SEIZURE DISORDERS

MECHANISM OF SEIZURE TERMINATION

Physiological mechanisms contributing to seizure termination and organized according to membranes, synapses, networks, and circuits are reviewed by researchers from Albert Einstein College of Medicine, and Montefiore Medical Center, Bronx, New York. A better understanding of these mechanisms may lead to novel anticonvulsant therapies. Agents that enhance termination of paroxysmal depolarizing shifts might decrease excitatory amplification in epileptic neurons. Modification of extracellular environment or intracellular ion gradients across membranes may raise seizure threshold and speed seizure termination (Ochoa, 2006). Disrupting gap junction connections between neurons and interneurons may reduce neuronal synchrony. Drugs targeting the GABA receptor to enhance local inhibition without increasing sedation or tachyphylaxis would provide an improvement over benzodiazepines that are of value mainly in acute seizure control. Drugs that alter chloride transporters and gradients might control age-dependent seizure syndromes. (Dzhala et al, 2005). Drugs targeting adenosine kinase, and endocannibanoid and NPY receptors, and altering the hormonal milieu may enhance seizure control and termination. Vagal nerve stimulation (Blount JP et al. 2006), initiated by a patient, will halt seizure activity and may be extended to seizure modifying circuits such as the anterior thalamus, substantia nigra pars reticulata and subthalamic nucleus. Implantable drug infusions systems to regulate seizure onset are a transmeningeal form of therapy under consideration. (Ludvig et al, 2006). (Lado FA, Moshe SL. How do seizures stop? **Epilepsia** Oct 2008;49(10):1651-1664). (Respond: Dr Fred A Lado, EEG Laboratory, Montefiore Medical Center, 111 E 210 St, Bronx, NY 10461. E-mail: flado@montefiore.org).

COMMENT. Factors influencing seizure termination are less well understood than those responsible for seizure initiation, propagation and recurrence. Several factors may be responsible for seizure initiation and termination, and these mechanisms may be modified by age, sex, fever and infection, structural brain injury, and genetics. Mechanisms that operate in the normal brain may be different from those affecting the diseased or epileptic brain. Children with a history of status epilepticus are likely to have status epilepticus with a seizure recurrence. Neuron excitability may be influenced by the extracellular environment, gap junctions, neuromodulators, and circuits. Sites of action of seizure terminating mechanisms include substantia nigra pars reticulata, subthalamic nucleus, superior colliculus, thalamus, and reticular activating system.

CDKL5 MUTATIONS IN BOYS WITH ENCEPHALOPATHY AND EARLY-ONSET INTRACTABLE EPILEPSY

Clinical and EEG data of 3 Italian boys (ages 3, 9, and 13 years) with severe early-onset encephalopathy, mental retardation, facial dysmorphisms, and intractable epilepsy were found to carry missense mutations in the *CDKL5* gene, in a report from Troina, Italy. Seizures were myoclonic, tonic, and partial or spasms, and the EEG abnormalities were multifocal epileptiform discharges while awake and pseudoperiodic bisynchronous