

Researchers identify role gender-biased protein may play in autism

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Researchers at the University of New Hampshire are one step closer to helping answer the question of why autism is four times more common in boys than in girls after identifying and characterizing the connection



of certain proteins in the brain to autism spectrum disorders (ASD).

"Our study is the first to look at the gender-biased regulation of proteins in the brain and how they may play a role in affecting abnormal changes in the body that results in autism," said Xuanmao (Mao) Chen, assistant professor of neurobiology. "Our findings point to a new direction for <u>autism research</u> and suggest promising possibilities for creating novel treatment strategies."

In the study, recently published in the journal *Frontiers in Cellular Neuroscience*, the researchers looked at an enzyme called AC3 which is genetically connected to <u>major depressive disorder</u> (MDD), obesity, and <u>autism spectrum disorders</u> (ASD). However, not much is known about how AC3 functions in the brain. What is known is that many neurodevelopmental disorders or psychiatric diseases, such as depression and autism, exhibit profound differences between males and females, known as sexual dimorphism. For example, females have a higher risk of depression, whereas autism affects more males, with a boy to girl ratio of four to one. The problem is that it is unclear what causes the differences.

The researchers took a closer look at the phosphorylation in the brain, a process when groups of chemicals called phosphates attach to proteins to regulate them, to see which were influenced based on gender. They identified 204 proteins that were more highly regulated in females than in males. Of those, a large percentage (31%) were associated with autism.

"Our results suggest that proteins in the female brain, particularly autismrelated proteins, are more tightly regulated than those in the male <u>brain</u> possibly helping to prevent the development of <u>autism</u> in females," said Chen.



The researchers point to evolution for possibly playing a part in how these proteins behave based on the key roles or functions of each sex. The female role has traditionally been multi-tasking several activities like childrearing, caring for the family, the home, and preparing meals whereas male tasks were more specifically focused on functions like hunting and gathering. You can see this highly focused trait in autistic males who are very smart but tend to be fixated on one thing and not interested in, or cannot handle, other social interactions.

Chen says that this research is still in the early phase with mouse models and more studies are needed, but he is hopeful that it may open up a new research direction and one day could possibly lead to a new pharmacological treatment.

More information: Yuxin Zhou et al, Comparative Phosphoproteomic Profiling of Type III Adenylyl Cyclase Knockout and Control, Male, and Female Mice, *Frontiers in Cellular Neuroscience* (2019). DOI: 10.3389/fncel.2019.00034

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