Gene linked to persistent stuttering into adulthood uncovered

November 20 2023, by Danielle Galvin

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A new study led by University of Melbourne researchers has discovered a link between a new gene pathway and structural brain anomalies in some people who stutter into adulthood, opening up promising research avenues to enhance the understanding of persistent developmental stuttering.

Published in the journal *Brain*, researchers studied 27 members of a four-generation Australian family, 13 of whom have stuttering.

Stuttering is a speech disorder affecting around 5% of children and 1% of adults worldwide. In over two-thirds of cases of stuttering in childhood, the stuttering eventually resolves with therapy. However, in severe cases like most individuals in the family studied here, the disorder can persist into adulthood.

Despite stuttering being commonly inherited, as shown by earlier twin studies, only four genes have previously been implicated in stuttering.

Professor Michael Hildebrand and Professor Angela Morgan led a large team of international researchers across 18 institutions to implicate a fifth gene, called PPID, in severe developmental stuttering, linking a new 'chaperone pathway' to the disorder.

Chaperones are proteins that shuttle other proteins to the correct part of a cell so they can complete their function. The researchers suspect the damaged gene will change the movement and function of proteins during brain development, triggering neural changes that cause persistent stuttering.

Consistent with this a mouse model generated with the same gene defect developed structural changes in similar brain regions to those of family members with stuttering.

"We have known for some time that there is a genetic link to stuttering, but this study is novel in that it is the first study to link structural brain anomalies to developmental stuttering," geneticist Professor Hildebrand said.

"These findings support changing the genetic diagnostic protocol for

some people who stutter to include brain imaging studies.

"It is significant because it shows that genetic changes passed on in families can alter brain development leading to structural anomalies that underly stuttering."

Professor Angela Morgan, a speech pathologist from the Murdoch Children's Research Institute (MCRI), said the study goes some way to understanding the genetic predisposition for the speech disorder.

"We know that there are environmental and genetic factors at play when it comes to stuttering," she said.

"But the study also opens up further research into this new chaperone pathway, and related pathways, enhancing our understanding of the genetic architecture of persistent developmental stuttering."

More information: Angela T Morgan et al, Stuttering associated with a pathogenic variant in the chaperone protein cyclophilin 40, *Brain* (2023). DOI: 10.1093/brain/awad314

Provided by University of Melbourne