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A Glutamate Receptor May Be A Target For Future Treatment Of Some Forms Of ASD

What is this research about?

It has been challenging to understand the different organization and connections of brain cells that underlie behaviours associated with autism spectrum disorder (ASD). Most research in this area has targeted syndromic ASD (secondary trait of another disease or known biological process), rather than the less well understood, non-syndromic forms of ASD (primary condition).

A well-studied case of ASD is the syndromic form associated with “Fragile X Syndrome”. In Fragile X Syndrome, a key defect is decreased communication between brain cells due to an overactive protein. This protein is a receptor that binds glutamate, a molecule that passes signals on to other brain cells.

More rare, and less well understood, are non-syndromic cases; some that are associated with changes in a protein called “neuroligin”. This study examines whether changes in glutamate receptor signalling (seen in Fragile X Syndrome) could also be involved in the cause of ASD in non-syndromic cases that have changes in the “neuroligins”.

What did the researchers do?

The researchers gave mice a defective version of the neuroligin protein, which resulted in impaired social interactions and social memory compared to healthy mice. They examined the connections between neurons in the cerebellum of these mice, an area that is known be altered in some cases of ASD. Here they measured the signalling between brain cells as well as the number and location of the glutamate receptor.

What you need to know:

Patients with Fragile X Syndrome may develop syndromic ASD due to an overactive glutamate receptor that weakens communication in the cerebellum. This study shows that some cases of non-syndromic ASD can be caused by the same mechanism, and that these cases may be treated by targeting these glutamate receptors.

Then, in order to see if the defective neuroligin had an effect on the function of the cerebellum, which is important for coordination of movement, the researchers measured the climbing patterns of mice.

What did the researchers find?

The researchers found that mice with a defective neuroligin had more of this glutamate receptor, which weakened connections between the neurons - similar to what is seen in patients with Fragile X Syndrome. Neuroligin-defective mice also performed slower climbing movements, indicating that the weakened neural connections resulted in functional decrease. Importantly, when the researchers reintroduced a functional neuroligin in mice that had developed without one, they restored the receptor levels back to normal and even reversed these functional alterations.

How can you use this research?

While it is not possible to directly reintroduce proteins in humans, this study indicates that treatments that inhibit this glutamate signalling may alleviate certain autistic symptoms, even in the adult brain. This

study shows that there may be common biological pathways that result in the autistic condition.

About the Researchers

S.J. Baudouin (PhD), postdoctoral researcher, S. Gerharz, researcher, L. Burklé, former Hatstatt, technical assistant, K. Vogt (PhD), assistant professor and P. Scheiffele (PhD) professor at the Biozentrum, University of Basel, Switzerland.

J. Gaudias (PhD) Regulatory Affairs Project Manager at SFL in Basel, Switzerland.

W. Spooren (PhD) Hoffmann-La Roche in Basel, Switzerland.

P. Punnakkal (PhD) fellow, Sree Chitra Tirunal Institute for Medical Sciences and Technology in Thiruvananthapuram, India.

C.L. De Zeeuw (PhD) professor, Institute for Neuroscience at the Royal Netherlands Academy of Arts and Sciences in Amsterdam, Netherlands and at the Dept of Neuroscience, Erasmus University Medical Centre, Rotterdam, Netherlands, where K. Zhou is a PhD student.

K.F. Tanaka (PhD) researcher at the Dept of Neuropsychiatry at Keio University, Tokyo, Japan, and at the Dept of Neuroscience, Columbia University, New York, USA.

R. Hen (PhD) professor, Dept of Neuroscience, Columbia University, New York, USA.

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About the Chair

The Chair in Autism Spectrum Disorders Treatment and Care Research is dedicated to studying ways to improve the mental health and well-being of people with Autism Spectrum Disorders (ASD) and their families in Canada.

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For more information, visit the Chair in Autism Spectrum Disorders Treatment and Care Research website at asdmentalhealth.ca

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