

# The effects of oxytocin on social anxiety depend on location, location, location

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Studies have long suggested that oxytocin—a hormone that can also act as a neurotransmitter—regulates prosocial behavior such as empathy, trust and bonding, which led to its popular labeling as the "love

hormone." Mysteriously, oxytocin has also been shown to play a role in antisocial behaviors and emotions, including reduced cooperation, envy and anxiety. How oxytocin could exert such opposite roles had largely remained a mystery, but a new UC Davis study sheds light on how this may work.

While most [oxytocin](#) is produced in an area of the brain known as the hypothalamus, some oxytocin is produced in another brain area known as the bed nucleus of the stria terminalis, or BNST. The BNST is known for its role in the [stress response](#), and it may play a key role in psychiatric disorders such as depression, addiction and anxiety.

The findings of the study, published this week in *Proceedings of the National Academy of Sciences U.S.*, show that oxytocin produced in the BNST increases stress-induced social anxiety behaviors in mice. This may provide an explanation as to why oxytocin can sometimes have antisocial effects. The lead author is Natalia Duque-Wilckens, a former doctoral researcher at UC Davis who is now at Michigan State University. The senior author is Brian Trainor, professor of psychology and director of the Behavioral Neuroendocrinology Lab at UC Davis.

"Before this study, we knew that stress increased the activity of the oxytocin-producing [neurons](#) located in the BNST, but we didn't know if they could affect behavior. Our experiments show that production of oxytocin in the BNST is necessary for social anxiety behaviors in California mice," said Duque-Wilckens.

## **Social stress stronger in females**

The researchers were able to show this by using a tool called morpholino-oligos, which, when injected directly into the BNST, prevents oxytocin from being produced in this area. Interestingly, while oxytocin neurons in the BNST are present in both males and females, previous studies

from this group showed that social stress has stronger long term effects on these neurons in females. This is interesting because social anxiety disorders are more common and more severe in women compared to men.

This study further showed that oxytocin-producing neurons in the BNST are connected to brain regions that control anxiety-related [behavior](#). This was achieved by using a virus to express a fluorescent molecule only in oxytocin neurons.

Remarkably, "simply infusing oxytocin into the parts of the brain that BNST oxytocin neurons connect to caused ordinarily non-stressed mice to show social anxiety behaviors as if they had experienced social stress," said Trainor. Previous studies from this and other labs had shown that oxytocin acting in other areas of the brain, including areas involved in motivated behaviors, had prosocial effects. This suggests that whether the effects of oxytocin are pro- or antisocial will largely depend on which areas of the brain oxytocin is acting in, he said.

"The results are exciting because they provide a potential explanation for why oxytocin sometimes increases anxiety in humans. The vast majority of previous work has focused on the neural mechanisms that underlie the anxiety-reducing effects of oxytocin," Trainor said. "If combined with further studies of how anxiety is connected with [brain](#) circuits in humans, these results could give us a better understanding of what conditions oxytocin could be beneficial or harmful for treating anxiety."

It's also possible that in some situations, using a drug that blocks the actions of oxytocin could reduce anxiety, he said. In future studies, researchers will try to understand how these neurons activate in response to stress and why this effect is long-lasting in females, with the final aim of finding therapeutic strategies that could help patients suffering from social [anxiety](#) disorder.

**More information:** Natalia Duque-Wilckens et al, Extrahypothalamic oxytocin neurons drive stress-induced social vigilance and avoidance, *Proceedings of the National Academy of Sciences* (2020). [DOI: 10.1073/pnas.2011890117](https://doi.org/10.1073/pnas.2011890117)

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