

Low ghrelin—reducing appetite at the cost of increased stress?

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Ghrelin is a hormone released by the lining of the stomach that promotes feeding behavior. Decreasing ghrelin levels could potentially help combat obesity—in fact, a vaccine that lowers ghrelin levels in order to reduce appetite is being studied as a treatment for obesity.

However, many people eat as a way to relieve stress. If low ghrelin levels increase stress, its effectiveness as a treatment for obesity may be reduced. In the current issue of [Biological Psychiatry](#), researchers led by Dr. Zane Andrews of Monash University in Australia show that mice with no ghrelin are more anxious after stress, but that administration of endogenous ghrelin prevents the over-anxious response.

Previous studies have indicated that ghrelin can be either anxiety-causing or anxiety-relieving. This new set of studies now reveals that this dual role in anxiety behavior is context-dependent. Under non-stressed conditions, normal mice show mild anxiety relative to mice without ghrelin. Under acute stress, normal mice mount an appropriate ghrelin response to stress and are less anxious than no-ghrelin [mice](#). In other words, stress-induced ghrelin release targets the body's stress system to stimulate a hormonal response that will combat the stress.

Ghrelin promotes the drive for [food intake](#) and maintains [blood glucose](#) during negative energy balance as well as subserving the rewarding nature of food. "We postulate that, under conditions of acute stress, ghrelin limits excessive anxious behavior by promoting the feeling of reward to ensure appropriate food-seeking behavior and maintain energy

homeostasis. Consistent with this idea, studies from Jeff Zigman and colleagues showed that elevated ghrelin during [calorie restriction](#) produced anxiolytic responses in a test of anxious behavior," said Andrews.

"We hypothesize that ghrelin suppresses anxiety under acutely [stressful conditions](#) to encourage food seeking and maintain appropriate energy homeostasis. Indeed, the importance of ghrelin in controlling stress-induced anxiety might manifest only during conditions of elevated plasma ghrelin, such as negative energy balance and calorie restriction," he continued. "This phenomenon represents an important evolutionary adaptation that maintains food-seeking behavior in the face of acutely stressful environments."

"This study highlights the complexity of approaches for reducing the epidemic in obesity," commented Dr. John Krystal, Editor of *Biological Psychiatry*. "In this case, low [ghrelin](#) levels stimulate anxiety and anxiety is a factor that increases food consumption in humans, particularly sweet and fatty comfort foods. These studies highlight complex relationships between systems in the body and brain that regulate mood and food consumption."

More information: The article is "Ghrelin Regulates the Hypothalamic-Pituitary-Adrenal Axis and Restricts Anxiety After Acute Stress" by Sarah J. Spencer, Lu Xu, Melanie A. Clarke, Moyra Lemus, Alex Reichenbach, Bram Geenen, Tamás Kozicz, and Zane B. Andrews ([doi: 10.1016/j.biopsych.2012.03.010](https://doi.org/10.1016/j.biopsych.2012.03.010)). The article appears in *Biological Psychiatry*, Volume 72, Issue 6 (September 15, 2012)

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