

Study finds two genes affect anxiety, behavior in mice with too much MeCP2

8 January 2012

The anxiety and behavioral issues associated with excess MeCP2 protein result from overexpression of two genes (Crh [corticotropin-releasing hormone] and Oprm 1 [mu-opioid receptor MOR 1]), which may point the way to treating these problems in patients with too much of the protein, said [Baylor College of Medicine](#) scientists in a report that appears online in the journal *Nature Genetics*.

Much of the work was done at the Jan and Dan L. Duncan [Neurological Research](#) Institute at Texas Children's Hospital.

MeCP2 is a "Goldilocks" in the protein world. When the protein is lacking or defective, girls develop the [neurological disorder](#) Rett syndrome early in life. Too much protein results in the more recently identified MeCP2 duplication syndrome, which usually affects boys, who may inherit the gene duplications either from their mothers or, in rare cases, develop it sporadically. In both cases, anxiety and social [behavioral deficits](#) are typical of those with the disease, along with other motor problems and cognitive defects.

"This is a nice example of a translational story," said Dr. Rodney Samaco, assistant professor of molecular and [human genetics](#) at BCM and first author of the paper. "We first identified the [mouse model](#) for MeCP2 duplication syndrome and then found people with the disorder in the clinic. We went back to the lab and found out that MeCP2 was indeed the major contributor to this phenotype in patients. We have now identified two [genes](#) involved in two major symptoms of the syndrome. Eventually, we may take the information back to the clinic to develop a treatment for patients."

"Loss or Gain of MeCP2 affects the expression of hundreds of genes, but discovering that two genes are the culprits in mediating anxiety and social behavioral problems is surprising," said Dr. Huda Zoghbi, professor of molecular and human

genetics, neurology, neuroscience, and pediatrics at BCM and director of the NRI. She is the corresponding author of the report and a Howard Hughes Medical Institute Investigator.

Patients with MeCP2 duplication disorder have a duplication in chromosomes that span both the MECP2 gene and another called IRAK1. But with this new study, it is now clear that excess MeCP2 accounts for the neuropsychiatric symptoms.

In mice, doubled MeCP2 levels caused both anxiety and autism-like behaviors and altered the expression of several hundred genes. Of these, two genes - Crh and Oprm1, are implicated in anxiety and social behavior, said Samaco.

"Then, when we reduced the levels of Crh, we saw reduced anxiety," he said. "When we reduced levels of Oprm1, we improved the social behavior problems."

This finding is important because it shows that tweaking the expression of genes that the protein affects, rather than trying to adjust the levels of the finicky MeCP2 protein itself, can modify symptoms of MeCP2 disorders.

In fact, Samaco also reduced levels of the [protein](#) that is a cellular receptor for Crh, both through molecular means and with the use of a drug, and found that anxiety levels also went down. That could provide another means of dealing with [anxiety](#) associated with the duplication syndrome.

More information: *Nature Genetics*: www.nature.com/ng/index.html

Provided by Baylor College of Medicine

APA citation: Study finds two genes affect anxiety, behavior in mice with too much MeCP2 (2012, January 8) retrieved 30 April 2021 from <https://medicalxpress.com/news/2012-01-genes-affect-anxiety-behavior-mice.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.