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Study finds novel compound switches off epilepsy development

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Researchers at the LSU Health New Orleans Neuroscience Center of Excellence have found that a novel compound they discovered helps curtail the onset and progression of temporal lobe epilepsy. The finding, which may contribute to the development of anti-epileptic therapies, is published online in the journal *PLOS ONE*.

In temporal lobe epilepsy, seizures arise in the hippocampus and other structures of the limbic system located in the temporal lobe when a cascade of molecular and cellular events results in aberrant brain wiring. (The limbic system is the region of the brain associated with memory and emotions.) Seizures reflect uncontrolled electrical brain activity. The period between a brain injury and the onset of seizures, called epileptogenesis, is a "silent" period because this brain abnormality cannot be detected by current neurological exams or electroencephalography (EEG).

Temporal lobe epilepsy (TLE), or limbic epilepsy, is a common adult epileptic disorder characterized by spontaneous recurrent seizures that may also spread to other brain regions, triggering secondary severe generalized seizures. Aside from neurosurgery, which benefits only a small population of TLE patients, there are no other effective treatments or preventive strategies.

Working in a mouse model, the research team led by Drs. Nicolas Bazan, Boyd Professor and Director of the LSU Health New Orleans Neuroscience Center of Excellence, and Alberto Musto, Assistant

Professor of Research, Neurosurgery and Neuroscience, found that brief, small electrical microbursts, or microseizures, occur before the onset of clinical recurrent seizures. When they systemically administered Neuroprotectin D-1 (NPD1), the researchers discovered that NPD1 regulated these bursts of brain electrical activity that not only reduced the aberrant brain cell signaling leading to severe generalized seizures, but also spontaneous recurrent seizures. Neuroprotectin D-1, discovered in the Bazan lab, is derived from docosahexaenoic acid (DHA), an essential omega 3 fatty acid found in fish oil.

"We have searched for years to unravel the significance of the mechanism by which DHA is released in the brain at the onset of seizures," notes Dr. Bazan. Called the "Bazan Effect" in the literature, with the discovery of NDP1, another piece of the puzzle fell into place.

Epilepsy is a chronic neurological disorder characterized by recurrent seizures. It's estimated that 66 million people in the world have epilepsy. In the US, 1 in 26 people will develop epilepsy at some time during their lifetime. The incidence of epilepsy is higher in young children and older adults. Although the cause of epilepsy is unknown, there are some types of epilepsy associated with previous brain injury. Recurrent seizures might cause brain damage.

According to the Epilepsy Foundation, temporal lobe epilepsy is the most common form of partial or localization related epilepsy. It accounts for approximately 60% of all patients with epilepsy. The medial form accounts for almost 80% of all temporal lobe seizures. While medial temporal lobe epilepsy is a very common form of epilepsy, it is also frequently resistant to medications. The overall prognosis for patients with drug-resistant medial temporal lobe epilepsy includes a higher risk for memory and mood difficulties. This in turn leads to impairments in quality of life and an increased risk for death, as observed in patients who have frequent seizures failing to respond to treatment.

"These observations will contribute to our ability to predict epileptic events, define key modulators of brain circuits, especially after a brain injury, and provide potential biomarkers and therapeutic approaches for epileptogenesis," says Dr. Musto.

More information: *PLOS ONE*, journals.plos.org/plosone/arti … journal.pone.0116543

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