Clock gene mutation found to contribute to the development of autism

March 24 2022

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In *Molecular Psychiatry*, a team of scientists from the University of Minnesota Medical School, University of Texas Health San Antonio, and the Biomedical Research Institute (BRI) of the Foundation for Research

and Technology Hellas (FORTH) in Greece found that the disruption of a circadian clock gene may be involved in the development of autism spectrum disorder.

Autism spectrum disorder, or ASD, refers to a neurodevelopmental disorder characterized by a wide range of behavioral conditions including challenges with social skills, repetitive behaviors, speech and nonverbal communication. According to the Centers for Disease Control and Prevention, ASD affects one in 44 children in the U.S.

About 50-80% of children with ASD have sleep problems, compared to less than 30% in the general population. The causes of sleep problems in ASD are not entirely clear, but a malfunctioning body clock could be the culprit.

"It has long been recognized that the function of the body clock is frequently disrupted in autism patients and these patients often exhibit various sleep problems," said Ruifeng Cao, MD, Ph.D., an assistant professor of neuroscience at the U of M Medical School, Duluth Campus and co-author of the study. "But, it is not known whether clock gene disruption can directly cause autism."

The study found that the disruption of an essential clock gene in preclinical models can lead to autistic-like phenotypes. Specifically, the global or cerebellar deletion of the Bmal1 gene can cause severe impairments in sociability, social communication and excessive repetitive behaviors.

The models also illustrated damages to their cerebellum—or cerebellar ataxia. The research team further studied the pathological changes in the cerebellum and found a number of cellular and molecular changes that indicate neurodevelopmental deficits.

"Clock gene disruption could be a mechanism underlying several forms of autism and potentially other neurodevelopmental conditions, and this finding paves the way for further exciting research," said Christos Gkogkas, Ph.D., a lab principal investigator in neurobiology at BRI of FORTH.

The research team plans to continue to study other clock genes that are found mutated in ASD. More importantly, they recommend development of novel therapeutic strategies based on their findings.

More information: Dong Liu et al, Autistic-like behavior and cerebellar dysfunction in Bmal1 mutant mice ameliorated by mTORC1 inhibition, *Molecular Psychiatry* (2022). DOI: 10.1038/s41380-022-01499-6

Provided by University of Minnesota Medical School