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RESEARCH HIGHLIGHT

Study May Explain Fear Response in PTSD

Nearly all of us have had a traumatic experience at some point in our lives, but most of us can move on and go about our daily business. People with post-traumatic stress disorder (PTSD), however, experience recurrent fear and anxiety that never seems to go away, even long after the traumatic event is over. An MBRS-supported researcher in Puerto Rico was part of a team that identified one area of the brain that may be essential for learning how not to be afraid. The researchers suggest that people with PTSD may have impaired function in the front part of the brain, called the prefrontal cortex.

MBRS researcher Dr. Gregory Quirk and graduate student Mohammed Milad at the Ponce School of Medicine have studied this area of the brain by recording electrical activity in the prefrontal cortex of laboratory rats. The team conditioned the rats to fear a sound the scientists played while delivering a foot shock to the rats. They measured fear by the degree to which the rats became immobilized, known as the freezing response. Repeated presentations of the sound without the shock caused fear responses to slowly disappear, a process researchers call extinction of the response.

Classic behavioral experiments dating back to Pavlov's dogs have suggested that extinction does not erase a fear association from memory, but instead generates a new safety memory to block the fear response. According to this theory, some part of the brain must create the safety memory by increasing its activity after extinction. In the November 7, 2002, issue of the journal *Nature*, Milad and Quirk showed for the first time that nerve cells in the prefrontal cortex increased their activity in response to the sound only after extinction, creating what the researchers called a "safety signal." The team found that the more active this brain region was, the less afraid the rats were when they heard the sound. The rats with the most prefrontal cortex activity acted as if they had never been conditioned to fear at all. The scientists' findings lend support to the idea that fear reduction is an active process.

Milad and Quirk, who both receive funding from the National Institute of Mental Health, did more experiments with the rats and learned that stimulating one particular region of the prefrontal cortex diminished the rats' fear response. When the researchers electrically stimulated the prefrontal cortex in rats that had never exhibited extinction and paired the stimulation with the sound, the stimulated rats displayed little fear, acting as if their fear response had been erased. Later, these rats continued to be unafraid of the sound even without stimulation.

What could be going on?

The researchers speculate that since the prefrontal cortex sends signals to the amygdala, which is a cluster of nerve cells in the brain that stores memories, including those of fear, stimulating the prefrontal cortex may directly impact the ability to remember a fear response. The findings also suggest the exciting possibility that stimulating the prefrontal cortex could someday be used to strengthen the extinction response in people with anxiety disorders.

Reference: Milad MR, Quirk GJ. Neurons in medial prefrontal cortex signal memory for fear extinction. ***Nature*** *2002;420:70-4.*

Research Highlights features the research being done by current and former students and faculty in the MARC, MBRS, and other NIGMS minority programs. ***We welcome your story ideas and suggestions for future Research Highlights items.***