

New model for treatment of obsessive-compulsive disorder created

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A new model of obsessive-compulsive disorder (OCD) that mirrors both symptoms of the disease and the timing of its treatment in humans has been created by University of Chicago researchers, according to a new study.

Using the model, researchers isolated a single neurotransmitter receptor in a specific brain region responsible for their model's OCD-like symptoms, offering new insight into the cause of the disorder. Further research with the model may point the way to new treatments for both OCD and autism, said Nancy Shanahan, PhD, lead author of the paper in [Biological Psychiatry](#).

"Treatment for these people is greatly needed, and there really are very few highly valid animal models of the disorder," said Shanahan, a postdoctoral researcher at the University of Chicago. "Having one that seems to mimic the disorder so well, especially in terms of the time course of treatments that work in humans, is potentially very useful for researching novel therapeutics."

Stephanie Dulawa, PhD, assistant professor in the Department of Psychiatry and [Behavioral Neuroscience](#) at the University of Chicago Medical Center and senior author of the study, said, "Our model can make accurate predictions about what you see in OCD, and that gives us confidence that the underlying neurobiology is likely to be similar between the model and the actual disorder."

About 2.2 million people in the United States have been diagnosed with OCD, according to the National Institute of Mental Health. OCD patients struggle with repetitive rituals (such as hand-washing, counting and cleaning) and unwanted thoughts that can cause [severe anxiety](#).

Psychiatrists have found some success treating patients with a class of drugs called serotonin reuptake inhibitors (SRIs) initially developed for depression. However, these drugs fail to reduce symptoms in as many as 60 percent of OCD patients and require four to eight weeks of treatment for therapeutic effects to begin.

"OCD is very mysterious and very prevalent," Shanahan said. "The development of OCD-specific treatments will be an extremely important step toward helping these people and preventing the disorder's cost to society."

With an [animal model](#) that replicates at least some aspects of OCD, researchers can dig deeper into the specific neurotransmitters and systems involved in the disorder. In Dulawa's laboratory, a team led by Shanahan found inspiration in a drug that activates the 1b class of receptors for the neurotransmitter serotonin. Clinically, the drug is used to treat migraines, but it is also known to have the unintended effect of increasing anxiety and compulsions in people with OCD.

When the drug was given to mice, they showed highly repetitive patterns of locomotion when placed into an open arena. The drug-treated mice also exhibited deficits in prepulse inhibition, a form of startle plasticity thought to measure the brain's ability to filter out intrusive thoughts, which plague OCD patients.

To determine whether these drug-induced behaviors reflected the neurobiology of OCD, the researchers tested the same drugs used to treat the disorder in humans. After four weeks of pre-treatment with SRIs —

the same duration required to see therapeutic effects in humans — drug-induced OCD behaviors were reduced in the mice. Shorter SRI treatment or treatment with other antidepressant drugs that do not work in humans with OCD were unsuccessful in reducing the behaviors caused by the drug.

"We have this time course that nicely parallels or mimics the human therapeutic response," Shanahan said. "In order to study how these drugs are working and the pathophysiology of the disorder, we need a model where this delayed onset exists. So we are really excited about that."

The researchers then looked for a specific brain region where activation of 1b serotonin receptors creates OCD-like symptoms. In humans, scientists have identified a region called the orbitofrontal cortex that is more active in OCD subjects. Again matching the human data, selectively activating 1b receptors in the orbitofrontal cortex with the drug was sufficient to produce the OCD-like symptoms in the mice.

"We found that the 1b receptors in the orbitofrontal cortex were really the critical receptors," Dulawa said. "It was very affirming to our research because it is the brain region most heavily implicated in OCD throughout all of the human literature."

The results offer promising ideas about developing new treatments for OCD. A drug that blocks the serotonin 1b receptors may be effective in reducing OCD symptoms; however, no such chemical is currently available, Dulawa said. Alternatively, treating OCD patients with an activator of these receptors may exacerbate symptoms initially, but have long-term benefits as the number of serotonin 1b receptors decreases from over-stimulation.

"These treatments could potentially be much more specific and work much faster," Dulawa said. "Now that we have this model, we actually

could pursue these ideas for better treatments in a disease where there is only one successful therapy."

More information: The paper, "Essential role for orbitofrontal 5-HT1B receptors in OCD-like behavior and SRI response in mice," was published online September 15, 2011 by *Biological Psychiatry* ([doi:10.1016/j.biopsych.2011.07.032](https://doi.org/10.1016/j.biopsych.2011.07.032)).

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