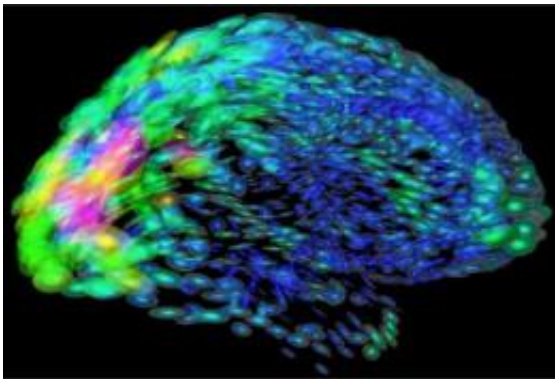


# Epileptic seizures may be linked to an ancient gene family

August 1 2010

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This is an artist's visualization of the human brain. New research points to a genetic route to understanding and treating epilepsy. Timothy Jegla, an assistant professor of biology at Penn State University, has identified an ancient gene family that plays a role in regulating the excitability of nerves within the brain. The research is scheduled to be published in the early online version of the journal *Nature Neuroscience* on Aug. 1, 2010. Credit: Arthur Toga, University of California at Los Angeles via the National Institute of General Medical Sciences

New research points to a genetic route to understanding and treating epilepsy. Timothy Jegla, an assistant professor of biology at Penn State University, has identified an ancient gene family that plays a role in regulating the excitability of nerves within the brain.

"In healthy people, nerves do not fire excessively in response to small stimuli. This function allows us to focus on what really matters. [Nerve](#)

[cells](#) maintain a threshold between rest and excitement, and a stimulus has to cross this threshold to cause the nerve cells to fire," Jegla explained. "However, when this threshold is set too low, neurons can become hyperactive and fire in synchrony. As excessive firing spreads across the brain, the result is an epileptic seizure."

Managing this delicate rest-excitement balance are [ion channels](#) -- neuronal "gates" that control the flow of electrical signals between cells. While sodium and [calcium channels](#) help to excite neurons, potassium channels help to suppress signaling between cells, increasing the threshold at which nerves fire. However, the genetic mechanisms that control the [potassium channels](#) and set this threshold are not fully understood. Jegla's team focused on a particular potassium-channel gene -- called Kv12.2 -- that is active in resting nerve cells and is expressed in [brain regions](#) prone to seizure. "We decided that Kv12.2 was a good candidate for study because it is part of an old gene family that has been conserved throughout animal evolution," Jegla said. "This ancient gene family probably first appeared in the genomes of sea-dwelling creatures prior to the Cambrian era about 542-million years ago. It is still with us and doing something very important in present-day animals." Previous studies have suggested that the Kv12.2 potassium channel has a role in spatial memory, but Jegla and his team focused on how it might be related to seizure disorders.

In collaboration with Jeffrey Noebels at Baylor College of Medicine, the team used an electroencephalography (EEG) device to monitor the brains of mice. They found that mice missing the Kv12.2 gene did indeed have frequent seizures, albeit without convulsions. The team then stimulated mice with a chemical that induces convulsive seizures. They found that normal mice had a much higher convulsive-seizure threshold than mice with a defective Kv12.2 gene. The team also found the same results when they used a chemical inhibitor to block the Kv12.2 potassium channel in normal mice.

"In mice without a functioning Kv12.2 gene, nerve cells had abnormally low firing thresholds. Even small stimuli caused seizures," Jegla explained. "We think that this potassium channel plays a role in the brain's ability to remain 'quiet' and to respond selectively to strong stimuli."

Jegla hopes to open up new avenues of epilepsy research by studying whether activation of the Kv12.2 potassium channel in normal animals can block seizures. "Ion-channel defects have been identified in inherited [seizure disorders](#), but many types of epilepsy don't have a genetic cause to begin with," Jegla explained. "They are often caused by environmental factors, such as a brain injury or a high fever. However, the most effective drugs used to treat epilepsy target ion channels. If we can learn more about how ion channels influence seizure thresholds, we should be able to develop better drugs with fewer side effects."

**More information:** The research results were published in *Nature Neuroscience*.

Provided by Pennsylvania State University

Citation: Epileptic seizures may be linked to an ancient gene family (2010, August 1) retrieved 18 April 2024 from <https://medicalxpress.com/news/2010-08-epileptic-seizures-linked-ancient-gene.html>

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