

Researchers Explore Genetic Basis of Early Childhood Epilepsies

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SEATTLE, December 6, 2014 – Technological advances in genetic analysis have uncovered changes in single genes that account for a surprising number of infantile and early-childhood epilepsies. Though some of the affected genes have been identified, the physical manifestations of these alterations remain largely uncharacterized. A pair of studies to be presented at the American Epilepsy Society's (AES) 68th Annual Meeting provides innovative insights into the genetic underpinnings of childhood epilepsies.

A study (Poster 1.105) by researchers at the Nishi-Niigata Chuo National Hospital in Niigata, Japan describes a host of genetic, physical, and clinical features associated with *SPTAN1* mutations, which have been implicated in epilepsies of early infancy.

“This study could facilitate the rapid diagnosis of *SPTAN1*-related disorders,” says Jun Tohyama, MD, a director of the Epilepsy Center and Pediatrics at the Nishi-Niigata Chuo National Hospital in Niigata, Japan. “Knowledge of clinical profiles and MRI features in *SPTAN1* encephalopathy will help clinicians perform the proper diagnostic work-up.”

The authors obtained clinical histories, neurological examinations, and neurophysiological and neuroradiological data from seven patients with epilepsy and *SPTAN1* mutations. Their findings link mutations in the *SPTAN1* gene, which encodes α -II spectrin, with a distinctive phenotype: intractable infantile spasms accompanied by abnormal brain activity between seizures, lack of visual attention, development of an abnormally small head, severe brain atrophy, spastic quadriplegia, and severe intellectual disability. These phenotypes appear to result from mutations in a specific portion of the *SPTAN1* coding sequence, and preliminary findings indicate that the location of the mutation could potentially predict disease severity.

“Known Spectrin-related disorders include spherocytosis caused by *SPTA1* and *SPTB* mutations and spinocerebellar ataxia type 5 or Lincoln ataxia caused by *SPTBN2* mutations. *SPTAN1* encephalopathy may be a new clinical syndrome with specific genotypes. More patients are needed to clarify the possible correlation between the location of the mutation and disease severity, but understanding this relationship could be of great value in identifying molecules directly involved in clinical phenotypes and in providing new targets for drug discovery,” says Dr. Tohyama.

In a second study (Platform Session C.06), researchers from The Children's Hospital of Philadelphia and The University of Pennsylvania investigate the connections between epilepsy and genetic aberrations on the X chromosome; such aberrations are thought to underlie approximately 1 in 10 cases of intellectual disability and are frequently accompanied by epilepsy.

The authors unveil a novel mouse model of chromosome Xq22.1 deletion syndrome, a human disease characterized by developmental delay, intellectual disability, epilepsy, dysmorphic features, and an X-linked pattern of inheritance. The findings suggest that the epilepsy component of this syndrome may stem from faulty protein transport in the cell, which in turn may overexcite brain networks in the cerebral cortex.

“Although Xq22.1 deletion syndrome is likely a rare cause of epilepsy in our patient population, this mouse model offers an opportunity to investigate mechanisms of epilepsy that may be more generalizable. The genes involved encode proteins that control the activity of a very important and ubiquitous class of molecules that are a major target of pharmacologic agents across medicine,” says Ethan Goldberg, MD, PhD, an attending physician and instructor of neurology at the Children’s Hospital of Philadelphia and The Perelman School of Medicine at The University of Pennsylvania.

Both research studies will be provided in full at the American Epilepsy Society Annual Meeting in Seattle, December 5-9. Abstracts referenced above can be found on the American Epilepsy Society’s [Annual Meeting Page](#).

Editor’s Note: Authors of these studies will be available at a press briefing on **December 6, 2014 at 2:15 PM (PT)/ 5:15 PM (ET)**, in the onsite press room, Room 304, Level 3 of the Washington State Convention Center. The call-in number for off-site journalists is 1-605-475-4000, passcode 521653#.

About the American Epilepsy Society

The American Epilepsy Society (AES) is a non-profit medical and scientific society. Our individual members are professionals engaged in both research and clinical care for people with epilepsy from private practice, academia and government. For more than 75 years, AES has been unlocking the potential of the clinical and research community by creating a dynamic global forum where professionals can share, learn and grow. AES champions the use of sound science and clinical care through the exchange of knowledge, by providing education and by furthering the advancement of the profession.

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