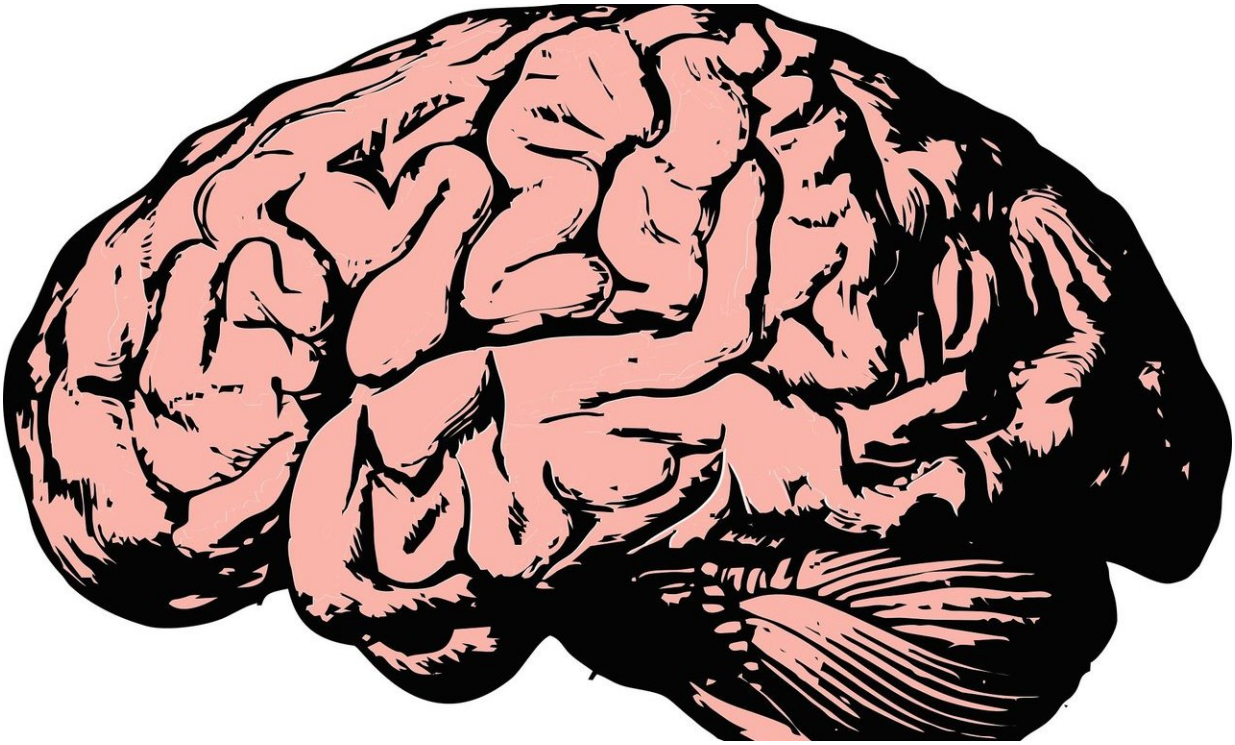
Researchers discover new genetic brain disease

October 30 2019



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Manchester researchers have contributed towards the discovery of a genetic brain disease which can cause paraplegia and epilepsy in sufferers.

Hereditary spastic paraplegias (HSP) are a group of genetic disorders

that cause weakness and stiffness in the leg muscles. Generally symptoms gradually get worse over time, and severely affected patients are wheelchair dependent.

Changes in several genes are known to cause HSP. However, the underlying cause in a substantial number of patients remains unknown. Currently, there is no cure for HSP.

Via human genetic studies and international collaboration, teams in Manchester and Amsterdam worked together to identify a new cause of HSP. They found that this disease is caused by mutations in a gene called PCYT2, which caused the gene to be less active.

The researchers studied the effects of the condition using zebrafish and cell samples from patients with the disease.

They found that zebrafish with normal or reduced PCYT2 activity had significantly better survival rates than those with absent PCYT2 activity, leading Dr. Siddharth Banka—Clinical Senior Lecturer at The University of Manchester and Consultant Clinical Geneticist at Manchester University NHS Foundation Trust (MFT) – and his colleagues to conclude that complete loss of PCYT2 activity is likely to be, 'incompatible with life in vertebrates'.

The gene encodes an enzyme which produces a lipid (a fatty molecule) that is used to build cell membranes in every cell of the body. The lipid produced by the enzyme is particularly abundant in brain cell membranes.

A team in Amsterdam was also able to identify abnormal biochemical signatures in the cells and blood of the patients who donated samples. It is hoped that these signatures could be used as markers to help diagnose patients with the condition.

Dr. Banka runs a Clinical Genetics clinics at Saint Mary's Hospital, which is part of MFT. His research group uses a combination of genomics, clinical and functional studies to identify the cause of disease in patient with unsolved genetic conditions.

Dr. Banka said: "Saint Mary's Hospital is one of the leading NHS and internationally recognised large-scale providers of genomic services. Being able to combine my clinical role at the hospital, with my academic research at The University of Manchester, has been crucial to this outcome.

"This link between academia and the NHS means we can translate research from the bench to the bedside, for the benefit of our patients.

"The identification of more patients in future will help in better understanding of the effects of HSP."

It is thought that studying this crucial gene will help in understanding other types of HSP and other neurodegenerative diseases.

The paper was published in the neurological journal *Brain*.

More information: Frédéric M Vaz et al. Mutations in PCYT2 disrupt etherlipid biosynthesis and cause a complex hereditary spastic paraplegia, *Brain* (2019). DOI: 10.1093/brain/awz291

Provided by University of Manchester