Genetic risk scores can aid accurate diagnosis of epilepsy

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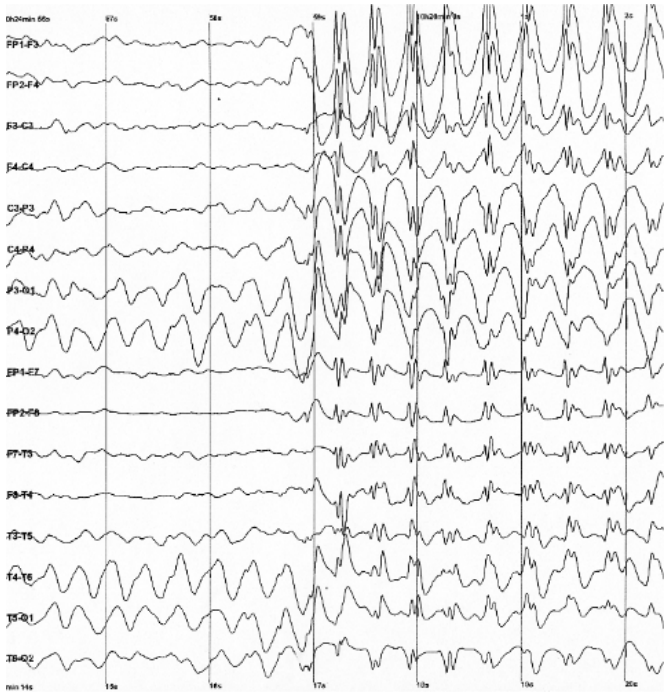

Generalized 3 Hz spike and wave discharges in a child with childhood absence epilepsy. Credit: Wikipedia.

Although epilepsy is a relatively common condition, affecting approximately 1% of individuals worldwide, it is often difficult to diagnose in clinical practice, and it is estimated that up to a quarter of all cases may be misdiagnosed initially. Epilepsy is often inherited, and recent research has shown that sufferers have elevated polygenic risk scores (PRSs) for the condition. Now, investigators from Finland have proposed that PRSs could be used as a tool to help diagnose epilepsy in those individuals who have had a single seizure and distinguish them from those where the seizure has another cause. The results will be presented at the annual conference of the European Society of Human Genetics today.

Together with other colleagues at the Institute for Molecular Medicine (FIMM), University of Helsinki, Finland, Henrike Heyne, MD (now working at the Hasso Plattner Institute, Potsdam, Germany) extracted data on 9660 individuals with epilepsy-related diagnoses from the over 269K people included in the FinnGen project and looked at their polygenic risk scores as compared to those of healthy controls. As expected, the individuals with epilepsy had a higher polygenic risk for the condition.

"In FinnGen we could also investigate the health records of participants who had suffered convulsions where the cause was unclear. Although some of them had later received a specific diagnosis of epilepsy, the majority had not. And we found that the genetic risk for epilepsy was significantly higher in individuals who received a specific epilepsy diagnosis than in those with only one seizure where the case was unclear," says Dr. Heyne.

Participants in the study ranged in age from a few months to over 90. In those under 40, the researchers found that the influence of the genetic factors was larger than in older individuals. This genetic influence was particularly high in those with adolescent myoclonic epilepsy, the type that made up the largest proportion of cases in the international epilepsy consortium used to identify which genetic variants convey highest risk to epilepsy. Although the sample size was relatively small, the results clearly showed the potential for the use of PRSs in the diagnosis of epilepsy, and the researchers hope to see them replicated in further studies with the larger sample sizes that are more usual in other common diseases such as high blood pressure or diabetes.

"Genetic risk could serve in future as a biomarker for epilepsy," says Dr. Heyne. "This could prove to be a very useful addition to existing methods, such as electroencephalograms. PRSs have been shown to be useful in many other diseases and it is

likely that in the future their use may become standard practice, meaning that genetic data could help to make an epilepsy diagnosis immediately after a seizure.

Chair of the ESHG conference, Professor Alexandre Reymond, Director of the Center for Integrative Genomics, University of Lausanne, Lausanne, Switzerland, said: "Genetic information often tells us whether a person is at increased risk to develop a disorder or not. In this study, the authors have pioneered the use of a genetic risk score to identify people at risk for epilepsy. Combining genetic data with other more traditional methods such as electroencephalograms could help identification of epileptic individuals, potentially allowing early treatment. Of note is that about 25% of epilepsy patients are under an effective regimen."

More information: Abstract no: PL2.6: Epilepsy polygenic risk scores in > 269k individuals with and without epilepsy

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