

Exploring the antidepressant effects of testosterone

April 2 2012

Testosterone, the primary male sex hormone, appears to have antidepressant properties, but the exact mechanisms underlying its effects have remained unclear. Nicole Carrier and Mohamed Kabbaj, scientists at Florida State University, are actively working to elucidate these mechanisms.

They've discovered that a specific pathway in the hippocampus, a brain region involved in [memory formation](#) and regulation of stress responses, plays a major role in mediating testosterone's effects, according to their new report in [Biological Psychiatry](#).

Compared to men, women are twice as likely to suffer from an affective disorder like depression. Men with hypogonadism, a condition where the body produces no or low testosterone, also suffer increased levels of depression and anxiety. Testosterone replacement therapy has been shown to effectively improve mood.

Although it may seem that much is already known, it is of vital importance to fully characterize how and where these effects are occurring so that scientists can better target the development of future antidepressant therapies.

To advance this goal, the scientists performed multiple experiments in neutered adult male rats. The rats developed depressive-like behaviors that were reversed with testosterone replacement.

They also "identified a molecular pathway called MAPK/ERK2 (mitogen activated protein kinase/ extracellular regulated kinase 2) in the hippocampus that plays a major role in mediating the protective effects of testosterone," said Kabbaj.

This suggests that the proper functioning of ERK2 is necessary before the antidepressant effects of testosterone can occur. It also suggests that this pathway may be a promising target for antidepressant therapies.

Kabbaj added, "Interestingly, the beneficial effects of testosterone were not associated with changes in neurogenesis (generation of new neurons) in the hippocampus as it is the case with other classical antidepressants like imipramine (Tofranil) and fluoxetine (Prozac)."

In results published elsewhere by the same group, testosterone has shown beneficial effects only in male rats, not in female rats.

More information: The article is "Extracellular Signal-Regulated Kinase 2 Signaling in the Hippocampal Dentate Gyrus Mediates the Antidepressant Effects of Testosterone" by Nicole Carrier and Mohamed Kabbaj ([doi: 10.1016/j.biopsych.2011.11.028](https://doi.org/10.1016/j.biopsych.2011.11.028)). The article appears in *Biological Psychiatry*, Volume 71, Issue 7 (April 1, 2012)

Provided by Elsevier

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