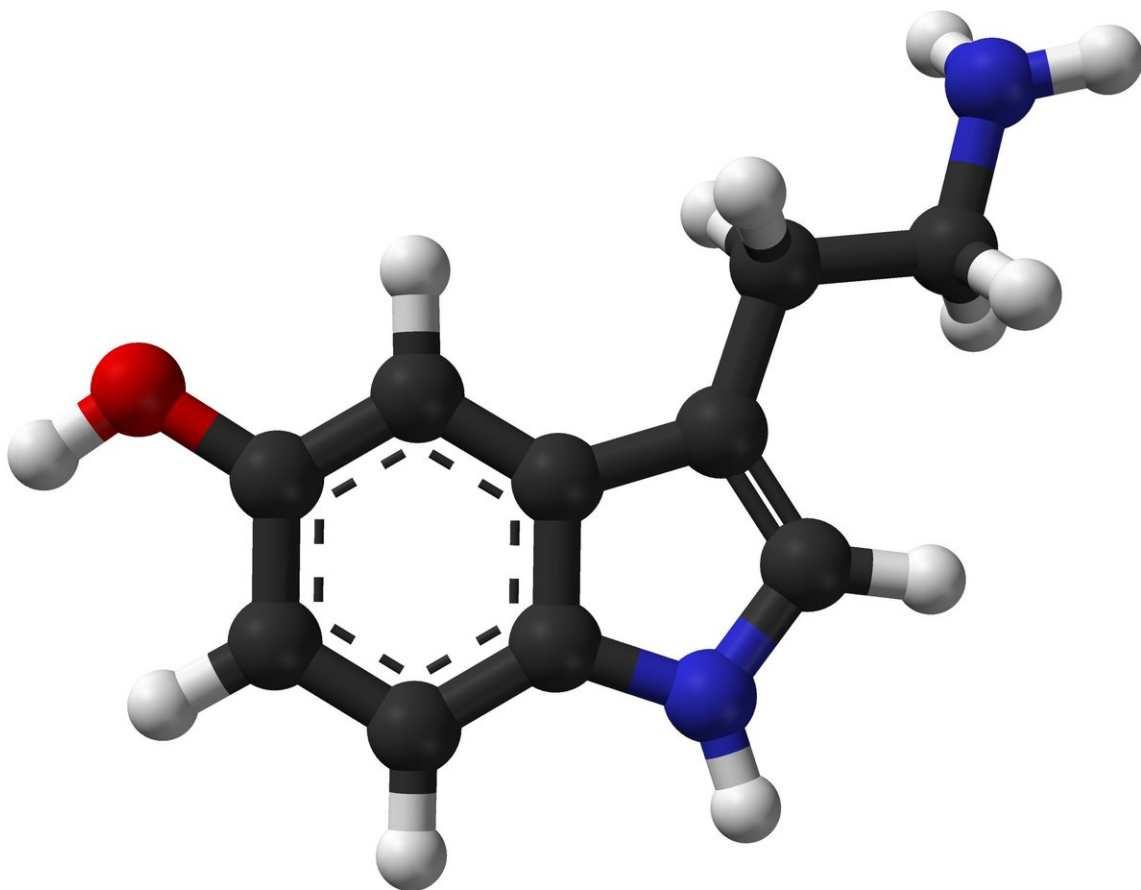


Study focuses on atomic structure of the serotonin transporter bound to SSRIs

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Ball-and-stick model of the serotonin molecule. Credit: Public Domain

New molecular research shows how chemically diverse drugs used to treat depression and anxiety disorders interact with the protein that transports serotonin in the brain. The discovery by researchers at the OHSU Vollum Institute could open the way for the development of additional forms of antidepressants collectively known as selective serotonin reuptake inhibitors, or SSRIs.

The study will be published Jan. 29 in the journal *Nature Structural & Molecular Biology*.

"This work tells a great deal about how clinically relevant antidepressants work," said senior author Eric Gouaux, Ph.D., senior scientist in the OHSU Vollum Institute.

Serotonin is a chemical messenger that acts as a neurotransmitter, carrying signals between neurons. Serotonin signaling controls many aspects of human behavior, including memory, learning, sleep, hunger, pain, sexual function and mood. SSRIs are chemical compounds that block the reabsorption (or reuptake) of [serotonin](#) into nerve cells. This has the effect of increasing the level of serotonin in synapses, allowing for prolonged serotonin signaling in patients suffering from [anxiety disorders](#) or depression.

The six most commonly prescribed SSRIs approved by the Food and Drug Administration for clinical treatment of depression can have varying levels of success and side effects depending on the patient. The OHSU researchers found that while these SSRI molecules are chemically quite different, they all bind to a central site in the serotonin transporter, locking the transporter in a state that blocks serotonin binding and reabsorption into [nerve cells](#).

"We wondered how these drugs, which are quite different, managed to accomplish a similar action on the transporter," said lead author Jonathan

Coleman, Ph.D., a researcher in the Gouaux Lab.

Coleman and colleagues used X-ray crystallography techniques to deduce the atomic structure of the serotonin transporter as it binds to each drug. This involved purifying the transporter-[drug](#) complexes and forming ordered arrays of protein crystals that could be used to map the position of the drugs. In discovering the atomic structure of the different molecules - and how they bind to the [serotonin transporter](#) - the study provides a pathway for the development of additional SSRIs to treat anxiety disorders while potentially limiting side effects such as sexual dysfunction, insomnia, nausea, headaches and diarrhea.

"We anticipate these studies should provide a blueprint for the development of new therapeutic agents for the treatment of depression and anxiety disorders," the authors concluded.

More information: Jonathan A. Coleman et al, Structural basis for recognition of diverse antidepressants by the human serotonin transporter, *Nature Structural & Molecular Biology* (2018). [DOI: 10.1038/s41594-018-0026-8](#)

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