean co-twin. In these obese co-twins, SAT expression of mitochondrial oxidative phosphorylation, branched-chain, amino acid catabolism, fatty acid oxidation and adipocyte differentiation pathways were downregulated and chronic inflammation upregulated, all of which are metabolic problems that can lead to complications and disease.

In the other eight pairs, the obese co-twin did not differ from the non-obese co-twin in liver fat, insulin sensitivity, CRP, lipids, blood pressure or SAT metabolic characteristics.

The authors discuss that it is also possible that the MHO stage will change with age or with advanced obesity. However, at present the two metabolically distinct groups were of the same age and had similar age of onset of obesity difference between the twin pair. They speculate: "Weight differences between the groups were similar, but a given weight difference may have different metabolic effects depending on where in the distribution of BMI a pair is located."

The authors conclude: "Our results suggest that maintenance of high mitochondrial transcription and lack of inflammation in SAT are associated with low liver fat and MHO...Future studies of the MHO

phenotype may suggest new potentially drug targets—with the most effective intervention point perhaps being improving mitochondrial function and prevention of inflammation in adipose tissue.

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