New gene discovery unlocks mystery to epilepsy in infants

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(Medical Xpress) -- A team of Australian researchers has come a step closer to unlocking a mystery that causes epileptic seizures in babies.

Benign familial infantile epilepsy (BFIE) has been recognised for some time as infantile seizures, without fever, that run in families but the cause has so far eluded researchers. However clinical researchers at the University of Melbourne and Florey Neurosciences Institute and molecular geneticists at the University of South Australia have discovered a gene.

BFIE is a disorder that occurs in previously healthy infants who are developing normally. Seizures commence when a baby is about six months old and stop by the age of two years. BFIE is a rare form of epilepsy with the Australian researchers having studied about 40 families from around the world. Some of the children with this gene abnormality develop an unusual movement disorder later in childhood or adolescence called Paroxysmal Kinesigenic Choreoathetosis (PKC).

This movement disorder causes sudden, brief stiffening or twisting of their muscles as the person starts to move, for instance, people with this condition often have difficulty crossing the road when the traffic lights change to green. While this condition can be easily controlled by medication, it impacts on quality of life and may prevent people from participating in some activities.

Families with this condition have now been found to carry a variation in

a gene called PRRT2, which may cause the protein the gene encodes to form incorrectly. The function of this gene is not yet known nor is it understood how the changes in this gene cause an infant to have seizures. This gene discovery provides valuable opportunities for learning more about brain function and what causes seizures.

Professor Ingrid Scheffer, Chair of Paediatric Neurology Research said the finding would help families understand why their baby has seizures and will provide reassurance that the baby will grow out of the seizures and not have long term problems. It will also help with early diagnosis and appropriate treatment of the movement disorder.

The research was published on Friday, 13 January 2012 in the *American Journal of Human Genetics.*

More information: PRRT2 mutations cause Benign Familial Infantile Epilepsy (BFIE) and Infantile Convulsions with Choreoathetosis (ICCA) syndrome, *American Journal of Human Genetics.*

Abstract

Benign familial infantile epilepsy (BFIE) is a self-limited seizure disorder of infancy with autosomal dominant inheritance. We have identified heterozygous mutations in PRRT2, which encodes Proline Rich Transmembrane protein 2, in fourteen of seventeen families (82%) with BFIE, indicating that PRRT2 mutations are the most frequent cause of this disorder. We also report PRRT2 mutations in five of six (83%) families with Infantile Convulsions and Choreoathetosis (ICCA) syndrome, a familial syndrome in which infantile seizures and an adolescent onset movement disorder, paroxysmal kinesigenic choreoathetosis (PKC), co-occur. These findings show that mutations in PRRT2 causes both epilepsy and a movement disorder. Furthermore, PRRT2 mutations elicit pleiotropy both in terms of age of expression

(infantile versus later childhood) and in anatomical substrate (cortex versus basal ganglia).

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