Researchers use AI-powered method to identify genetic epilepsies earlier than current genetic diagnosis

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Diagnosing the genetic cause of a disease can aid in finding therapies and directing treatment, but often these diagnoses occur long after the disease has impacted a patient's life. In a new study, researchers from Children's Hospital of Philadelphia (CHOP) used machine learning and artificial intelligence to comb through medical records and use clinical notes to match symptoms with specific genetic epilepsies. The results of

their study could significantly improve the time to diagnosis and treatment.

The findings were recently published in the journal *Genetics in Medicine*.

More than 100 epilepsies caused by a single gene mutation have been identified, with several therapies being designed to target the genes responsible for these epilepsies. However, genetic testing can take a long time to confirm a particular genetic epilepsy. For example, in Dravet Syndrome, one of the most common genetic epilepsies, symptoms can be observed between the ages of 6 to 9 months, yet the average age for diagnosis is 4.2 years. Cost and access barriers continue to be an issue, meaning that researchers must develop methods for making diagnoses more timely and more widely accessible.

Prior studies from the Epilepsy Genetics Initiative (ENGIN) at CHOP--one of the largest epilepsy genetics programs in the country, with more than 5,000 individuals assessed for epilepsy genetics evaluations so far--have demonstrated that standardized data from Electronic Medical Records can be used to study clinical data at very large scales and better predict onset of epilepsy based on symptoms instead of relying solely on a confirmed genetic diagnosis. Building upon these previously developed techniques, researchers in this study aimed to identify early clinical features that could suggest a genetic diagnosis of epilepsy.

"We wanted to determine whether the type of information captured in electronic medical records prior to genetic testing could provide clinicians with clues for a later diagnosis," said first study author Peter D. Galer, MSc, a Ph.D. student with ENGIN at CHOP and the Center for Neuroengineering and Therapeutics at the University of Pennsylvania. "In this instance, we found that a wide range of genetic epilepsies have key clinical features that present prior to genetic testing

and diagnosis."

Using Natural Language Processing, an AI-driven standardized method for processing clinical information from text in Electronic Medical Records, the researchers extracted 89 million timestamped clinical annotations from 4,572,783 clinical notes from 32,112 individuals with childhood epilepsy, including 1,925 individuals with known or presumed genetic epilepsies.

The researchers identified 47,774 age-dependent associations of clinical features with genetic epilepsies a median of 3.6 years prior to when those diagnoses were confirmed with a genetic test. A total of 710 genetic etiologies were identified in the cohort, and in that group, neurodevelopmental differences observed between the ages of 6 and 9 months increased the likelihood of a later genetic diagnosis fivefold.

"By examining a very large dataset of individuals with childhood epilepsies, we believe that our results could be used prospectively for new diagnoses. Since most clinicians use Electronic Medical Records, we believe this system could be widely adapted and utilized even in patient populations where genetic testing is not immediately available after symptom onset," said senior study author Ingo Helbig, MD, pediatric neurologist in the Division of Neurology, co-director of ENGIN, and Clinical Director of the CHOP/Penn Center for Epilepsy and Neurodevelopmental Disorders (ENDD).

Helbig also serves as the Scientific Director of Arcus Omics, an institution-wide initiative that allows for genomics and clinical data at CHOP to be analyzed jointly. The analysis of the combined dataset was only made possible through the resources of the Arcus Omics team.

"In the era of precision medicine, quicker, more accurate prognoses could make an enormous difference in the lives of individuals living

with genetic epilepsies," said Helbig.

More information: Peter D. Galer et al, Clinical signatures of genetic epilepsies precede diagnosis in electronic medical records of 32,000 individuals, *Genetics in Medicine* (2024). DOI: 10.1016/j.gim.2024.101211

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