Researchers pinpoint genetic connection to traumatic experience

February 1 2012

Rutgers scientists have uncovered genetic clues as to why some mice no longer in danger are still fearful while others are resilient to traumatic experiences - knowledge that could help those suffering with crippling anxiety and PTSD.

"Our work with mice demonstrates how genes play a role in developing and extinguishing pathological fear like Post Traumatic Stress Disorder," says Gleb Shumyatsky, an associate professor in the Department of Genetics in the School of Arts and Sciences. "It is clear that previous life experiences are not the only cause of PTSD - genetic predispositions may make some people more sensitive and others more resilient to PTSD."

Since humans and animals register fear in the brain similarly, the discovery being reported today in the journal *PLoS ONE*, is an important step to understanding how genes work in the brain to control learning and memory as well as reactions to fearful and traumatic experiences.

In the study, mice bred missing either one of the two fear memory-related genes were trained to be afraid of the cage and a tone associated with a mild shock. Next, by repeatedly putting the mice in the training cage or presenting them with the tone - but now without the shock - the scientists taught them not to be afraid, a process called fear memory extinction. When extinction was performed using the fearful context, a training cage, the knockout mice behaved normally, similar to wild type control mice.

These same mutant mice acted quite differently, however, when they heard a quiet, fear-evoking tone that had previously been followed by the same shock. Mice bred without the gastrin-related peptide receptor (GRPR) gene were more fearful of the tone and froze up more often than normal mice, despite no longer being in danger of receiving a shock. By contrast, mice bred without the stathmin gene forgot that they had been afraid of the dangerous tones and stopped freezing.

Next, the scientists analyzed the neural activities of portions of the brain that deal with fear and anxiety in humans - the amygdala, hippocampus, and medial prefrontal cortex. What they discovered: Genetic evidence of a connection between the amygdala - the portion of the brain where unconscious fears are stored - and the prefrontal cortex, the area that enables animals and humans to inhibit excessive fear to better react to potential danger.

The "fearless" stathmin-deficient mice exhibited an increase in brain activity in the prefrontal cortex and a decrease in the amygdala. The opposite occurred in the timid, GRPR deficient mice that were overly afraid in spite of the fact that they were no longer in danger.

Shumyatsky says scientists need to continue identifying molecules involved in the neural circuits of the brain responsible for specific memories and behaviors in order to develop psychotherapeutic, pharmacological and genetic therapies to treat disabling anxiety disorders like PTSD which is estimated to affect 30 percent of combat veterans.

"The research suggests that there are different types of PTSD and that different medical treatments could be applied to treat the cue-related versus the context-related PTSD symptoms, Shumyatsky says.