Study connects the genetic background of autistic spectrum disorders with stem cell dysfunction

December 4 2018

Credit: CC0 Public Domain

Disorders of the autistic spectrum have been associated with hundreds of genetic variations, which have helped in identifying disturbed

intracellular signalling pathways and molecular mechanisms typical to autism.

Many gene mutations related to the autism spectrum disorders reside in a gene that produces a protein relevant to synapses, or is important for the connections between neurons. Gene defects linked with developmental disorders are often located in genes involved in brain development.

In a study recently published in the *Stem Cell Reports* journal, researchers from the University of Helsinki examined molecular mechanisms leading to disturbed neuronal network function in autistic spectrum disorders by utilising patient-specific neuronal progenitors differentiated from stem cells induced from blood or fibroblasts of skin. Functional changes in the voltage-dependent L-type calcium channels were detected in fragile X syndrome (FraX), the disease model used in the study.

FraX is the most common cause of genetic mental retardation and a variant of the autistic spectrum.

"In genetic studies, the L-type calcium channels have been previously linked with autism, and a dysfunction in the channels aptly connects the changes identified in genetic studies to abnormalities of neural network formation and function in autistic spectrum disorders," says Maija Castrén, an Academy of Finland research fellow at the University of Helsinki,

The new research finding increases our understanding of the developmental disorders of the nervous system and provides an opportunity for further research, which can help in identifying the factors that individually increase or decrease vulnerability to defects of neuronal connectivity underlying autistic spectrum disorders and its co-morbid neuropsychiatric diseases.

"Even though functional changes are clearly expressed in similar manner in relation to distinct neurodevelopmental disorders, in human neural progenitor cultures there are a lot of individual variations that presumably regulate the effects of each gene mutation on the individual phenotype," Castrén says.

More information: Claudia Danesi et al. Increased Calcium Influx through L-type Calcium Channels in Human and Mouse Neural Progenitors Lacking Fragile X Mental Retardation Protein, *Stem Cell Reports* (2018). DOI: 10.1016/j.stemcr.2018.11.003

Provided by University of Helsinki