Animal behavioral studies can mimic human behavior

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Studying animals in behavioral experiments has been a cornerstone of psychological research, but whether the observations are relevant for human behavior has been unclear. Weill Cornell Medical College researchers have identified an alteration to the DNA of a gene that imparts similar anxiety-related behavior in both humans and mice, demonstrating that laboratory animals can be accurately used to study these human behaviors.

The findings may help researchers develop new clinical strategies to treat humans with anxiety disorders, such as phobias and post-traumatic stress disorder (PTSD).

Results from the study, funded by the National Institutes of Health, are published today in the journal *Science*.

"We found that humans and mice who had the same human genetic alteration also had greater difficulty in extinguishing an anxious-like response to adverse stimuli," explains Dr. B.J. Casey, co-senior author of the study and professor of psychology in psychiatry from The Sackler Institute for Developmental Psychobiology at Weill Cornell Medical College.

The researchers observed common behavioral responses between humans and mice that possess an alteration in the brain-derived neurotrophic factor (BDNF) gene. The mice were genetically altered -- meaning that they had a human genetic variation inserted within their

genome.

To make their comparison, the researchers paired a harmless stimulus with an aversive one, which elicits an anxious-like response, known as conditioned fear. Following fear learning, exposure to numerous presentations of the harmless stimulus alone, in the absence of the aversive stimulus, normally leads to subjects extinguishing this fear response. That is, a subject should eventually stop having an anxious response towards the harmless stimulus.

"But both the mice and humans found to have the alternation in the BDNF gene took significantly longer to 'get over' the innocuous stimuli and stop having a conditioned fear response," explains Dr. Fatima Soliman, lead author of the study, who is currently a Tri-Institutional MD-PhD student, and has completed her Ph.D. in the labs of Drs. B.J. Casey and Francis S. Lee.

In addition to the observational testing, the researchers also performed brain scans using functional magnetic resonance imaging (fMRI), on the human participants, to see if brain function differed between people with the abnormal BDNF gene and those with normal BDNF genes.

They found that a circuit in the brain involving the frontal cortex and amygdala -- responsible for learning about cues that signal safety and danger -- was altered in people with the abnormality, when compared with control participants who did not have the abnormality.

"Testing for this gene may one day help doctors make more informed decisions for treatment of anxiety disorders," explains Dr. Francis S. Lee, co-senior author of the study and associate professor of psychiatry and pharmacology at Weill Cornell Medical College.

Therapists use exposure therapy -- a type of behavior therapy in which

the patient confronts a feared situation, object, thought, or memory -- to treat individuals who experience stress and anxiety due to certain situations. Sometimes, exposure therapy involves reliving a traumatic experience in a controlled, therapeutic environment and is based on principles of extinction learning. The goal is to reduce the distress, physical or emotional, felt in situations that trigger negative emotion. Exposure therapy is often used for the treatment of anxiety, phobias and PTSD.

"Exposure therapy may still work for patients with this gene abnormality, but a positive test for the BDNF genetic variant may let doctors know that exposure therapy may take longer, and that the use of newer drugs may be necessary to accelerate extinction learning," explains Dr. Soliman.

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