SOUTHWESTERN NEWS

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INHERITED GENE MAY PLACE SOME AT HIGHER RISK OF POST-TRAUMATIC INJURY SEIZURES

DALLAS – June 16, 2003 – People who inherit a particular gene involved in lipid metabolism in the brain appear to be at higher risk of developing seizures after traumatic brain injury, according to researchers at UT Southwestern Medical Center at Dallas.

A study published in the June issue of *Archives of Neurology* found that patients with moderate to severe brain injuries who had inherited the *epsilon 4* variation of the *apolipoprotein E* (*apoE*) gene were 2.41 times more likely to develop seizures than patients without the gene.

The finding sheds new light on the pathophysiology of post-traumatic epilepsy and may lead to new therapies that could prevent brain-injury patients from developing seizures, said Dr. Ramon Diaz-Arrastia, associate professor of neurology at UT Southwestern and lead author of the paper.

"Post-traumatic epilepsy is a common and frequently disabling complication of traumatic brain injury, for which there is no effective prophylactic therapy," Dr. Diaz-Arrastia said. "What this finding indicates is that if we learn to manipulate aspects of lipid or lipoprotein metabolism in the brain we may be able to develop therapies to prevent post-traumatic epilepsy."

Approximately 20 percent to 25 percent of patients with moderate to severe brain injury – such as injuries sustained during a car crash – develop epilepsy.

"After the injury, there is rewiring and sprouting of the nerve cells," Dr. Diaz-Arrastia said. "That is often a good thing, because it allows recovery. It can also be bad if that rewiring results in a circuit that is, in a sense, misfiring."

Researchers obtained information on 106 patients with diagnoses of moderate or severe brain injury who were admitted to the neurological surgery service at Parkland Memorial Hospital. The patients were evaluated six months after admittance to determine the outcome

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of their injuries. Scientists also obtained DNA samples to determine which variation of the *apoE* gene was present in each patient.

Of the 106 patients, 29 had the *epsilon 4* variation of *apoE,* and 77 did not. Of the *apoE* carriers, 34 percent had post-traumatic seizures, while only 14 percent of those without the gene had seizures.

ApoE first came to the attention of neurologists in 1993 when it was found to be associated with an increased risk of developing Alzheimer's disease. Since then, the gene, which is the major lipid-carrying protein in the central nervous system, has been linked to the development of dementia in boxers following chronic concussive injury, faster progression to disability in multiple-sclerosis patients and poor outcome after traumatic brain injury.

"We were interested in a complication of brain injury that had not been explored in previous studies – the development of post-traumatic epilepsy," Dr. Diaz-Arrastia said.

Dr. Paul Van Ness, associate professor of neurology at UT Southwestern, is senior author of the study. Other contributing authors from UT Southwestern are Dr. Yun-Hua Gong, senior research associate in neurology, Dr. Maria Garcia, postdoctoral fellow, and Dr. Mark Agostini, assistant professor of neurology. Also contributing was Dr. Mary C. Carlile from the Baylor Institute for Rehabilitation in Dallas, where some patients received rehabilitative care.

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