

OCD Breakthrough Finding from Sapap 3 Knockout Mice

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Obsessive Compulsive Disorder (OCD) is a chronic, debilitating psychiatric disorder characterized by obsessions and compulsions. Obsessions are intrusive thoughts that cause intense discomfort for the afflicted individual. Common examples of obsessions include the fear of contamination, order and symmetry, perfectionism, and the fear of losing control. Obsessions produce a tremendous amount of anxiety in the afflicted person, often making individuals feel as though there is imminent danger. Compulsions are unwanted urges by the afflicted person to engage in repetitive behaviors in an attempt to alleviate the psychological and physical discomfort produced by obsessions. Common examples of compulsions include excessive hand-washing, excessive checking behaviors, and repetition of certain numbers or words. These compulsions may provide momentary relief, but oftentimes the same intense discomfort will arise shortly afterwards, oftentimes stronger than the initial discomfort, leading to a vicious cycle of compulsive behaviors without any relief in sight. OCD can be particularly time and energy consuming, and as a result can interfere with all aspects of a person's life.

Although there are several known risk factors for developing OCD, the causes of OCD are still a mystery to scientists and health care professionals. The known risk factors for developing OCD are based upon a combination of biological, psychological, and social factors.

The most effective treatments for OCD to date are a combination of pharmacotherapy and psychotherapy. The most successful drugs that have been used to treat OCD are SSRI's (Selective Serotonin Reuptake Inhibitors, such as Prozac). Although these drugs help to alleviate the symptoms of OCD, they do not cure the disease. The most successful psychotherapies to date are Exposure and Response Prevention (ERP) and Cognitive Behavioral Therapy (CBT). ERP, a form of CBT, is a treatment that desensitizes the patient to certain environmental stimuli that trigger their particular obsessions and compulsions by having the patient refrain from engaging in compulsive behaviors. CBT, a term that encapsulates a wide variety of different psychotherapies, provides the patient with a variety of different coping techniques to help manage their OCD.

OCD cannot currently be diagnosed using medical technology, so as a result, health care providers rely on psychological measures based upon DSM-V criteria in order to determine whether an individual qualifies for a diagnosis of OCD. An estimated 2.3% of the population has a lifetime prevalence of OCD, whereas an estimated 1.2% of the population has a 12-month prevalence of OCD. The onset of OCD typically occurs before individuals are twenty-five years of age, and often begins in childhood or adolescence. The age of onset is typically earlier in males than females. Based upon these statistics, it is evident that OCD is a serious public health issue that needs to be further researched in order to lead to more effective treatments.

Although researchers have begun to develop some understanding of the neurobiological mechanism underlying OCD, there is still a tremendous amount of information that remains a mystery to scientists. In particular, researchers have long struggled to understand the molecular signaling that underlies OCD. On May 13, 2016, researchers published groundbreaking research findings in the prestigious scientific journal- Biological Psychiatry, that has illuminated an exciting discovery regarding a particular metabotropic receptor, mGluR5, which shows promise in being an influential protein involved in the molecular signaling underlying OCD. Previous studies have linked OCD to an increase in the activity of neural circuits, called frontostriatal circuits, that connect the basal ganglia, a structure deep inside the brain that is responsible for various motor functions, to the frontal lobe of the brain, which is responsible for a variety of cognitive functions, most notably for an individual's executive function. In addition, in a previous research paper from 2007, researchers from Duke University had discovered that when deleting a gene that codes for Sapap3 in mice, a protein that is involved in neuronal communication through the use of glutamate, that the mice began to develop behaviors characteristic of OCD.

In this exciting new research paper, another group of researchers from Duke University wanted to build upon the previous research findings from 2007 by determining whether there is a causal connection between increased signaling of a particular glutamate receptor, mGluR5, and an increase in frontostriatal activity and observable characteristic OCD behaviors using a mouse model. In this study, there was a Sapap3 knockout group of mice and a wild-type group of mice. The researcher's first big discovery was that through several experiments, they were able to demonstrate that in Sapap3 knockout mice that exhibited characteristic OCD behaviors, there is increased mGluR5 signaling, as well as increased striatal activity. When these mice were given an antagonist drug that acts upon the mGluR5 receptor, their characteristic OCD behaviors vanished within minutes. The researcher's second big discovery was that when delivering an agonist drug that increased mGluR5 signaling in wild-type mice initially without any observable behavioral abnormalities, within minutes the wild-type mice began to exhibit the same characteristic OCD behaviors that the Sapap3 knockout mice group originally displayed. This remarkable discovery is an exciting breakthrough in both the medical and scientific communities. The current first-line pharmacological therapies for OCD (SSRI's), can take from weeks to months to begin to alleviate OCD symptoms in the patient. This study is able to show that it is possible to alleviate OCD symptoms within minutes in mouse models, giving hope to the possibility that new pharmacological therapies for OCD may be able to have a more immediate impact in human patients. In addition, this discovery allows scientists to gain a deeper understanding of the underlying molecular signaling mechanisms that underlie this extraordinarily complex psychiatric disorder.

This new research finding is particularly exciting and personal for me. I was diagnosed with OCD at the age of six. It has without a doubt been the hardest challenge of my life. I have myself received a combination of pharmacotherapy (SSRI's), and extensive mindfulness-based psychotherapy throughout my life. Although the SSRI's have helped to alleviate my OCD symptoms over the years, the drugs have never completely cured my OCD. In addition, the SSRI's take a long time to take effect. As a result, I have had to rely heavily on developing solid coping techniques to help me when I get "stuck in quicksand." Mindfulness-based psychotherapy has been extremely beneficial for me. I have learned to effectively shift my attention away from the mental anguish that is a product of the OCD mechanism to the present moment, such as by focusing my attention on the current task at hand, or simply being and focusing my attention on the sensations of breathing. The challenge is to keep coming back to the present moment when my attention gets caught in the drama created by the OCD, and to resist the urge of giving into any compulsions. It is a challenge that I still work with on a day to day basis, but I have discovered that it is possible for me to live a full and productive life without having to be controlled by my OCD. Although psychotherapy has been extremely beneficial for me, I would without a doubt welcome a more effective drug to treat my OCD, because it can be exhausting to cope with, particularly when it happens to be higher than its normal baseline level. Hopefully more research studies will be able to build upon this article's breakthrough findings and bring the scientific and medical communities one step closer to providing more effective treatments for OCD patients.

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