

New Study Shows Link Between Testosterone and Anxiety

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February 16, 2024

STORY AT-A-GLANCE

- › Researchers have now identified the molecular connection between testosterone, genetic expression in the brain, and anxiety, calling the relationship a "mutual regulation" that may be positively affected by administration of testosterone
- › Symptoms of low testosterone levels may be associated with physical conditions such as metabolic syndrome, Type 2 diabetes and obesity. Other factors that influence levels include certain medications and exposure to environmental toxins. Nonprescription drugs that impact levels are alcohol, anabolic steroids and illicit drugs
- › Men with androgen deficiency may experience decreased libido, reduced frequency and quality of erections, gynecomastia (enlarged breast tissue), sweating, fatigue, reduced muscle mass and increased body fat
- › There are several contraindications to using testosterone replacement therapy, including severe lower urinary tract symptoms, erythrocytosis, congestive heart failure, and prostate or breast cancers. Nonpharmacological treatments include controlling lifestyle factors and avoiding medications that affect testosterone levels
- › Testosterone replacement can affect fertility in the future, so many experts recommend gonadotropin hormone replacement to stimulate testosterone production. You can support treatment by avoiding plastics and phthalates, which are endocrine-disrupting chemicals

Researchers have recognized that testosterone plays a role in anxiety and depression-like behavior. A study¹ from Ben-Gurion University in Israel used genetic sequencing to

reveal the connection between a protein in the brain, low testosterone levels and anxiety, which offers a possible explanation for how testosterone affects mental health.

In the U.S., anxiety disorders are common and affect 19.1% of the population.² People between the ages of 18 and 24 are more likely to experience symptoms of anxiety than older adults and women are more likely than men. It is normal to have anxious feelings in certain circumstances, but when it becomes overwhelming and affects your ability to function, it may have crossed the line into an anxiety disorder.

According to a federal survey, 32.3% of U.S. adults reported experiencing symptoms of anxiety and depression in 2023. An estimated 31.1% reported experiencing an anxiety disorder at some point during their life. While 3.1% of the population has generalized anxiety disorder, only 43.2% of that group are receiving treatment.

Although a low testosterone level is not an explanation for all anxiety disorders, researchers believe that identifying males with low testosterone and applying appropriate treatment may help reduce symptoms.³

Molecular Connection Found Between Testosterone and Anxiety

Sex hormones, including testosterone and estrogen, affect brain function. Past research has demonstrated a link between testosterone, anxiety and depression. This effect has been found in animal studies,⁴ which found that both excess and under-exposure to testosterone during brain development have a significant effect on anxiety levels in males.

"Testosterone exposure or deficiency during critical periods of development may have long-lasting consequences persisting into middle or old age,"⁵ concluded the authors of one study. The same effect has been found in men.⁶ After six months of replacement therapy, the men demonstrated improvements in anxiety, depression, quality of life and sexual function, which suggested that low endogenous levels could increase the incidence of psychological symptoms.

Moving forward, researchers in the current study were interested in the missing piece of the puzzle, which was the nature of the connection between testosterone and anxiety.⁷ The research was led by Shira Knafo, who is head of the molecular cognitive lab at the university. The researchers first began observing hundreds of laboratory rats, trying to determine why those from the same litter behaved differently.

"Some showed a very high level of anxiety, some a very low level of anxiety, and the majority were in the middle with a normal amount of anxiety," Knafo told The Times of Israel.⁸ Following this observation, the team separated highly anxious male rats and those with very low levels of anxiety to test their behavior.

They then examined gene expression in the ventral hippocampus of the brain to try to identify the genetic link involved in the variation of anxiety expression. They found the tachykinin receptor 3 (TACR3) that encodes the TACR3 protein was expressed differently in the two groups of rats.

The Connection Between TACR3 and Anxiety

Additional lab testing confirmed the initial findings, and a literature search revealed a study that showed male children with a TACR3 protein mutation had congenital hypogonadism. This is a condition in which young males do not produce enough testosterone, which reduces puberty expression and sexual function.

"So, at that point, we had a link between this TACR3 and puberty. But what was the connection to anxiety? Then I found that people with hypogonadism have problems with anxiety and depression," Knafo said.⁹ The researcher's next step was to measure blood testosterone levels in rats. They found that the more testosterone the rats had, the less anxiety they exhibited, in "a direct linear correlation."

After injecting testosterone into some of the rats, which raised the blood level of testosterone, the researchers found that it also boosted the level of TACR3 protein in the brains. "So, it's like a mutual regulation. The TACR3 affects the amount of testosterone, and the testosterone affects the amount of TACR3," Knafo said.¹⁰

Knafo was excited to have established a molecular connection between anxiety and depression, low testosterone, and TACR3. He hopes to move research forward by investigating whether testosterone administration to people with anxiety might help. She cautions that this should never be done on your own as testosterone administration has significant side effects, including a higher risk for cancer.¹¹

More Symptoms of Low Testosterone Levels

Low levels of circulating testosterone will result in symptoms of androgen deficiency. Androgens are a group of sex hormones, of which testosterone is one. The clinical presentations of low testosterone will vary and are dependent on when androgen deficiency begins, whether it's a defect in spermatogenesis or testosterone production, is associated with a genetic factor or the man has a history of androgen therapy.¹²

Primary hypogonadism can result from testicular disease or secondary hypogonadism, which results from dysfunction of the hypothalamic-pituitary axis.¹³ Symptoms of androgen deficiency can include fatigue, irritability, infertility, poor feeling of well-being, or decreased libido and reduced frequency and quality of erections.¹⁴ Men may also experience gynecomastia (enlarged breast tissue), hot flushes, sweating, fatigue, reduced muscle mass and increased body fat.¹⁵

In some cases, men may present with unrelated concerns,¹⁶ such as a history of Type 2 diabetes, obesity, metabolic syndrome or systemic diseases that impact testosterone physiology. Researchers from the featured study also suggest that anxiety may be a part of the presentation in men with androgen deficiency.

Hypogonadism can also result from medications or exposure to environmental toxins. Medications with known effects on androgens include steroids, opioids, statins, dopamine antagonists and 5-alpha reductase inhibitors. Nonprescription drugs can also affect testosterone levels, including alcohol, anabolic steroids and illicit drugs such as marijuana.

Environmental Factors Can Affect Testosterone Levels

Shanna H. Swan, Ph.D., a leading environmental and reproductive epidemiologist and professor of environmental medicine and public health at the Icahn School of Medicine at Mount Sinai in New York City, has examined the [role of environmental toxins in reproductive health](#).

After a 1992 study that demonstrated the quality of sperm counts in men had been nearly cut in half over the past 50 years, Swan decided to investigate further and spent the next 20 years looking at why human reproduction is plummeting.

In 2017, she published a systematic review and meta-regression analysis,¹⁷ which showed a 50% to 60% drop in total sperm count among men in North America, Europe, Australia and New Zealand between 1973 and 2011. Overall, men in these countries had a 52.4% decline in sperm concentration and a 59.3% decline in total sperm count (sperm concentration multiplied by the total volume of an ejaculate).

As discussed above, a defect in spermatogenesis, or the production of mature sperm, is one sign of androgen deficiency. Swan refers to this 30-year decline as "the 1% effect," meaning the cumulative effect that an annual change of just 1% has over time. In tandem with lower sperm counts, testosterone has also declined and miscarriage rates among women and erectile dysfunction among men have been steadily rising.

A 2020 study¹⁸ that evaluated the trends in anxiety in adults from 2008 to 2018, well before the pandemic, found that anxiety prevalence has consistently increased among adult Americans and the most notable increase was in the 18 to 25-year-old range where it rose from 7.97% to 14.66% during the study years.

According to Swan, there are likely a host of factors that have contributed to this decline in fertility. As I detail further in "[Are These Chemicals Part of a Depopulation Agenda?](#)" the causes are likely related to lifestyle and chemical exposure.

Lifestyle factors that are known to negatively impact fertility include binge drinking, stress, smoking and obesity. Chemical exposures that are most concerning are

endocrine-disrupting chemicals (EDCs) that mimic hormones and effectively take their place.

A 2024 study identified plastics, known EDCs, as a substantial contributor to disease and estimated the associated cost in the U.S. to be 1.22% of the gross domestic product, which the researchers estimated to be \$249 billion in 2018.¹⁹

Swan suspects EDCs are a primary culprit in infertility, in part because we're surrounded by them every day of our lives. We're exposed to them through our food, water, personal care products, furniture, building materials, plastics and much more.

Support Your Hormonal Balance

In a 2018 paper²⁰ published in *Metabolism*, researchers found that symptoms of hypogonadism are frequent in aging men but the diagnosis is typically neglected. While the need to treat young adults with pituitary or testicular failure using testosterone replacement is universally accepted, there are some controversies in treating older men, especially since it is not risk-free.

There are several contraindications to using testosterone replacement therapy, including severe lower urinary tract symptoms, erythrocytosis, congestive heart failure, and prostate or breast cancers.²¹

Several of the nonpharmacological treatments that have been used include controlling chronic diseases such as obesity and type 2 diabetes, and eliminating certain drugs as these can help normalize testosterone levels. Experts also understand that testosterone replacement therapy can negatively impact fertility and so recommend gonadotropin hormone replacement to help stimulate sperm production and induce puberty to promote testicular growth and maturation.

You can support treatment by avoiding as many plastics and phthalates as possible. Phthalates are what make plastic soft and flexible, which you can find in raincoats, rubber boots, plastic shower curtains, plastic tubing and foods that have been

processed in plastic. Phthalates are also found in cosmetics, perfumes and personal care products as well as scented products such as laundry soap and air fresheners.

Phthalates are just one class of EDCs, and there are others. However, they are the most hazardous for male reproductive health because of their ability to block testosterone.

As I've written before, another option to discuss with your physician before beginning medication is [supplementing with fenugreek](#), which is known to promote increased testosterone levels. Although it increases testosterone levels, it does not convert to dihydrotestosterone (DHT) which contributes to male pattern hair loss and prostate cancer. Instead, fenugreek lowers DHT levels, helps to modulate blood sugar, and helps improve glucose tolerance in those with Type 2 diabetes.

Sources and References

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