Press Release

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A Common Medication Restores Social Deficits in Autism Mouse Model

Reports new study in Biological Psychiatry

Philadelphia, PA, January 26, 2017 – Reducing the function of the autism-associated gene *Pcdh10* leads to impairments in social behavior, according to a study published in *Biological Psychiatry*. Reducing *Pcdh10* function also disrupted the structure and function of circuitry in the amygdala, a brain region implicated in the behavior symptoms of autism spectrum disorder (ASD).

In the study, first authors Dr. Hannah Schoch and Dr. Arati Kreibich, both of the University of Pennsylvania, and colleagues found that neurons in the amygdala of mice lacking one copy of *Pcdh10* (*Pcdh10*$^{+/-}$) had reduced levels of NMDA glutamate receptor subunits, indicating disrupted excitatory neural circuitry.

"Our study of *Pcdh10*$^{+/-}$ mice gives us greater insight into the biology of social behaviors and into the function of a gene associated with ASD," said senior author Professor Edward Brodkin, also of the University of Pennsylvania.

The study also suggests a possible target for treatment of ASD. When the researchers gave the mice a medication called d-cycloserine, the impaired social behavior improved. D-cycloserine is an old medication that was developed as a treatment for tuberculosis. However, nearly 30 years ago, it was discovered that this drug targets the NMDA glutamate receptor to enhance its function.

Brodkin cautions that although much more work would be necessary in both animal models and humans to establish the medication as safe and effective for this use, preliminary clinical studies in humans with ASD have also shown promise for its use to improve social interactions.

"This study is an example of a principle that we will hold for more psychiatric conditions," said John Krystal, Editor of *Biological Psychiatry.* "That hypothesis is that when psychiatric syndromes can be targeted to specific genes, then specific treatments may be implicated."

Reducing the function of the *Pcdh10* gene had a more prominent effect in male mice — female mice did not exhibit the social behavior deficits seen in males. The finding parallels the male predominance of ASD in humans, and will be an important line of future research to understand the genetic underpinnings of sex differences in ASD.

Notes for editors

The article is "Sociability Deficits and Altered Amygdala Circuits in Mice Lacking Pcdh10, an Autism Associated Gene," by Hannah Schoch, Arati S. Kreibich, Sarah L. Ferri, Rachel S. White, Dominique Bohorquez, Anamika Banerjee, Russell G. Port, Holly C. Dow, Lucero Cordero, Ashley A. Pallathra,

Hyong Kim, Hongzhe Li, Warren B. Bilker, Shinji Hirano, Robert T. Schultz, Karin Borgmann-Winter, Chang-Gyu Hahn, Dirk Feldmeyer, Gregory C. Carlson, Ted Abel, and Edward S. Brodkin (http://dx.doi.org/10.1016/j.biopsych.2016.06.008). It appears in *Biological Psychiatry*, volume 81, issue 3 (2017), published by Elsevier.

Copies of this paper are available to credentialed journalists upon request; please contact Rhiannon Bugno at +1 214 648 0880 or biol.psych@utsouthwestern.edu. Journalists wishing to interview the authors may contact Edward S. Brodkin, M.D., at ebrodkin@mail.med.upenn.edu.

The authors' affiliations, and disclosures of financial and conflicts of interests are available in the article.

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The journal publishes novel results of original research which represent an important new lead or significant impact on the field, particularly those addressing genetic and environmental risk factors, neural circuitry and neurochemistry, and important new therapeutic approaches. Reviews and commentaries that focus on topics of current research and interest are also encouraged.

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