

How brain injury leads to seizures, memory problems

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In a finding that may provide a scientific basis for eventual treatment, neurology researchers have shown that traumatic brain injury reduces the level of a protein that helps keep brain activity in balance. The resulting abnormal activity, in turn, is thought to be an underlying reason for seizures and memory defects experienced by people who have suffered a traumatic brain injury (TBI).

"A traumatic brain injury occurs to someone in the United States every 23 seconds," said study team leader Akiva S. Cohen, Ph.D., of The Children's Hospital of Philadelphia, adding that, "TBI is the leading cause of death among children and young adults in this country. There are no cures known for traumatic brain injury. Our hope is that our research may contribute to potential therapies for TBI patients."

Transportation accidents such as car crashes are responsible for the majority of TBIs in people under age 75. According to the National Institutes of Health, over 5 million Americans currently have permanent disabilities resulting from TBIs.

The study, which was done in animals, appears in the journal *Neurobiology of Disease*, published online on Oct. 10.

Using mice, the researchers showed for the first time that TBI reduces the levels of a protein called potassium-chloride co-transporter 2 (KCC2) within a portion of the brain called the dentate gyrus. The dentate gyrus controls overactivity from reaching seizure-prone brain

cells further along the circuit.

The dentate gyrus is a gatekeeper in maintaining a balance between two systems of neurotransmitters in the brain: the glutamate system and the gamma-aminobutyric acid system, abbreviated GABA(A). Glutamate stimulates neurons to fire, while GABA(A) inhibits that activity. "When lower levels of the KCC2 transporter weaken the dentate gyrus's ability to act as a gatekeeper," said Dr. Cohen, "neurons become more excitable, and seizures can occur."

In addition to its role in inhibiting seizures, the dentate gyrus is also believed to be important in memory formation. Therefore, said Dr. Cohen, "Interfering with normal function in the dentate gyrus may impair memory formation--especially antegrade memory, the ability to learn new things." Epileptic seizures and impaired memory are two of the disabilities caused by TBI.

Further animal studies, said Dr. Cohen, will investigate whether supplying KCC2 directly to the dentate gyrus will restore normal functioning in that structure, and whether it may improve symptoms in brain-injured mice. If this proves to be the case, the protein may someday be used as a medical treatment for patients with TBI.

Source: Children's Hospital of Philadelphia

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