Role of a gene known as FTO in the coexistence of depression and obesity

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The UGR research team that carried out this work. Credit: University of Granada

Scientists from the University of Granada (UGR) have highlighted that the possible role attributed to the 'fat mass and obesity-associated' (FTO) gene in the comorbidity of depression and obesity can only be confirmed by conducting more studies involving individuals suffering from both diseases, together with more in-depth analysis of the different clinical

subtypes of depression, as some are more prone to being accompanied by obesity than others.

In their study, which has been published in the journal *Neuroscience & Biobehavioral Reviews*, the researchers conducted an exhaustive systematic review of the scientific literature published to date on this topic, to better understand the role of this gene in the relationship between these two diseases.

Depression and obesity are both extremely common diseases in our society, with serious implications not only on a personal and family level but also for public, occupational, and economic health. Depression is currently considered the world's leading cause of disability. No less serious, obesity is considered a pandemic constituting the main risk factor for other diseases that cause mortality, such as cardiovascular disease, type-2 diabetes, or cancer.

Juan Antonio Zarza Rebollo, a researcher from the UGR's Department of Biochemistry and Molecular Biology II and the main author of this work, explains: "Depression and obesity have a strong bidirectional relationship—that is, obesity increases the risk of developing depression; and vice-versa, people with depression are at higher risk of becoming obese. Furthermore, it is common for depression and obesity to present as comorbidities—that is, they appear at the same time and coexist in the same individual, which poses an even greater health risk."

There are different factors that increase the risk that an individual will develop depression and obesity simultaneously. These factors include having low self-esteem, having suffered maltreatment or abuse in childhood, social stigma, or a low level of family and social support. All of these can impact on the biology of each individual, where there are certain physiological mechanisms (which involve the hypothalamic-pituitary-adrenal axis or inflammation) or genetic risk variants that can

play an important role in the appearance of these pathologies.

According to the "Ramón y Cajal" research fellow Margarita Rivera (coordinator of this work and of the research on physical health and mental health of this group and also a lecturer in the UGR's Department of Biochemistry and Molecular Biology II): "The study of the underlying genetic factors involved in the comorbidity between depression and obesity is one of the active lines of research of our group. Specifically, the FTO gene has been investigated by this and other international research groups as a possible genetic link between both pathologies."

A limited but important role

The role of genes in the development of these diseases is limited and cannot be considered a determining factor (that is, there is no "obesity gene" or "depression gene"). Esther Molina, a co-author of this research and lecturer at the UGR's Department of Nursing, explains, however, that "there are genetic variants common to both disorders that confer a greater risk of developing these diseases on those who carry those variants because they can interact with the environment, giving rise to an individual risk for these pathologies. Hence, we find that some individuals are more likely to develop them than others."

This systematic review was undertaken to derive insights from the published scientific evidence on the possible role that one particular gene, the FTO gene, may play in comorbid depression and obesity. This gene contains an area that varies from person to person, known as a polymorphism.

"The presence of the so-called 'risk' variant of this polymorphism has been linked by numerous studies to a greater probability of suffering from obesity and to an increase in body weight in humans. Although there are no studies that associate it with depression independently, the

FTO gene is highly expressed in the brain, and recent studies have described functions that may participate in important brain mechanisms. All of this leads us to believe that this gene may play a key role in the appearance of comorbid depression and obesity," notes Zarza-Rebollo.

The authors of this work, all of whom belong to the "Federico Olóriz" Institute of Neurosciences and the Biomedical Research Centre of the UGR, have shown that there are very few studies analyzing the role of this gene in comorbid obesity and depression. Therefore, it is necessary to conduct more studies where individuals with both pathologies are analyzed simultaneously. According to Margarita Rivera, "at the same time, it is important that future studies take into account the different subtypes of depression, since they have different characteristics not only at the clinical level but also in terms of metabolism and weight-gain. Different subtypes of depression are likely to have different genetic profiles. By characterizing the samples by the different depression subtypes, we may be able to illuminate the role played by the FTO gene and possibly other genes in those depression subtypes that are more prone to triggering weight-gain."

"A better understanding of the role of genetics in comorbid depression and obesity opens the door to early detection of those individuals with a higher risk of developing this comorbidity and to being able to design more personalized (and more effective) prevention and treatment strategies for them," stresses Esther Molina.

More information: Juan Antonio Zarza-Rebollo et al, The role of the FTO gene in the relationship between depression and obesity. A systematic review, *Neuroscience & Biobehavioral Reviews* (2021). DOI: 10.1016/j.neubiorev.2021.05.013