UPR researchers break ground in anxiety study

By CB Online Staff

Recent findings of researchers at the University of Puerto Rico School of Medicine suggest new treatments exist for individuals suffering from anxiety disorders.

The researchers pharmacologically induced the memory of safety by administering a protein directly into the brain of rats, achieving the same effect as extinction training. The protein, brain-derived neurotrophic factor or BDNF, is one of a class of proteins that support the growth and survival of neurons.

In a classical conditioning model, the rats used in research normally freeze when they hear a tone they have been conditioned to associate with an electric shock. The reaction can be extinguished by repeatedly exposing the rats to the tone with no shock.

Importantly, prior work has shown that extinction training does not erase a previously conditioned fear memory, but creates a new memory associating the tone with safety.

"The surprising finding here is that the drug substituted the extinction training, suggesting that it induced such a [safe] memory," said Dr. Gregory Quirk, a professor of the UPR School of Medicine’s Department of Psychiatry, who led the investigation with support from the National Institute of Mental Health.

The work is also reported in the June 4 issue of Science magazine.

Memory formation involves changes in the connections, or synapses, between neurons, a process known as synaptic plasticity. One brain structure critical for extinction memory in rats is the infra-limbic prefrontal cortex (ILC). Drugs that block synaptic plasticity impair the formation of extinction memory when injected into the ILC, causing rats to continue freezing at high levels after extinction training.

BDNF, on the other hand, allows a learning experience to increase the size and strength of synaptic contacts between neurons.

Previous work from other groups is consistent with those findings, implicating BDNF in extinction learning. In the UPR study, after rats were conditioned to fear a tone by pairing it with a footshock, BDNF was infused directly into the ILC. The next day, BDNF-infused rats showed little freezing to the tone, as if they had received extinction training.

Experiments showed that BDNF-induced extinction did not erase the original fear memory. The scientists reported that training to reinstate the tone-shock association was just as effective in both experimental and control groups. Also, the effect of BDNF was specific to extinction. It did not reduce general anxiety or change the animals' tendency to move around.
The researchers also found that rats that were naturally deficient in BDNF were more likely to do poorly in extinction trials. These rats were deficient in BDNF in the hippocampus, a brain structure that plays an important role in memory and extinction, and which has connections to the ILC. Failure to extinguish fear is thought to contribute to anxiety disorders, such as post-traumatic stress disorder (PTSD). People with PTSD have a smaller than normal hippocampus and ILC.

“Many lines of evidence implicate BDNF in mental disorders,” said NIMH Director Dr. Thomas Insel. “This work supports the idea that medications could be developed to augment the effects of BDNF, providing opportunities for pharmaceutical treatment of post-traumatic stress disorder and other anxiety disorders.”

The focus now, say the scientists, is to look for ways to augment BDNF’s actions in the brain, which might include anti-depressant medications and even exercise.

Also collaborating on the study were Dr. Jamie Peters, Dr. Loyda Meléndez and Laura Dieppa-Perea, all assigned to the University of Puerto Rico.

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