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Mimicking brain's "all clear" quells fear in rats

Researchers funded by the National Institute of Mental Health (NIMH) have discovered a high tech way to quell panic in rats. They have detected the brain's equivalent of an "all clear" signal, that, when simulated, turns off fear. The discovery could lead to non-drug, physiological treatments for runaway fear responses seen in anxiety disorders.

Rats normally freeze with fear when they hear a tone they have been conditioned to associate with an electric shock. Dr. Gregory Quirk and Mohammed Milad, Ponce School of Medicine, Puerto Rico, have now demonstrated that stimulating a site in the front part of the brain, the prefrontal cortex, extinguishes this fear response by mimicking the brain's own "safety signal." They report on their findings in the November 7, 2002 *Nature*.

"Repeated exposure to traumatic reminders without any adverse consequences causes fear responses to gradually disappear," explained Quirk. "Such reduction of fear appears to be an active rather than passive process. It doesn't erase the fear association from memory, but generates a new memory for safety."

The researchers recorded electrical activity of neurons in the prefrontal cortex as rats were fear-conditioned - taught to fear a tone by repeatedly pairing it with a shock. Then they abolished this conditioned fear by presenting the tone without the shock; the animals no longer froze when they heard the tone.

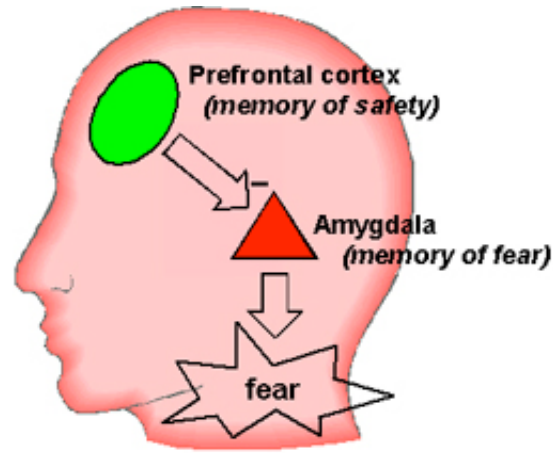
Although inactive during both procedures, neurons near the middle of the prefrontal cortex, the infralimbic area, fired conspicuously when the tone was sounded on the following day. This activity proved to be the brain's way of signaling that the tone no longer presaged a shock. The more the cells fired -- i.e., the louder this safety signal -- the less the rats froze. Animals that showed the most infralimbic activity behaved as if they had never been fear conditioned at all.

The researchers then electrically stimulated the infralimbic area in rats that had been fear conditioned but not extinguished -- in effect simulating the safety signal, while pairing it with the tone. Remarkably, the rats showed little freezing. Later, the rats continued to be unafraid of the tone even without the stimulation, suggesting that memory for extinction was strengthened by experimentally mimicking the safety signal.

Since the prefrontal cortex is known to project to the amygdala, a hub of fear memory deep in the brain, the researchers propose that increased activity of infralimbic neurons in the prefrontal cortex strengthens memory of safety by inhibiting the amygdala's memory of fear. They speculate that stimulating parts of the prefrontal cortex in anxiety disorder patients, using an experimental technique called transcranial magnetic stimulation, might help them control fear.

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