World's first genetic and environmental risks identified for common form of childhood epilepsy

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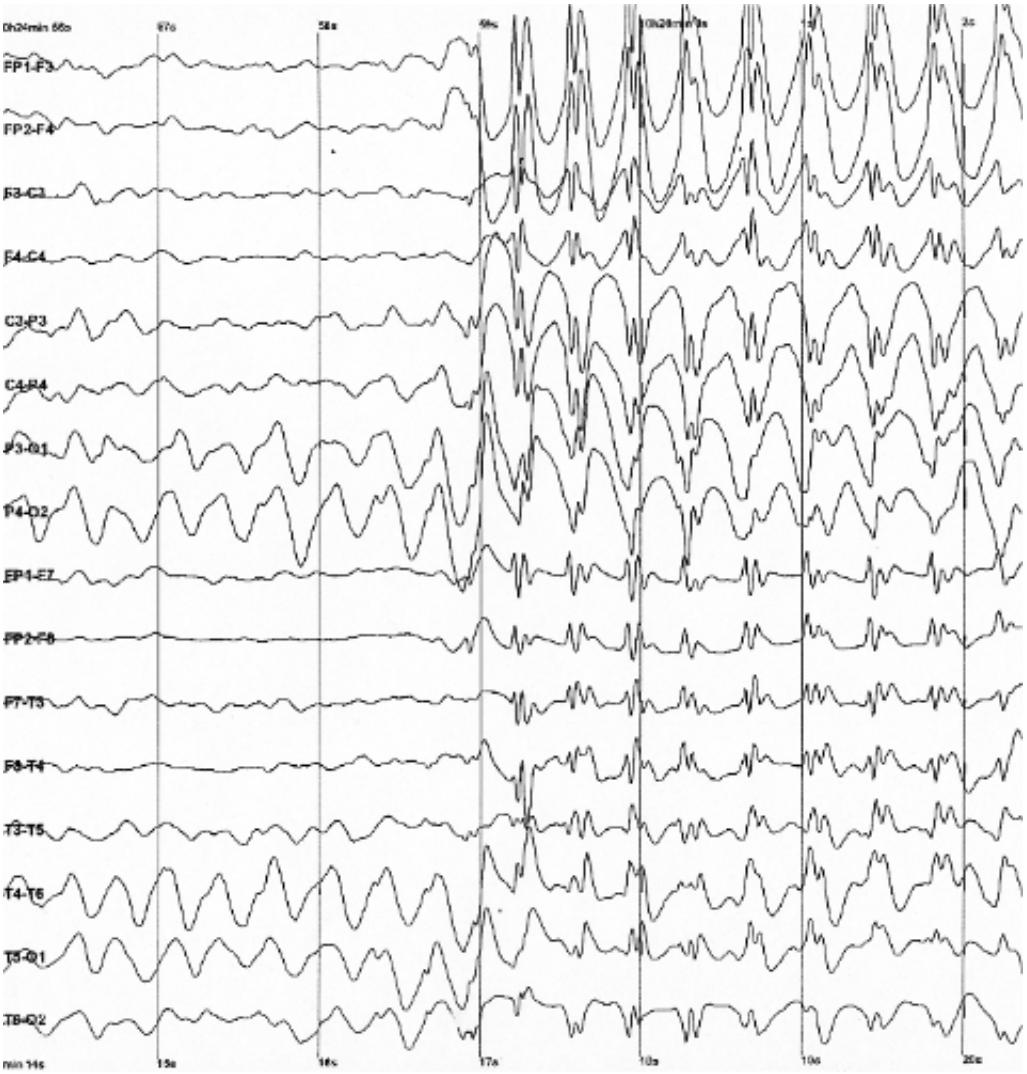

Generalized 3 Hz spike and wave discharges in a child with childhood absence epilepsy. Credit: Wikipedia.

A new study of childhood epilepsy has identified the world's first environmental risk factor for the disease—maternal smoking in pregnancy, and discovered a new genetic association with the condition, pointing to potential new treatments for the disease.

The research was led by an international team of clinicians and scientists including Professor Matt Brown, Professor of Medicine at King's College London and Director of the National Institute for Health Research Biomedical Research Centre at Guy's and St Thomas'.

The study focussed on one of the most common forms of childhood epilepsy, Benign Childhood Epilepsy with Centrotemporal Spikes (BECTS). Around 1% of children globally suffer with epilepsy with around 15% of those affected by BECTS. Driven by tendency for BECTS to run in families, previous research efforts focussed on identifying potential rare genetic mutations associated with the disease, but offered no robust evidence for the genetic association for the condition.

Unlike previous studies, the study team used genome wide complex trait analysis to examine and explain the most common type of genetic variations in people with BECTS.

This enabled the team to demonstrate that BECTS does indeed have a significant common genetic component, for the first time demonstrating that the reason that BECTS runs in families is because of genetic variants carried by patients. The study identified an association with a gene called CHRNA5 being involved in BECTS risk.

It is commonly known that genetic variations within the CHRNA5 and related genes are associated with nicotine dependence and smoking

associated lung disease. This along with suggestive evidence that smoking increases the risk of epilepsy overall led the team to perform analysis between risk factors and disease using summary-level data from independent genome-wide association studies from the UK Biobank. The analysis demonstrated that maternal smoking during pregnancy quadrupled the risk of BECTS. This is the first ever environmental risk factor identified for the disease.

Commenting on the findings Professor Matt Brown from King's College London said: "The new evidence in our study showing that common genetic variants play an important role in BECTS susceptibility opens up immense research possibilities to better understand how epilepsy is caused.

Maternal smoking in pregnancy being identified as the first ever environmental risk factor described in the development of BECTS offers a very clear message to clinicians and mothers about what can and should be done to limit the risk of children developing this common form of epilepsy."

He added: "With the association of the CHRNA5 gene which encodes a cholinergic receptor expressed in the brain involved in BECTS risk, our research also suggests that a class of drugs called 'anticholinergics' may be effective in the treatment of BECTS, however, further research into this is needed."

The study is published in *EBioMedicine*.

Provided by King's College London