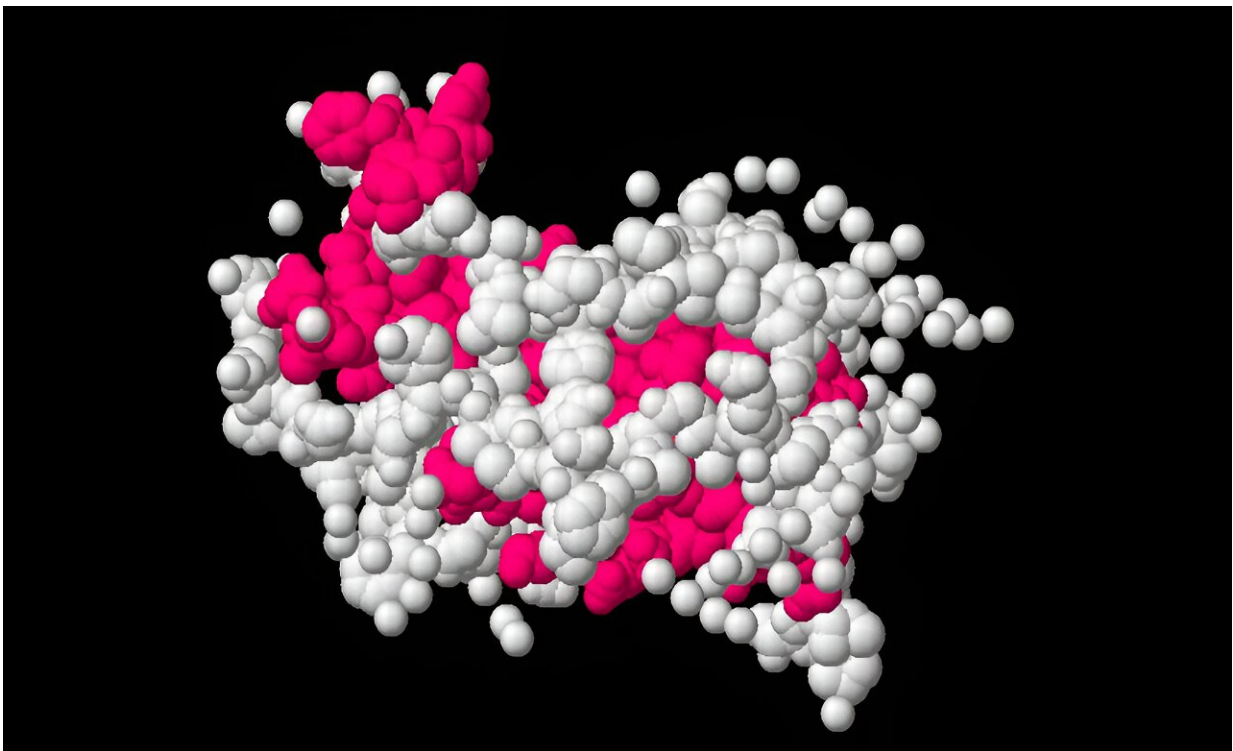


# Growth hormone found to influence regulation of anxiety via a specific group of neurons

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The study showed that growth hormone modifies synapses and structurally alters the neurons that secrete somatostatin. Credit: Wikipedia

Growth hormone (GH) acts on many tissues throughout the body, helping build bones and muscles, among other functions. It is also a

powerful anxiolytic. A study conducted by researchers at the University of São Paulo (USP) in Brazil has produced a deeper understanding of the role of GH in mitigating anxiety and, for the first time, identified the population of neurons responsible for modulating the influence of GH on the development of neuropsychiatric disorders involving anxiety, depression, and post-traumatic stress.

The study is [published](#) in the *Journal of Neuroscience*.

In the study, the researchers found that [male mice](#) lacking the GH receptor in a group of somatostatin-expressing neurons displayed increased anxiety. Somatostatin is a peptide that regulates several physiological processes, including the release of GH and other hormones, such as insulin.

On the other hand, they also found that the absence of the GH receptor in somatostatin-expressing neurons decreased [fear memory](#), a key feature of post-traumatic stress disorder, in males and females. The discovery could contribute to the future development of novel classes of anxiolytic drugs.

"Our discovery of the mechanism involving anxiolytic effects of GH offers a possible, merely chemical, explanation for these disorders, suggesting why patients with more or less GH secretion are more or less susceptible to them," said José Donato Júnior, the last author of the article and a professor at the university's Biomedical Sciences Institute (ICB-USP).

In the study, the researchers conducted three types of experiments involving mice (open field, elevated plus maze, and light/dark box) to test the animals' capacity to explore the environment and take risks. "These are well-established experiments to analyze behavior similar to anxiety and memory of fear, which is an element in post-traumatic

stress. As a result, we were able to explore the role of GH in these animals," Donato explained.

The study's results did not point to any reasons for the lack of increased anxiety-like behavior in female mice. "We believe it may be related to sexual dimorphism. We know the brain region containing the neurons we studied is a bit different in males and females. Some neurological disorders are also different in men and women, probably not by chance," he said.

Thousands of people suffer from neuropsychiatric disorders all over the world. Although anxiety and depression are the most common, their causes have yet to be fully elucidated. Scientists think they may be due to multiple factors, such as stress, genetics, [social pressures](#), economic difficulties, and/or gender issues, among others.

There is also growing evidence that hormones are important in regulating various neurological processes and influencing susceptibility to neuropsychiatric disorders. Alterations in levels of sex hormones such as estradiol affect anxiety, depression, and fear memory in rodents and humans, for example.

Preliminary results of other studies suggest that glucocorticoids (steroid hormones such as cortisol as well as synthetic forms such as prednisone and dexamethasone) may be involved in the development of neuropsychiatric disorders.

In the case of GH, the regulatory mechanism in neurons associated with such disorders had not yet been discovered. "We demonstrated that GH changes the synapses and structurally alters the neurons that secrete somatostatin," Donato said.

The study also showed that anxiety, post-traumatic stress, and fear

memory are different facets of the same neuronal circuit. According to Donato, anxiety can be defined as excessive fear or distrust, while fear memory relates to an adverse past event that produces a brain alteration, which triggers an exacerbated response whenever the subject is exposed to a similar stimulus. This response may range from weeping to tremors and even paralysis.

"All this happens in the same neuron population expressing the GH receptor. In our experiment, fear memory was reduced in mice when we switched the GH receptor off. This means the capacity to form fear memory is impaired. It may be the case that GH contributes to the development of post-traumatic stress," he said.

Another evidence for this is that chronic stress raises the hormone ghrelin, a powerful trigger of GH secretion. "The role of ghrelin in post-traumatic stress has been studied for some time. Research has shown that ghrelin-induced GH secretion increases in chronic stress, favoring the development of fear memory and post-traumatic stress in the animal's brain," he said.

## **How GH affects neurological disorders**

In humans, GH is secreted by the pituitary gland into the bloodstream, promoting tissue growth throughout the body by means of protein formation, cell multiplication, and cell differentiation. GH is indispensable during childhood, adolescence, and pregnancy when its secretion peaks. In old age, it naturally declines.

GH deficiency can lead to dwarfism, which is mostly manifested from 2 years of age, preventing growth during childhood and adolescence.

"Previous research involving patients with GH deficiency showed a higher prevalence of anxiety and depression in these individuals, but the cause hadn't yet been established. Some authors blame it on problems of

self-image and bullying due to short stature," Donato said.

The study involving mice demonstrated the key role played by GH in these disorders without the presence of potential confounders, such as body image issues. "We were able to find out how much is due directly to the effects of GH or the indirect effects of growth deficit. Because we were able to identify the mechanism involving GH, we know it's a direct cause of anxiety disorder, and this knowledge can facilitate the development of therapies," Donato said.

The next steps for the research group include an investigation of the role played by GH during pregnancy.

"We know one of the peaks in GH production occurs during pregnancy. We also know that the prevalence of depression rises in this period owing to post-partum depression. Of course, these disorders also reflect social, economic, and other kinds of pressure, but we mustn't forget that the rise in hormone secretion during and after pregnancy can dysregulate brain functioning, also leading to this kind of mental illness," he said.

**More information:** Willian O. dos Santos et al, Growth Hormone Action in Somatostatin Neurons Regulates Anxiety and Fear Memory, *The Journal of Neuroscience* (2023). [DOI: 10.1523/JNEUROSCI.0254-23.2023](https://doi.org/10.1523/JNEUROSCI.0254-23.2023)

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