EPILEPSY MAY BE GENETICALLY LINKED TO NEURODEGENERATIVE DISORDERS

Mutations in prickle genes cause epilepsy, but the mechanism responsible for generating prickle-associated seizures was unknown.

A new University of Iowa study, published online in the *Proceedings of the National Academy of Sciences*, reveals a novel pathway in the pathophysiology of epilepsy. UI researchers have identified the basic cellular mechanism that goes awry in prickle mutant flies, leading to the epilepsy-like seizures.

"This is to our knowledge the first direct genetic evidence demonstrating that mutations in the fly version of a known human epilepsy gene produce seizures through altered vesicle transport," says John Manak, senior author and associate professor of biology in the College of Liberal Arts and Sciences and pediatrics in the Carver College of Medicine.

Manak and his fellow researchers show that seizure-prone prickle mutant flies have behavioral defects (such as uncoordinated gait) and electrophysiological defects (problems in the electrical properties of biological cells) similar to other fly mutants used to study seizures. The researchers also show that altering the balance of two forms of the prickle gene disrupts neural information flow and causes epilepsy.

Further, they demonstrate that reducing either of two motor proteins responsible for directional movement of vesicles (small organelles within a cell that contain biologically important molecules) along tracks of structural proteins in axons can suppress the seizures.

— PNAS 111: 3011187-11192

VIMPAT DATA PRESENTED AT THE EUROPEAN CONGRESS ON EPILEPTOLOGY

UCB showcased data from two studies evaluating the efficacy and safety of Vimpat® (lacosamide) as early adjunctive treatment in adults with partial-onset seizures. The results are presented this week at the 11th European Congress on Epileptology (ECE) in Stockholm, Sweden.

"The open-label and real-life data presented at ECE show that early adjunctive therapy with Vimpat can support patients with partial-onset seizures towards the goal of seizure freedom with manageable side effects." said Dr. Plamen Tzvetanov from the Military Medical Academy, Pleven, Bulgaria.

Results from an open-label study showed that lacosamide as first adjunctive therapy was efficacious in achieving seizure freedom and was well-tolerated in patients with uncontrolled partial-onset seizures. Final results from the VITOBA™ study showed that in clinical practice lacosamide improved partial-onset seizure control and was generally well-tolerated when used as adjunctive treatment to one baseline antiepileptic drug.

This open-label trial enrolled 456 patients with partial-onset seizures. Patients received lacosamide as first adjunctive therapy to a first monotherapy within 2 years of diagnosis, or as later add-on to 1-3 concomitant antiepileptic drugs, after 2 or more previous antiepileptic drugs, at ≥5 years since diagnosis. The primary efficacy variable was the proportion of patients achieving seizure freedom for the first 12 weeks of the 24-week maintenance phase.
Of the 333 patients who completed 12 weeks' treatment, 19.8 percent were seizure-free. Among 96 patients who received lacosamide as first add-on, 72 completed 12 weeks' treatment and 68 patients completed 24 weeks. 37.5 percent of patients who completed 12-weeks' treatment and 26.5 percent of patients who completed 24-weeks' treatment were seizure-free for the respective treatment periods.

Among 360 patients who received lacosamide as later add-on, 261 completed 12 weeks' treatment and 249 completed 24 weeks. 14.9 percent of patients who completed 12-weeks' treatment and 11.6 percent of patients who completed 24-weeks' treatment were seizure-free for the respective treatment periods.

ZEBINIX DATA PRESENTED

The results of an interim analysis of the non-interventional EPOS (Eslicarbazepine acetate in Partial-Onset

Seizure) study presented at the XXI European Congress on Epileptology (ECE) in Stockholm, Sweden, show that once-daily Zebinix (eslicarbazepine acetate) is effective, retained and well-tolerated when given as an add-on to antiepileptic monotherapy to adults in routine clinical practice. Eslicarbazepine acetate, a novel anti-epilepsy treatment for adult individuals with partial epilepsy, targets sodium channels, stabilizing their inactive state. It is indicated as adjunctive therapy in adults with partial onset seizures, with or without secondary generalization.

The interim analysis reviewed data from 109 adults (mean age 45.3±16.5 years; 59.6% male) with uncontrolled partial onset seizure under antiepileptic monotherapy for whom the physician had independently decided to initiate add-on treatment with eslicarbazepine acetate. The mean eslicarbazepine acetate daily dose after titration was 907.1mg±300.0 mg. Levetiracetam (32.1 percent) and lamotrigine (23.9 percent) were the most frequently preferred combination treatments.

At six-months, the eslicarbazepine acetate retention rate was 82.6 percent, with seizure freedom reported over the same period by 47.8 percent of patients. Adverse events occurred in 29 people during the observation period. The most frequently reported adverse events were dizziness (6.4 percent), headache (5.5 percent) and fatigue (4.6 percent).

PROTEIN S100B MAY TRIGGER BRAIN-DAMAGING IMMUNE RESPONSE

The body's own immune system might play a role in memory impairment and cognitive dysfunction associated with conditions like chronic epilepsy, Alzheimer's dementia and concussions, Cleveland Clinic researchers believe, based on a study published online by PLoS ONE.

The study focuses on the role of a protein known as S100B, which serves as a biomarker for brain damage. Normally, S100B is found only in the brain and spinal column. However, following a brain injury, it can leak through the blood-brain barrier into the blood.

Once S100B enters the bloodstream, it is identified as an intruder by the immune system, which releases antibodies to attack the protein.

"Our results show an unexpected role for S100B in the regulation of a neuro-immune response, connecting the function of the brain to the immune system," said Damir Janigro, Ph.D., senior author and molecular medicine researcher at Cleveland Clinic's Lerner Research Institute. "Uptake of S100B was prominent in cells that are known to be involved in regulating immune responses. Repeated increases of S100B—whether due to epileptic seizures, Alzheimer's disease, or repeated hits to the head in sporting events—may thus become boosters of an autoimmune response against the brain, which may slowly but inexorably result in chronic neurological disease."

These findings are the first to report a connection between a brain-derived protein and an immune response in the context of normal immunological function.

— PLoS ONE 9(7): e101477.

RESEARCH LINKS ANXIETY AND SEIZURES

New research by clinical psychologists from Arizona State University and the United Kingdom has revealed seizures that could be mistaken for epilepsy are linked to feelings of anxiety.

The team of researchers devised a new set of tests to determine whether there was a link between how people interpret and respond to anxiety, and incidences of psychogenic nonepileptic seizures (PNES).

The researchers used a series of questionnaires and computer tests to determine if a patient regularly avoids situations which might bring on anxiety.

These tests correctly predicted whether a patient had epilepsy or PNES—seizures that can be brought on by threatening situations, sensations, emotions, thoughts or memories—in 83 percent of study participants. Such seizures appear on the surface to be similar to epileptic fits, which are caused by abnormal brain activity.

Participants completed questionnaires to determine the level to which they suffered from anxiety, their awareness of their experiences and if they would avoid situations which would make them feel anxious.

They then completed a computer task, which required rapid responses to true or false statements. This test was designed to gather data on immediate, or implicit, beliefs about anxiety. Participants also answered questions about common physical complaints that may have no medical explanation, also called somatic symptoms. These can include things like gastrointestinal problems, tiredness and back pain.

Results showed that those with PNES reported significantly more somatic symptoms than others in the study, as well as avoidance of situations that might make them anxious. The group with PNES also scored significantly higher on a measure of how aware they were of their anxiety compared with the control group.

The test subjects were 30 adults with PNES, 25 with epilepsy and 31 with no reported history of seizures who served as a nonclinical control group.

The researchers suggest that including tests to determine levels of anxiety and avoidance behavior may enable health professionals to make earlier diagnosis, and develop more effective intervention plans. ■

— Epilepsy & Behavior (30):43–49