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Scientists make epilepsy breakthrough

Epilepsy could be prevented from passing down through families which causes the condition, new research suggests.

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Scientists claim to have made a breakthrough in eradicating inherited epilepsy after managing to breed the defect out of epileptic mice by balancing "good" and "bad" genes.

It is hoped that the research will lead to new ways of preventing the disorder in humans.

Scientists at the University of Leeds studied a strain of mouse called Myshkin, which has an inherited form of severe epilepsy.

The mice had a defective version of the gene Atp1a3 which led them to suffer spontaneous seizures.

Mice treated with the anti-epilepsy drug valproic acid had fewer, less severe attacks.

When the Myshkin mice were bred with genetically engineered animals having an extra copy of the normal Atp1a3 gene, they produced healthy offspring completely free of epilepsy.

The additional normal gene counterbalanced the effect of the faulty gene, said the researchers writing in the journal Proceedings of the National Academy of Sciences.

Dr Steve Clapcote, who led the research, said: "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."

The human equivalent of the mouse gene matched it by more than 99 per cent, he said.

DNA samples from epilepsy patients are now being screened to see if they have defective versions of the gene.

The gene makes an enzyme that regulates levels of sodium and potassium in the brain.

An imbalance of the two elements has long been suspected as a cause of epileptic seizures.

Epilepsy affects almost one in 200 people in the UK yet the causes of it are unknown in the majority of cases. Drug treatments are ineffective for around a third of patients.

Simon Wigglesworth, deputy chief executive of the charity Epilepsy Action, said: "This is encouraging news, although it is too early to say whether this treatment will work for humans.

"At the moment there is no treatment to cure epilepsy, other than surgery, which is only effective for small numbers."

Delphine van der Pauw, research and information executive at Epilepsy Research UK said: "If the findings can be repeated in human studies, new avenues for the prevention and treatment of inherited epilepsy will be opened."

THE TIMES

Discovery of epilepsy gene is key to future treatment

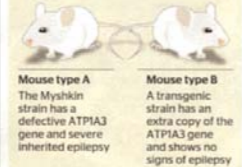
Flaw may predispose half of sufferers to disease

Hannah Devlin

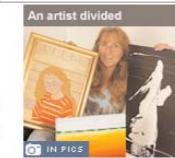
A genetic defect that could be responsible for up to half of all cases of epilepsy has been identified by scientists. In about 50 per cent of cases, the onset of epilepsy is linked with an obvious cause, such as a head injury, brain tumour or another neurological disease. In most other cases the condition is believed to have a genetic basis — but so far little progress has been made in identifying the genes responsible. The latest study, which is published today in the journal *PNAS* (Proceedings of the National Academy of Sciences), shows that a mutation in a gene called *ATP1A3* can lead to a severe form of epilepsy in mice. If the findings translate to human beings, they could pave the way for more effective treatments. The team behind the study has already begun screening a large archive of DNA samples from epileptic patients to ascertain whether the same genetic flaw predisposes people to the disease. They say that the 99 per cent match between the mouse and human versions of the gene means there is a good chance that it also plays a role in human epilepsy. In both species the gene is involved in regulating levels of sodium and potassium in the brain. Imbalances in these chemicals have already been linked with epilepsy in humans. In epilepsy sufferers, the brain is hyperexcitable, meaning that when stimulated there is a much bigger increase in neuronal firing than in a normal brain. Sodium and potassium affect how easily neurons fire. "It's equivalent to salty water conducting electricity better than tap water. When there's more sodium present in the brain, the conductivity of neurons increases and they fire more often," said Steve Clapcote, a neuroscientist from the University of Leeds, who led the study. The *ATP1A3* gene regulates the levels of sodium and potassium in the brain by producing an enzyme that works as a sodium-potassium pump. In a strain of mouse called Myshkin, which has been bred to have epilepsy, a defect in the *ATP1A3* gene means that an inactive version of the enzyme is produced, leading to sodium and potassium imbalances. As a consequence the mice have regular seizures. The study went a step further in isolating the cause of the epilepsy by cross-breeding the epileptic mice with normal mice that had been genetically engineered to have an extra copy of the *ATP1A3* gene, compensating for the resulting sodium-potassium imbalance. An imbalance of sodium 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," Dr Clapcote said. Epilepsy affects about 1 in 200 people in Britain. But despite being a relatively common condition, anti-convulsive medication — the most common treatment. One possibility would be to give patients a synthetic version of the sodium-potassium pump enzyme to help to regulate levels of these chemicals in their brain. Alternatively, drugs could be designed to stimulate the inactive enzyme. Designing specifically tailored drugs will be a long-range project, says

Curing epilepsy in mice

The *ATP1A3* gene makes an enzyme called a sodium-potassium pump that regulates levels of sodium and potassium in the brain's nerve cells.



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Gene study raises epilepsy hopes

Source PA News

Inherited epilepsy can be halted by silencing the gene responsible for its development, a study has shown.

Researchers bred the defect out of epileptic mice by balancing "good" and "bad" genes.

They hope the research will lead to new ways of preventing the disorder in humans.

Scientists at the University of Leeds studied an inherited form of severe epilepsy.

The mice had a defective version of the gene responsible for passing on the disorder.

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Fix for faulty gene may cure epilepsy

Test breakthrough in mice could provide clues to treatment for humans

By Kevin Rawlinson

Tuesday, 4 August 2009

Epilepsy sufferers have been given fresh hope that a cure may be found after scientists prevented the condition being passed on to mice offspring, in a breakthrough described as "very exciting" by epilepsy charities.

Scientists at Leeds University said they had proved that a faulty version of the gene which makes an enzyme called sodium-potassium pump is responsible for passing on the disorder.

The mice had a defective version of the gene, known as *ATP1A3*, which led them to suffer spontaneous seizures. The team behind the study has already begun screening a large archive of DNA samples from epileptic patients to ascertain whether the same genetic flaw predisposes people to the disease. They say that the 99 per cent match between the mouse and human versions of the gene means there is a good chance that it also plays a role in human epilepsy. In both species the gene is involved in regulating levels of sodium and potassium in the brain. Imbalances in these chemicals have already been linked with epilepsy in humans. In epilepsy sufferers, the brain is hyperexcitable, meaning that when stimulated there is a much bigger increase in neuronal firing than in a normal brain. Sodium and potassium affect how easily neurons fire. "It's equivalent to salty water conducting electricity better than tap water. When there's more sodium present in the brain, the conductivity of neurons increases and they fire more often," said Steve Clapcote, a neuroscientist from the University of Leeds, who led the study. The *ATP1A3* gene regulates the levels of sodium and potassium in the brain by producing an enzyme that works as a sodium-potassium pump. In a strain of mouse called Myshkin, which has been bred to have epilepsy, a defect in the *ATP1A3* gene means that an inactive version of the enzyme is produced, leading to sodium and potassium imbalances. As a consequence the mice have regular seizures. The study went a step further in isolating the cause of the epilepsy by cross-breeding the epileptic mice with normal mice that had been genetically engineered to have an extra copy of the *ATP1A3* gene, compensating for the resulting sodium-potassium imbalance. An imbalance of sodium 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," Dr Clapcote said. Epilepsy affects about 1 in 200 people in Britain. But despite being a relatively common condition, anti-convulsive medication — the most common treatment. One possibility would be to give patients a synthetic version of the sodium-potassium pump enzyme to help to regulate levels of these chemicals in their brain. Alternatively, drugs could be designed to stimulate the inactive enzyme. Designing specifically tailored drugs will be a long-range project, says

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THE INDEPENDENT

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The gene makes an enzyme that regulates levels of sodium and potassium in the brain.

Research has already begun on how the gene defects affect humans. "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," said Ms van der Pauw. However, she added that not all cases of epilepsy are caused by genetic disorders. "Epilepsy can be caused by brain trauma as well as a number of other things. But if it is shown that this is the cause of a lot of the cases in humans, then genetic screening should be made available on the NHS."

"Epilepsy is already quite low down on the Government's list of funding priorities and there is a stigma attached to the disease. Anything which helps remove that is good news."

Simon Wigglesworth, deputy chief executive of Epilepsy Action, agreed that while it was too early to say whether the treatment would work on humans, it was nevertheless "encouraging news."

He said: "At the moment there is no treatment to cure epilepsy, other than surgery, which is only effective for small numbers. Epilepsy Action welcomes any research which may have positive implications for people with epilepsy."

Current drug treatments are ineffective in around one third of epilepsy patients — an estimated 150,000 people in Britain.

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Integrity and sensitivity

With this potentially huge story, it was essential that the early-stage research findings weren't portrayed in the media as an imminent cure for epilepsy, no matter how exciting the discovery was. Pleasingly, the national and international coverage exemplified science journalism at its best, reporting the potential implications of the discovery rather than giving false hope to sufferers or their families.