



New Issue of *Epilepsy Currents* highlights the utility of genetic testing in epileptic encephalopathies, genetic generalized epilepsies and in epilepsy of infancy with migrating focal seizures, a novel mechanism of childhood absence epilepsy and preferential GABAergic neuron recruitment during interictal spikes.

CHICAGO, February 2, 2016 – The latest issue of *Epilepsy Currents* is now available featuring expert commentary on articles in basic and clinical science. Here are the editor's highlights from the latest issue of *Epilepsy Currents* Vol. 16, no. 1:

- **The utility of genetic testing in epileptic encephalopathy**
Epileptic encephalopathy is characterized by abnormal EEG, refractory seizures, behavioral and neurological deficits. Diagnosis involves history, physical exam, imaging and electroencephalography which may be followed by biochemical and genetic analyses. Genetic testing can hasten treatment, but is also associated with higher costs. A 2015 study in *Epilepsia* by Mercimek-Mahmutoglu and colleagues examined the diagnostic yield of genetic testing by doing a retrospective chart review of children with suspected epileptic encephalopathy. In a Commentary, Scott Perry, MD remarks that genetic testing combining inherited metabolic disorders and other genetic causes of epileptic encephalopathy had the greatest diagnostic yield. He suggests that it might be worthwhile considering genetic testing at presentation rather than at the end.
- **Microdeletions in genetic generalized epilepsies**
Given that the genomic variants involved in genetic generalized epilepsy are not fully understood, a 2015 study in *PLoS Genet* by Lal and colleagues investigated whether copy number variants (deletions or duplications of a stretch of chromosomal DNA) could be a risk factor for genetic generalized epilepsy. A Commentary by Huong Ha, BS and John Huguenard, PhD examines the findings and make recommendations for clinical practice. Microdeletions in genes implicated in neurodevelopmental disorders like autism and intellectual disability are more common in genetic generalized epilepsy than controls, suggesting a common neurobiological mechanism. Huong and Huguenard suggest that based on this study, individuals with genetic generalized epilepsy with comorbid neurodevelopmental conditions or with a family history for such conditions should be tested for microdeletions.
- **Novel genes discovered in epilepsy of infancy with migrating focal seizures**
Epilepsy of infancy with migrating focal seizures is characterized by electrographic seizures in multiple areas of onset. Two studies published in 2015 examined novel genes - Stöberg and colleagues in *Nat Commun* found SLC12A5, and Howell and colleagues in *Neurology* found SCN2A to be implicated in this syndrome. A Commentary by Jennifer A. Kearney, PhD summarizes these studies and gives guidance for clinical practice. SLC12A5 codes for the potassium- chloride co-transporter KCC2; a loss of function of KCC2 may result in depolarizing effects of GABA and hyperexcitability. Some subjects had SCN2A mutation and they benefitted from phenytoin – a sodium channel blocker. Kearney suggests that subjects with epilepsy of infancy with migrating focal seizures should be screened for SLC12A5 and SNC2A to better guide treatment.

- **A novel mechanism for childhood absence epilepsy**

CaV3.2 channels are implicated in childhood absence epilepsy, but how Cav3.2 channels cause or influence seizures is not known. In a 2015 study published in *Genes Dev*, Wang and colleagues used a variety of tools to investigate this. A Commentary by Huong Ha, BS and John Huguenard, PhD explains that by inducing local calcium influx, Cav3.2 channels control glutamatergic neurotransmission, and inserting mutant CaV3.2 channels into cortex of rats induces spikes suggestive of absence epilepsy. This direct link between CaV3.2 channels and glutamatergic transmission could lead to chronic remodeling of synapses and ultimately epilepsy. Huong and Huguenard suggest given the role of glutamatergic neurotransmission in cognition, the study will allow us to better understand the effect of seizures on cognition.

- **Role of GABAergic signaling in interictal spikes**

Interictal spikes are transient electrographic events that occur between seizures but the mechanisms underlying these events are still a mystery. A 2015 study by Muldoon and colleagues in *Brain* investigated the contribution of the GABAergic system in generation of interictal spikes. In a Commentary, Archana Proddutur, MS and Viji Santhakumar, MBBS, PhD probe into the findings, and find a preferential recruitment of GABAergic neurons as opposed to glutamatergic neurons during an interictal spike. They remark contrary to previous studies that suggested a collapse of GABAergic inhibition, this study shows a preferential recruitment of the GABAergic system during an interictal spike. They suggest that studies investigating specific interneuron class involved should be undertaken.

Epilepsy Currents is a literature surveillance publication, including brief expert commentary on research articles in basic and clinical science selected by the editorial board. The journal is available online to AES members and non-members.

About the American Epilepsy Society

The American Epilepsy Society is a medical and scientific society whose members are professionals from private practice, academia and government engaged in both research and clinical care for people with epilepsy. 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. For additional information, visit aesnet.org.

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