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Nervous mice lead researchers to regulator of anxiety

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University of Toronto researchers have uncovered a protein in brain receptors that regulates anxiety in mice - a finding that could one day lead to new clinical treatments of pathological anxiety in humans.

In the study, published online in the *Public Library of Science*, physiology professor Min Zhuo and his team outlined how brain receptors containing a protein called GluR5 help regulate GABA, a chemical messenger in the brain long associated with anxiety and depression. By breeding mice with genetically deleted GluR5 - or injecting a substance to inhibit GluR5 - researchers were able to track the role of the molecule inside the amygdala, an almond-shaped structure in the front of the brain that processes emotion.

"Many people suffer from constant anxiety, which studies have shown to negative effect on overall mental and physical health," says Zhuo, the EJLB-CIHR Michael Smith Chair in Neurosciences and Mental Health. "We know that GABA, as the main calming neurotransmitter, plays a crucial role in controlling anxiety and GluR5 plays a role in regulating GABA release."

Researchers used a standard test - the elevated plus maze (EPM) - to determine the GluR5 mice's anxiety levels. The EPM has a high wide-open space and an enclosed space to test a mouse's natural fear of heights. The GluR5 mice spent significantly less time in the open arms of the EPM compared with the wild-type animals, preferring to hide in the enclosed space. Having established the link between GluR5 mice and

anxiety, the researchers then wanted to determine whether activation of GluR5 in wild-type mice would decrease anxiety. They injected the mice with ATPA - a molecule that improves GluR5 - 30 minutes before testing in the EPM and found that the animals treated with ATPA spent significantly more time in the open arms. Zhuo says that the study also provides a nice cellular model for studying behavioural anxiety and explains how GluR5 is expressed in the inhibitory neurons - brain cells that decrease electrochemical activity - that may affect the release of GABA in the amygdala.

"Taken together, our results show that the deletion of GluR5 increases anxious behaviour in the EPM while the activation of GluR5 by ATPA decreases anxiety," Zhuo says. "The next step is to find ways of translating these findings into therapeutic drugs and we are working with Innovations at U of T for the translation of this finding into treatments."

Source: University of Toronto