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Simple DNA test could detect common neurological disorders, study says

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A simple test could end years of uncertainty for people with relatively common neurological conditions, new research has found.

Historically, obtaining a definitive diagnosis for conditions including Huntingdon's disease and some forms of amyotrophic lateral sclerosis has been difficult, because, although the cause of the symptoms is genetic, knowing which test to carry out has resulted in delays of many years.

Now, a new study suggests that whole genome sequencing (WGS) can quickly and accurately detect the most common inherited neurological disorders, and could be implemented in routine clinical practice with immediate effect.

"It is very exciting because it opens up the vista of a test that could end the diagnostic odyssey for many patients," said Prof Sir Mark Caulfield from Queen Mary University of London and former chief scientist at Genomics England.

"This work paves the way for this to be implemented immediately within the NHS."

WGS is already offered to people in England with rare disorders or childhood cancers through the NHS Genomic Medicine Service. However, the technique wasn't thought to work on people with 'repeat expansion disorders' caused by the insertion of short repetitive chunks of DNA into the genetic code – in some cases, stretching across long distances – because they can be difficult to quantify.

Such disorders are relatively common, affecting around one in 3,000 people, and include neurodegenerative and movement disorders such as Fragile X syndrome, Huntington's disease, Friedreich's ataxia, and some forms of amyotrophic lateral sclerosis or frontal lobe dementia.

Instead, those with neurological symptoms are subjected to multiple tests, each examining a single gene at a time, and taking six to eight weeks to return a result – meaning a long diagnostic odyssey for many patients. For those with atypical clinical presentations, especially children without a previous positive family history, the process can take years.

Prof Patrick Chinnery, clinical director at the Medical Research Council, said: "Many patients with neurological disorders never receive a precise diagnosis. This new study shows how

whole genome sequencing can address this challenge through a genuinely national programme, taking world-leading re
search to patients across the whole of England and improving their health care."

The new test utilises an algorithm that can spot repetitive elements in whole genome sequences, by comparing those from healthy people with those affected by repeat expansion disorders. "The advantage is that you can test multiple variants at the same time," said Dr Arianna Tucci at Queen Mary University of London, who led the research.

The study, published in The Lancet Neurology, assessed the accuracy of WGS to detect repeat expansion disorders in 404 patients who had previously been diagnosed using standard NHS tests, concluding that the accuracy and sensitivity of WGS was comparable.

Next, it was used to investigate 11,631 undiagnosed people with clinical symptoms potentially associated with a repeat expansion disorder, resulting in a new diagnosis for 68 of them.

Among those who benefited were six children, some of whom had no reported family history and are likely to have remained undiagnosed – including a 10-year-old girl with an intellectual disability and an 18-year-old teenager with dementia.

"Here in a single test, we have the capacity to diagnose the most common neurological diseases," said Caulfield.

Another of those who benefited is Eileen Flynn, a patient at The Ataxia Centre at University College London Hospitals who was diagnosed with Friedreich's ataxia through the study. She said: "Over the last 15 years I've gone from someone who was confident, loved to dance and socialise to now using a walker and having slurred speech.

"Before my diagnosis, I thought it would be better if I had cancer as there's usually a clear path of action to help you fight the disease. Having a diagnosis isn't a cure, but at last I know what is happening and understand what I need to do to delay the inevitable for as long as possible."

A definitive diagnosis also meant other family members could be tested – sadly, this confirmed that her younger sister also has the disorder.