

Anxiodepressive disorders: Much more than a matter of weight

December 8 2021



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Obese people run a higher-than-average risk of depression or anxiety, the result of a combination of factors: poor diet, lack of physical activity and an accumulation of fat cells called visceral adipocytes. However,

obesity alone can't cause anxious or depressive behaviors—far from it.

In a new review published in *Trends in Endocrinology & Metabolism*, Université de Montréal nutrition professor Stephanie Fulton explains that metabolic deficits, particularly inflammation and resistance to insulin or leptin (a hormone that also regulates appetite), are considered key elements in the development of anxiodepressive disorders in the obese.

"Excess intake of sugar and saturated fats such as palm oil increases the likelihood of such metabolic changes," notes Fulton, a researcher at the CHUM Research Centre (CRCHUM) affiliated with UdeM. The excess intake also causes enough inflammation in the brain to modify the neural circuits responsible for controlling mood, motivation and emotions.

Recent scientific literature, which Fulton cites in her review, shows that anxiodepressive disorders in obese men and obese women are more strongly associated with these types of metabolic deficiencies than with body weight itself.

Connecting metabolism to mental health

Depression and anxiety disorders are much more prevalent in women than in men, though the reasons have been less than clear, as the use of female animal models in psychiatric research has been limited.

In a new study, however, published in *Brain, Behavior, and Immunity - Health*, Fulton and her doctoral student Léa Décarie-Spain observe that depressive and anxious behaviors in female mice occur only if they are fed a diet high in sugar and saturated fat.

Diets that are high in sugar and monounsaturated fat such as olive oil do not cause these types of behaviors, they found. But in female mice these

two diets led to obesity and metabolic disorders.

In 2018, the same scientific team identified one of the causes of this phenomenon in [male mice](#): inflammation of the nucleus accumbens, a component of the limbic system of the brain involved in reward and mood regulation.

"In females, this metabolic inflammation was weaker and was not solely responsible for the observed anxiodepressive behaviors," said Fulton. "However, we found that their blood estrogen levels and the amount of an estrogen synthesis marker called aromatase, in the nucleus accumbens, increased with the saturated high-fat diet. This increase was also related to the observation of anxiodepressive behaviors."

The gender gap in health research

At the CRCHUM, Stephanie Fulton's team investigates the neurobiology of nutrition, obesity and mood disorders.

In a second study published in *Brain, Behavior, and Immunity*, Fulton and Marie F. Fernandes, a doctoral student trained in Fulton's lab, studied the impact of leptin, a hormone controlling the feeling of satiety, on motivation, physical activity and anxiety in [female mice](#).

Leptin serves as a signal to control hunger and body weight. It also influences brain systems that control emotions and cognition.

In 2015, Fulton had already used male mice to show that leptin targeted dopamine neurons, a neurotransmitter involved in motivation, and, by extension, modulated the mice's "desire" to engage in physical activity.

"Once again, we saw significant differences between males and females," said Fulton.

"When we manipulated the leptin signaling pathway, we noticed that doing so had no impact on food intake, weight or even motivation for physical activity in female rodents. It did, however, have an effect on anxious behavior," she added.

"In males, we noticed weight loss despite normal food intake, and also more energy expenditure than usual."

These recent studies build upon expanding area of research on sex differences, Fulton believes.

She and her team want to understand the neurometabolic mechanisms specific to females and also learn more about the influence of nutrition and hormones on motivation and anxiodepressive behaviors.

In so doing, they hope to bring a much stronger female focus to biomedical research.

More information: Stephanie Fulton et al, The menace of obesity to depression and anxiety prevalence, *Trends in Endocrinology & Metabolism* (2021). [DOI: 10.1016/j.tem.2021.10.005](https://doi.org/10.1016/j.tem.2021.10.005)

Léa Décarie-Spain et al, Prolonged saturated, but not monounsaturated, high-fat feeding provokes anxiodepressive-like behaviors in female mice despite similar metabolic consequences, *Brain, Behavior, & Immunity - Health* (2021). [DOI: 10.1016/j.bbih.2021.100324](https://doi.org/10.1016/j.bbih.2021.100324)

Maria F. Fernandes et al, Anxiety-like behavior in female mice is modulated by STAT3 signaling in midbrain dopamine neurons, *Brain, Behavior, and Immunity* (2021). [DOI: 10.1016/j.bbi.2021.04.013](https://doi.org/10.1016/j.bbi.2021.04.013)

Provided by University of Montreal Hospital Research Centre
(CRCHUM)

Citation: Anxiodepressive disorders: Much more than a matter of weight (2021, December 8)
retrieved 18 January 2023 from <https://medicalxpress.com/news/2021-12-anxiodepressive-disorders-weight.html>

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