

Gene identified for sudden unexpected death in epilepsy

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The pair of traces shows 25 seconds of simultaneous brain and heart activity, as recorded by electroencephalography-electrocardiography, during a seizure in a mouse lacking Kv1.1 ion channels shortly before it suffered sudden death. As the seizure progresses, the regular cardiac rhythm disappears temporarily and the heart beats only intermittently. Credit: Courtesy, with permission: Glasscock et al. *The Journal of Neuroscience* 2010.

A mutation in a brain protein gene may trigger irregular heart beat and sudden death in people with epilepsy, according to new research in the April 14 issue of *The Journal of Neuroscience*. People with epilepsy who are otherwise healthy are more than 10 times more likely to die suddenly and unexpectedly than the general population.

Researchers have long suspected that abnormal ion channels in the brains of individuals that cause epilepsy also put them at risk for sudden unexplained death in epilepsy, or SUDEP, perhaps by harming the heart. An ion channel is a protein that lets charged particles enter or leave a cell to generate electrical signals, a basic process of nerve cell communication.

A team of neuroscientists, led by Jeffrey Noebels, MD, PhD, of the Department of Neurology, Baylor

College of Medicine, used an animal model to study a particular type of potassium ion channel called Kv1.1, which helps regulate electrical signals in the brain. In humans, mutation of the gene for Kv1.1 has been associated with spontaneous seizures, abnormal muscle movements, and motor coordination problems. Now Noebels and his colleagues have found that these channels are also required for proper [heart function](#).

In this study, they focused on Kv1.1 because studies have shown that mice without these channels show signs of severe epilepsy and involuntary movement, and they die prematurely. Noebels and his team investigated why the mice die and whether Kv1.1, in particular, is a possible factor for SUDEP.

The authors recorded [electrical signals](#) from the brains and hearts of mice bred to lack the gene for Kv1.1 channels to determine where and how the lethal abnormalities originated. The results showed that the hearts of the mutated mice skipped beats intermittently. When the mice had epileptic seizures, their heart beats became even more erratic — suggesting the signals from their brains to their hearts were disordered. The mice soon died after several episodes of cardiac arrest.

The researchers determined that in healthy animals these specific potassium channels are present in the brain and the vagus nerve, a bundle of axons that helps regulate cardiac rhythms, but are barely detectable in the heart. In the mutant mice, the brain signals sent to the heart through the vagus nerve were crippled.

"In mice without Kv1.1 channels, we think the vagus nerve loses control and sends extra nerve impulses to the heart, telling it to slow down — and even stop beating — when it shouldn't," said Edward Glasscock, PhD, first author of the study.

This potassium [ion channel](#) gene is the second

such gene found by the group to cause abnormal electrical activity leading to death in epilepsy. "Now that we are starting to grasp the genes and proteins underlying SUDEP, we can begin to predict and find ways to reduce the risk of death in patients with epilepsy," Noebels said.

Philip Schwartzkroin, PhD, of the University of California at Davis, who studies [epileptic seizures](#) and was unaffiliated with the study, said this new finding could be of considerable significance. "The potential association of this deficit with SUDEP provides insights that could lead to better treatments for at-risk patients," he said. "Such progress would be very important given that SUDEP accounts for a high proportion of deaths in epilepsy patients."

Schwartzkroin also pointed out that similar tests have yet to be tried for humans, and there may be multiple genes that contribute to SUDEP in different people.

Provided by Society for Neuroscience

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