Medical Xpress

Global genomic collaboration provides diagnoses and informs care for infants with epilepsy

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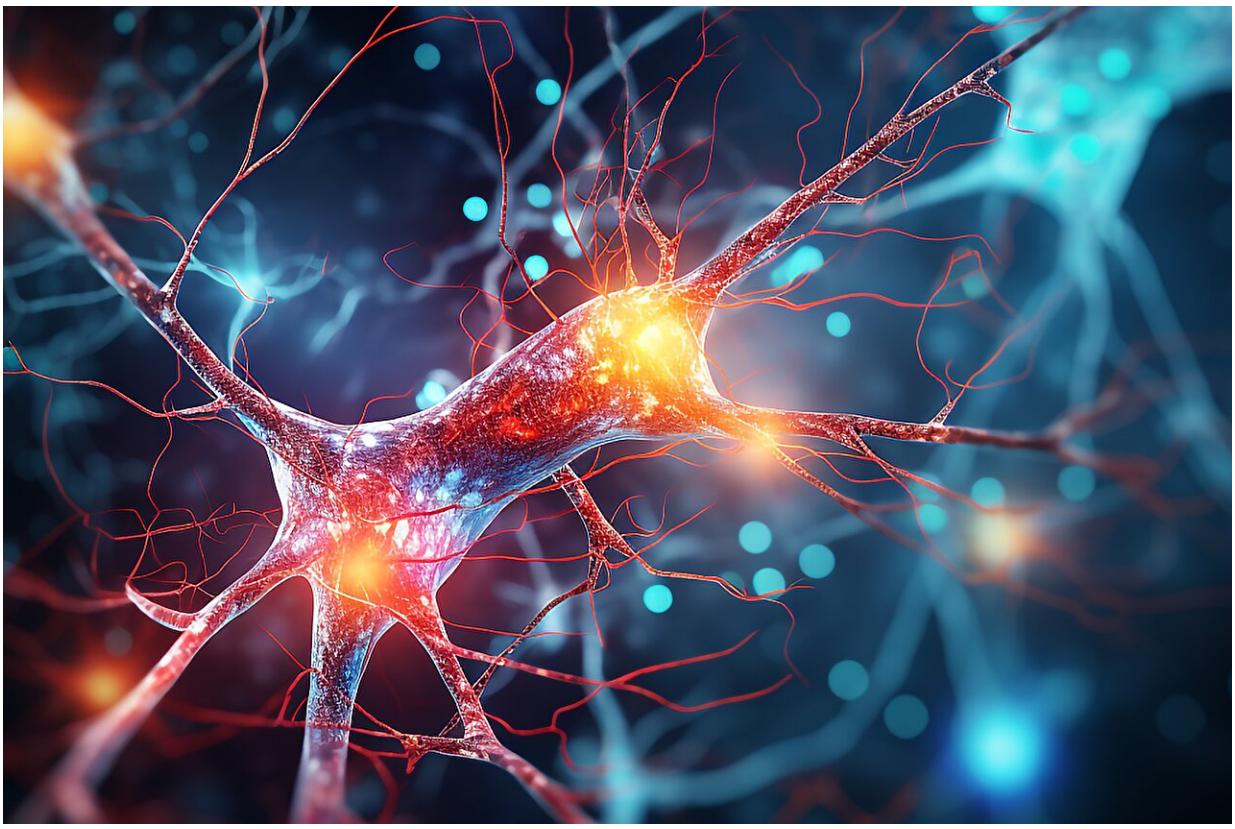

An illustration showing flashing neurons. Credit: The Hospital for Sick Children (SickKids).

Epilepsy in infants ranges in severity and can leave caregivers with

questions about their child's health. While genetic testing to help determine the cause of epilepsy is possible, comprehensive testing does not always happen routinely and it can take a long time, leaving families waiting for answers.

Published in *The Lancet Neurology*, this international study sequenced the genomes of 100 infants with unexplained seizures, along with their parents, from four countries (England, U.S., Canada and Australia) to better understand the potential strengths of early, broad genome sequencing (a process which looks for changes across the entire genome) for infantile epilepsy.

The researchers used rapid genome sequencing (rGS) to investigate the impact of an expedited genetic diagnosis on care for the first time. Across all children enrolled in the study, 43% received a diagnosis within weeks, and that diagnosis impacted prognosis in nearly 90% of those cases, guiding treatment options for over half.

Called Gene-STEPS (Shortening Time to Epilepsy Services), the study is the first collaboration launched through the International Precision Child Health Partnership (IPCHiP), an international consortium (Boston Children's Hospital, Murdoch Children's Research Institute with The Royal Children's Hospital in Melbourne Australia, The Hospital for Sick Children (SickKids) and UCL Great Ormond Street Institute of Child Health and Great Ormond Street Hospital) that leverages each institution's expertise and genomic infrastructure to accelerate discovery and the development of therapies for children.

Genetic insights inform course of care for infantile epilepsy

Currently, there are more than 800 different genetic causes of infantile

epilepsy and many have similar symptoms during infancy. Unlike more targeted genetic testing that is often used to confirm a suspected diagnosis, rapid genome sequencing looks for any changes in a person's DNA that may explain a medical condition, analyzing the entire genome.

In this study, both biological parents and the infant underwent rGS, known as "trio" sequencing, to more quickly understand whether gene changes in the children were inherited or new to the child (de novo). These insights are important for families to understand how the results may impact their lives and any future family planning.

For the participants for whom initial analysis did not provide a genetic explanation for their seizures, the research team noted that a "negative" result from this genetic test was also an important piece of information for families and clinicians, providing an informed path forward for the child's care.

The international research team is continuing to follow-up with clinicians and study participants to understand how rGS has influenced the child's development, but the work doesn't stop there. A greater understanding of the genetic variants involved in epilepsy may help identify eligibility for clinical trials and inform the development of tailored interventions.

More information: Evaluation of the feasibility, diagnostic yield, and clinical utility of rapid genome sequencing in infantile epilepsy (Gene-STEPS): an international, multicentre, pilot cohort study, *The Lancet Neurology* (2023).

Provided by The Hospital for Sick Children