Possible link between different forms of epilepsy found

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Carnegie Mellon University neuroscientists have identified what may be the first known common denominator underlying inherited and sporadic epilepsy — a disruption in an ion channel called the BK channel. Although BK channels have been linked to a rare, familial form of epilepsy, their involvement in other types of seizure disorders has never been demonstrated. These findings, published in the June issue of Neurobiology of Disease, indicate that BK channels are a new target for anticonvulsant therapies, and offer new hope to individuals suffering from epilepsy.

The researchers discovered that BK channels become abnormally active after a seizure. This disruption results in the neurons becoming overly excitable, which may be associated with the development of epilepsy. The Carnegie Mellon scientists were able to reverse this abnormal excitability using a BK channel antagonist, which returned the post-seizure electrical activity to normal levels.

"The fact that the BK channel previously has been linked with familial epilepsy and with generalized seizures in subjects without a genetic predisposition points to a common therapeutic pathway. We've shown that BK antagonists can be very effective in normalizing aberrant electrical activity in neurons, which suggests that BK channel antagonists might be a new weapon in the arsenal against epilepsy," said Alison Barth, an assistant professor of biological sciences at Carnegie Mellon's Mellon College of Science.

Epilepsy is a neurological disorder marked by abnormal electrical activity in the brain that leads to recurring seizures. According to the Epilepsy Foundation, no cause can be found in about seven out of 10 people with epilepsy. Researchers, however, have identified a genetic component in some types of epilepsy. This study establishes, for the first time, a shared component between different types of epilepsy.

"Although research has revealed that many types of inherited epilepsy are linked to mutations in different ion channels, there has been little overlap between these ion channels and those channels that are affected by sporadic or acquired forms of epilepsy," Barth said. "BK channels could represent a common pathway activated in familial and sporadic cases of epilepsy."

The BK channel allows electrically charged potassium ions into and out of cells. This activity starts and stops the electrical impulses by which neurons communicate with one another. Barth and her colleagues were specifically interested in investigating BK channels' function following a first seizure. Their in vitro studies revealed that, after a seizure, BK channel function was enhanced — neurons fired quicker, stronger and more spontaneously. This abnormal activity might underlie the transition between a single seizure and the emergence of epilepsy, characterized by recurrent seizures.

"We found that seizures caused cells to become more excitable, and that BK channel antagonists bring everything back to normal. These channels are at a nexus of control and represent a new target for anticonvulsant therapies," Barth said.

It is also possible that BK channel antagonists could be used early, perhaps after an initial seizure, to prevent cellular changes that lead to epilepsy, according to Barth.

Source: Carnegie Mellon University