Clinicians work together to improve diagnostic tools for epilepsy

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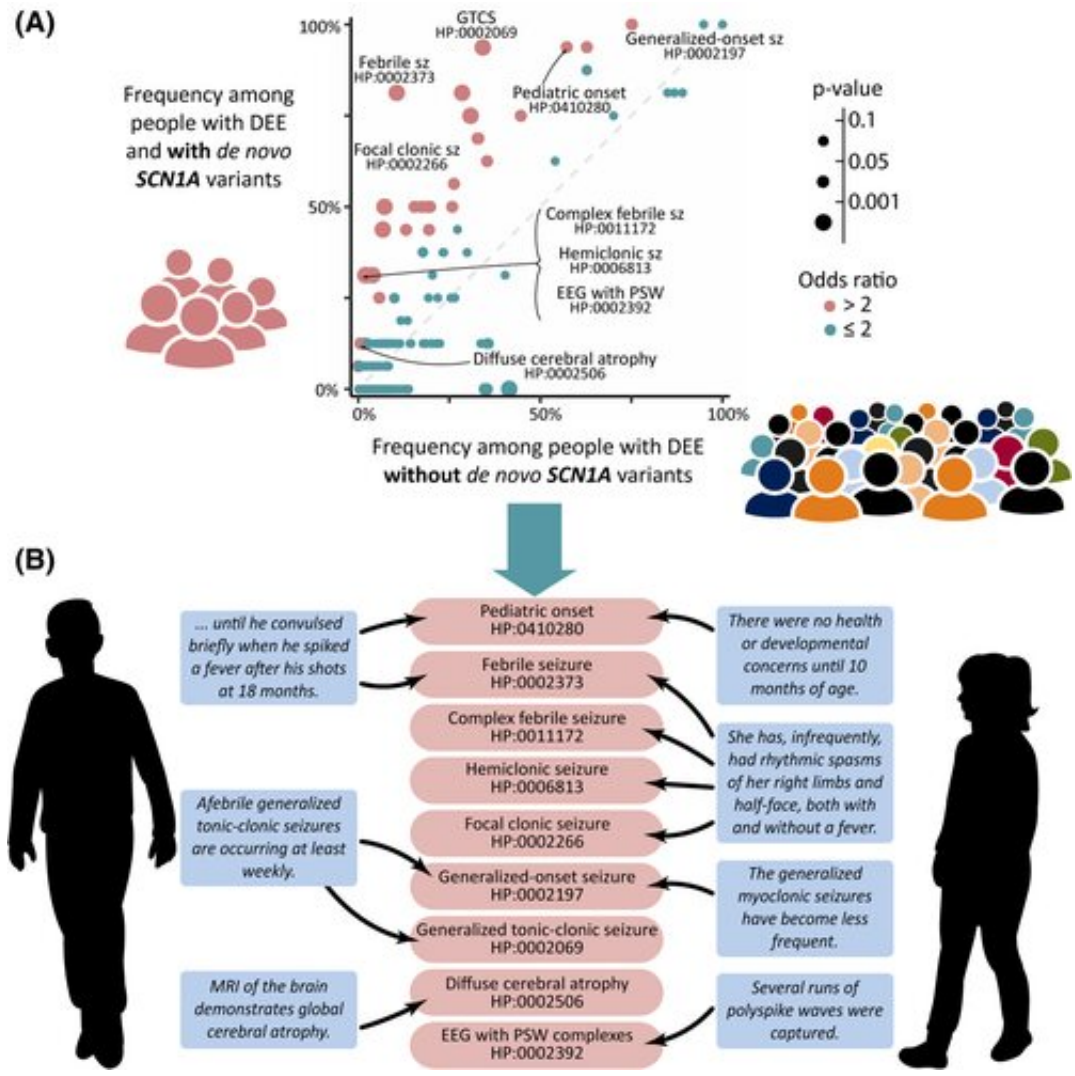

FIGURE 1 (A) The Human Phenotype Ontology (HPO) can harmonize phenotypic data from large cohorts to identify phenotypic associations with a particular genetic (or other) categorical factor, in this case de novo variants in SCN1A. Data from Galer et al. 2020;25 p-values and odds ratio obtained using

Fisher's exact test. (B) Once the set of HPO terms associated with this form of epilepsy is known, the clinical features of patients can be translated into HPO terms to assess how closely they match phenotypically. GTCS, generalized tonic-clonic seizure; PSW, polyspike-wave; sz, seizure. Credit: *Epilepsia* (2021). DOI: 10.1111/epi.16908

An international team of scientists have created a language to improve epilepsy research and diagnosis.

Researchers at Newcastle University have led an international team of epilepsy experts to redefine the language used to describe seizures in a tool used to diagnose patients with genetic diseases.

The Human Phenotype Ontology (HPO) is a freely available map of human symptoms used widely by medical and research teams around the world.

Its most important function is to select and interpret genetic tests. Identifying a genetic cause in epilepsy can help doctors to select which treatments to recommend and which to avoid.

The team led from Newcastle University, Newcastle Upon Tyne Hospitals NHS Foundation Trust and Children's Hospital of Philadelphia (Pennsylvania) redesigned the concepts of seizures in the HPO, using the latest expert opinions from the International League Against Epilepsy.

The new map consists of five times as many concepts by which a seizure can be described. When the research team used the new HPO to describe the seizures of 791 people with epilepsy, combining data from different studies, it provided nearly 40% more information than the previous version.

Consistent language

The central feature of the HPO is that it allows symptoms to be recorded and mapped out using terms with consistent meaning, making the most of the any descriptions available even when imprecise. This is essential when describing epileptic seizures as there are many different types and in some situations doctors cannot necessarily classify them to a high degree of detail.

After mapping their patient's symptoms onto the HPO, doctors can compare them to the symptoms seen in the range of potential diseases they are considering. This can help medics to select what genetic tests to do and improve interpretation of the test's results.

Lead author of the study, Dr. David Lewis-Smith is a Wellcome Trust Clinical Ph.D. Fellow at the Translational and Clinical Research Institute, Newcastle University, and a Specialist Registrar in neurology with Newcastle Hospitals NHS Foundation Trust.

He said: "We realized that whilst the HPO was becoming increasingly important for those people with epilepsy who might have a genetic cause, the representation of seizure types was inadequate.

"We formed an international team and spent two years arranging the current and historical expert classifications of seizures into a map that allows people's seizures to be compared precisely, even if described from different perspectives.

"This will help doctors to make genetic diagnoses for people with epilepsy, and researchers to make the most of data from large numbers of people with epilepsy, even reusing data from old studies, to discover new causes."

Genetic technology

Genetic technology has advanced at a pace that promises research breakthroughs through studies of thousands of people. However, current medical data is complex and difficult to fully exploit because of differences in terminology.

If doctors map their patients' symptoms to the HPO, computer algorithms can do the heavy lifting. They can use the map of the HPO to copy how experts compare seizure descriptions, but in larger numbers of people, allowing the experts to focus on interpreting the results to tease new genetic causes of epilepsy.

Dr. Rhys Thomas, Clinical Lecturer at Newcastle University and Honorary Consultant Neurologist, and author on the study explained the importance of the tool for digital medicine.

He said: "The next leap forward in the study of epilepsy will come from creating order out of the rich but complex data contained in medical records distilling the key features in a logical and ordered way so that we can benefit from the best of technological advances."

More information: David Lewis-Smith et al. Modeling seizures in the Human Phenotype Ontology according to contemporary ILAE concepts makes big phenotypic data tractable, *Epilepsia* (2021). DOI: 10.1111/epi.16908

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