

Scientists discover new genetic disease that delays brain development in children

June 24 2022



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Scientists have identified a new genetic disease, which causes some children's brains to develop abnormally, resulting in delayed intellectual development.

The majority of patients with the condition—a condition that is so new it doesn't have a name yet—have severe learning difficulties which affect

their quality of life.

An international team of researchers from the universities of Portsmouth, Southampton and Copenhagen found that changes in a protein coding gene called Glutamate Ionotropic Receptor AMPA Type Subunit 1 (GRIA1) caused this [rare genetic disease](#).

Now the variant has been identified, it will help clinicians come up with targeted interventions to help patients and their families, also opening the door to screening and [prenatal diagnosis](#).

The GRIA1 gene helps to move electrical signals around the brain. However, if this process is interrupted or made less efficient, it can cause a reduction in the brain's capacity to retain information.

The research team, made up of frog geneticists, biochemists and clinical geneticists, used tadpoles in which the human gene variants were mimicked using gene editing to show that GRIA1 changes are the underlying cause of the behavior-altering disease. The biochemical analysis of the variants was also performed in frog oocytes.

The findings are published in the *American Journal of Human Genetics*.

Study co-author Professor Matt Guille, who leads a laboratory in the Epigenetics and Developmental Biology research group at the University of Portsmouth, says that "next generation DNA sequencing is transforming our ability to make new diagnoses and discover new genetic causes of rare disorders."

"The main bottleneck in providing diagnoses for these patients is linking a change discovered in their genome firmly to their disease. Making the suspect genetic change in tadpoles allows us to test whether it causes the same illness in humans."

"The resulting data allow us to support our colleagues in providing the more timely, accurate diagnosis that patients and their families so desperately need."

Co-author Dr. Annie Goodwin, Research Fellow at the University of Portsmouth who performed much of the study, says that "this was a transformational piece of work for us; the ability to analyze human-like behaviors in tadpoles with sufficient accuracy to detect genetic disease-linked changes opens the opportunity to help identify a huge range of diseases. This is particularly important given that so many neurodevelopmental diseases are currently undiagnosed."

Co-author Professor Diana Baralle, Professor of Genomic Medicine and Associate Dean (Research) in the Faculty of Medicine at the University of Southampton, added that "discovering these new causes for genetic disorders ends our patients' diagnostic odyssey and this has been made possible by collaborative interdisciplinary working across universities."

One in 17 people will suffer from a rare disease at some time in their lives. Most of these rare diseases have a genetic cause and often affect children, but proving which gene change causes a disease is a huge challenge.

Professor Guille said that previously, while studies connecting a gene and a disease were mainly performed in mice; several labs, including his own at the University of Portsmouth, have recently shown that experiments in tadpoles can also provide very strong evidence about the function of variant human [genes](#). The process of re-creating some gene variants in tadpoles is straightforward and can be done in as little as three days.

Professor Guille added that they "are currently extending and improving our technology in a program funded by the Medical Research Council;

this is making it applicable to the wider range of [disease](#)-related DNA changes provided to us by our clinical collaborators."

"If the clinical researchers find the information sufficiently useful, then we will continue to work together to scale up the pipeline of gene function analysis so it can be used to direct effective interventions for a significant number of patients."

More information: Vardha Ismail et al, Identification and functional evaluation of GRIA1 missense and truncation variants in individuals with ID: An emerging neurodevelopmental syndrome, *The American Journal of Human Genetics* (2022). [DOI: 10.1016/j.ajhg.2022.05.009](https://doi.org/10.1016/j.ajhg.2022.05.009)

Provided by University of Portsmouth

Citation: Scientists discover new genetic disease that delays brain development in children (2022, June 24) retrieved 22 June 2024 from <https://medicalxpress.com/news/2022-06-scientists-genetic-disease-brain-children.html>

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