Regulating the formation of fear extinction memory

August 15 2011

(Medical Xpress) -- Neuroscientists at UQ's Queensland Brain Institute have discovered a previously unrecognized layer of gene regulation associated with fear extinction.

This is an inhibitory learning process thought to be critical for controlling fear-related behaviour when the fear response is no longer required.

Lead researcher Dr. Timothy Bredy said the findings shed new light on the processes involved in loosening the grip of fear-related memories, particularly those implicated in conditions such as phobias and post-traumatic stress disorder (PTSD).

Published in the latest issue of Nature Neuroscience, the study explores how fear-related memories are formed, updated, and extinguished at the molecular level.

It also provides fresh understanding of the actual function of genes expressed at the time of retrieval of fear memories, and how they are regulated to facilitate fear extinction.

“This is the first demonstration of how small non-coding RNAs contribute to the formation of fear extinction memory, and highlights the adaptive significance of activity-dependent microRNA expression in the adult brain,” Dr. Bredy said.

(Non-coding RNAs are believed to function by directing the epigenome to activate or silence genes although the genome itself remains the same. Small non-coding RNAs, such as the microRNAs studied here, can regulate gene function by complementary binding to the 3' untranslated end of their protein-coding target genes, resulting in transcriptional silencing.)

Dr. Bredy said that the extinction of fear-related memories occurred in the face of a competing memory process called reconsolidation, which saw memories potentially undergo modification every time they were retrieved.

“Contrary to popular belief, fear-related memories are not set in stone,” Dr. Bredy said.

“Extinction learning involves retrieval and expression of the original fear memory, which naturally permits either the restabilization of the original trace, or new extinction learning.

“And in order for new memories to be firmly established, the genes associated with the original fear memory trace must be transiently inhibited, so that the fear extinction process can proceed.”

QBI neuroscientists probed how fear memories could be strengthened or shaken loose by intervening during extinction training.

“These findings indicate that activity of this brain-specific non-coding RNA is necessary for the formation of fear extinction memory,” Dr. Bredy said.

It seems to do this by disrupting the stability of several plasticity-related target genes including one called regulator of calmodulin signalling (RCS), which is important for dopamine signalling in the brain.

“This research explains how fear extinction proceeds despite competition with the original fear memory for control over behaviour, where we have evidence to suggest that the brain specific microRNA miR-128b is essential for tipping the scale in favour of fear extinction memory rather than restabilization of the original fear,” Dr. Bredy said.

“These findings represent significant advance in our understanding of the neural mechanisms of memory updating and the processes by which fear memories can be inhibited through extinction learning."

Provided by University of Queensland