

## Excess body fat increases the risk of depression

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Carrying ten kilograms of excess body fat increases the risk of depression by seventeen per cent. The more fat, the greater the probability of developing depression. This is the main conclusion of a new study carried out by researchers from Aarhus University and Aarhus University Hospital, Denmark.

"Our study also indicated that the location of the fat on the <u>body</u> makes no difference to the risk of depression. This suggests that it is the psychological consequences of being overweight or obese which lead to the increased risk of depression, and not the direct biological effect of the fat. If the opposite was true we would have seen that fat located centrally on the body increased the risk the most, as it has the most damaging effect in biological terms," says the study's last author Dr. Søren Dinesen Østergaard.

He is professor at the Department of Clinical Medicine at Aarhus University and affiliated with the Department of Affective Disorders at Aarhus University Hospital.

Prior studies in the field have predominantly used Body Mass Index (BMI) to measure obesity. BMI is calculated solely on the basis of body weight and height and is therefore a fairly crude measure, that does not, for example, take build and muscle mass into account.

"BMI is an inaccurate way of measuring overweight and obesity. Many elite athletes with a large muscle mass and a low body fat mass will have a BMI above 25, which is classified as overweight according to the common definition. This obviously doesn't make much sense. Therefore, one of the strengths of our study is that we've been able to zoom in and look at the specific relationship between the amount of body fat and the risk of depression," explains Dr. Østergaard.

In the study, which has been published in the journal *Translational* 



Psychiatry, the researchers have analysed data from two large genetic data sets: the UK Biobank, which contains data on the correlation between genetic variants and physical measurements (including body fat mass distributed around parts of the body); and the Psychiatric Genomics Consortium, which contains information on the correlation between genetic variants and depression.

Dr. Østergaard also highlights his research group's choice of the 'Mendelian randomization' method as the main reason why the study was successful. He also emphasises that the findings are particularly significant in light of the fact that almost 40 per cent of the world's adult population is overweight.

"In addition to the known physical consequences of obesity such as diabetes and cardiovascular disease, there is also a significant and now well-documented psychological component, which needs to be dealt with as well. This is yet another argument for resolving the obesity epidemic," he says, before emphasising that it is important to have a balanced approach to the issue:

"As it appears to be the psychological consequences of obesity, such as a negative body image and low self-esteem that is the main driving force behind the increased risk of depression, society's efforts to combat obesity must not stigmatise, as this will probably increase the risk of depression even further. It is important to bear this in mind so we can avoid doing more harm than good in the effort to curb the obesity epidemic," says Dr. Østergaard.

## **Facts About Mendelian Randomization**

Mendelian randomization (named after the Austrian monk Gregor Mendel, who was the father of modern genetics) is a method which in recent years has helped researchers to overcome a major challenge



associated with observational studies—namely that of making causal inference. In <u>observational studies</u> researchers often find correlations between two conditions—e.g. between obesity and depression—where it is difficult, or rather impossible, to determine whether there is indeed a causal effect going from <u>obesity</u> to depression—or vice versa. Mendelian randomization may solve this challenge.

Mendelian randomization can be described as nature's version of the randomised controlled trials that are carried out when testing whether a new drug has the desired (causal) effect in the treatment of a disease. In the clinical trials of drugs, lots are drawn to determine whether individual participants will receive the active drug or a placebo, without them knowing which treatment they have been assigned to. Instead, Mendelian randomization takes advantage of the fact that a completely natural randomization takes place during the formation of the sex cells (egg cells and sperm cells), which represent the origin of all human beings. When sex cells are formed, the parents' genetic variants—including those that give rise to increased body fat- are randomly distributed. Therefore, some individuals will have received many of these variants and others less. In the study in question, the researchers have utilised this natural and random source of variation to determine whether people who have received many genetic variants for increased body fat have an increased risk of suffering depression.

## The Research Result—More Information

Genetic epidemiological study utilising data from the UK Biobank (with information on the association between genetic variants and fat mass based on a study of 330,000 people) and the Psychiatric Genomics Consortium (with information on the association between genetic variants and depression based on a study of 135,000 people with depression and 345,000 control subjects).



The research group comprises Maria S. Speed, Oskar H. Jefsen, Anders D. Børglum, Doug Speed and Søren D. Østergaard—all from Aarhus University.

**More information:** Maria S. Speed et al. Investigating the association between body fat and depression via Mendelian randomization, *Translational Psychiatry* (2019). DOI: 10.1038/s41398-019-0516-4

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