

Controlling fear by modifying DNA

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Neuroscientists from The University of Queensland's Queensland Brain Institute may have found a way to silence the gene that feeds fear.

(Medical Xpress)—For many people, fear of flying or of spiders skittering across the lounge room floor is more than just a momentary increase in heart rate and a pair of sweaty palms.

It's a hard-core phobia that can lead to crippling anxiety, but an international team of researchers, including neuroscientists from The University of Queensland's Queensland Brain Institute (QBI), may have found a way to silence the gene that feeds this fear.

QBI senior research fellow Dr Timothy Bredy said the team had shed



new light on the processes involved in loosening the grip of fear-related memories, particularly those implicated in conditions such as phobia and <u>post-traumatic stress disorder</u>.

Dr Bredy said they had discovered a novel mechanism of gene regulation associated with <u>fear extinction</u>, an inhibitory learning process thought to be critical for controlling fear when the response was no longer required.

"Rather than being static, the way genes function is incredibly dynamic and can be altered by our daily life experiences, with emotionally relevant events having a pronounced impact," Dr Bredy said.

He said that by understanding the fundamental relationship between the way in which DNA functions without a change in the underlying sequence, future targets for therapeutic intervention in fear-related <u>anxiety disorders</u> could be developed.

"This may be achieved through the selective enhancement of memory for fear extinction by targeting genes that are subject to this novel mode of epigenetic regulation," he said.

Mr Xiang Li, a PhD candidate and the study's lead author, said fear extinction was a clear example of rapid behavioural adaptation, and that impairments in this process were critically involved in the development of fear-related anxiety disorders.

"What is most exciting is that we have revealed an epigenetic state that appears to be quite specific for fear extinction," Mr Li said.

Dr Bredy said this was the first comprehensive analysis of how fear extinction was influenced by modifying DNA.

"It highlights the adaptive significance of experience-dependent changes



in the chromatin landscape in the adult brain," he said.

The collaborative research is being done by a team from QBI, the University of California, Irvine, and Harvard University.

The study was published this month in the *Proceedings of the National Academy of Sciences*.

More information: Xiang Li, Wei Wei, Qiong-Yi Zhao, Jocelyn Widagdo, Danay Baker-Andresen, Charlotte R. Flavell, Ana D'Alessio, Yi Zhang, and Timothy W. Bredy. "Neocortical Tet3-mediated accumulation of 5-hydroxymethylcytosine promotes rapid behavioral adaptation." *PNAS* 2014 ; published ahead of print April 22, 2014, DOI: 10.1073/pnas.1318906111

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