Epilepsy halted in mice

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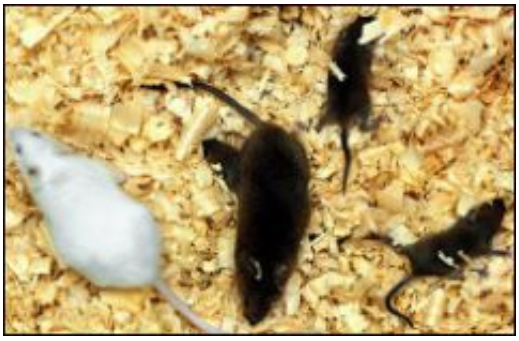

Scientists at Leeds have prevented epilepsy caused by a gene defect from being passed on to mice offspring - an achievement which may herald new therapies for people suffering from the condition.

The study is published today in the US journal Proceedings of the National Academy of Sciences (*PNAS*). It offers, for the first time, irrefutable proof that a faulty version of a gene known as Atp1a3 is responsible for causing epileptic seizures in mice.

Says lead researcher Dr Steve Clapcote, of the University of Leeds' Faculty of Biological Sciences: "Atp1a3 makes an enzyme called a sodium-potassium pump that regulates levels of sodium and potassium in the brain's nerve cells. An imbalance of sodium and potassium levels has long been suspected to lead to epileptic seizures, but our study is the first to show beyond any doubt that a defect in this gene is responsible."

Epilepsy is a common neurological condition that affects almost 1 in every 200 people, and yet the causes are unknown in the majority of cases. Current drug treatments are ineffective in around one third of epilepsy patients.

To prove the gene's role, the team studied a special strain of mouse, called Myshkin, which has an inherited form of severe epilepsy. The researchers found that these mice have a defective Atp1a3 gene, which led to them all having spontaneous seizures displaying the characteristic brain activity of epilepsy. To confirm that the seizures were epileptic, the team showed that mice treated with an antiepileptic drug, valproic acid, had fewer, less severe seizures.

When the epileptic Myshkin strain was bred with a transgenic mouse strain that has an extra copy of the normal Atp1a3 gene, the additional normal gene counteracted the faulty gene - resulting in offspring which were completely free from epilepsy.

"Our study has identified a new way in which epilepsy can be caused and prevented in mice, and therefore it may provide clues to potential causes, therapies and preventive measures in human epilepsy," says Dr Clapcote.

"Our results are very promising, but there's a long way to go before this research could yield new antiepileptic therapies. However, the human ATP1A3 gene matches the mouse version of the gene by more than 99 per cent, so we've already started to screen DNA samples from epilepsy patients to investigate whether ATP1A3 gene defects are involved the human condition."

Commenting on the research, Delphine van der Pauw, Research and Information Executive at Epilepsy Research UK said: "These results are promising. Not only have Dr Clapcote and his team highlighted a new culprit gene for epilepsy in mice; but they have also shown how normal

activity of the affected sodium-potassium pump can be restored. If the findings can be repeated in human studies, new avenues for the prevention and treatment of inherited epilepsy will be opened."

Source: University of Leeds (news : web)