

Partnership for Pediatric Epilepsy Research

Meritorious Research 2010- \$50,000 each

Mathew Jones, Ph.D.

Associate Professor

University of Wisconsin-Madison Madison, WI, United States

Application Title:

Mechanisms of Childhood Absence Epilepsy in GEFS+ Knock-in Mice

General Audience Summary:

The overall goal of this research is to understand the precise sequence of events in the brain that cause seizures in Childhood Absence Epilepsy (CAE). Absence seizures are pathological reverberations between the thalamus and cortex. To understand the sequence of events that generate a seizure, we will use a mouse brain slice preparation that preserves the thalamocortical loop, and use multi-electrode arrays to record the simultaneous activity of 30-50 cells. We will evaluate the excitability and specific patterns of thalamocortical communication and compare these between normal mice and mice genetically engineered to express a human CAE gene. These studies will reveal how malfunctions in thalamocortical signal processing can give rise to pathological rhythms, and will suggest ways to predict, and ideally to prevent, absence seizures.

Andre Lagrange, M.D. Ph.D.

Assistant Professor

Vanderbilt University Medical Center

Nashville, TN, United States

Application Title:

Regulation of Neuronal Development by RNA Editing of GABA-A Receptors

General Audience Summary:

GABA is a major developmental signal in embryonic brain, but is also the primary inhibitory neurotransmitter in adult brain. RNA editing produces a developmentally regulated change in the protein sequence of a major isoform of the GABA(A) receptor. Based on the spatial and temporal expression patterns of this isoform, it likely plays important roles in normal development, as well as a number of normal and pathophysiological processes, such as sleep and epilepsy

Yogendra H Raol, Ph.D.

Assistant Professor

University of Colorado Denver

Aurora, CO, United States

Application Title:

Potassium channel opener for the treatment of neonatal seizures

General Audience Summary:

The risk of seizures is highest in the neonatal period and survivors often experience long-term neurological problems. Currently available drugs are poorly effective in treating neonatal seizures and are associated with side effects. Recent research studies suggest significant differences between developing and mature brain that could provide better targets for treatment that is specifically designed to treat seizures that occur during development. Here we propose to study the efficacy of flupirtine, a potassium channel opener that may be uniquely effective for the treatment of neonatal seizures due to the important role potassium channels play in controlling brain excitability during early-life.

Santina Agnes Zanelli, M.D.
Assistant Professor of Pediatrics
University of Virginia
Charlottesville, VA, United States

General Audience Summary:

One of the most devastating problems babies can encounter around the time of birth is oxygen deprivation to the brain. This disorder, called hypoxic-ischemic encephalopathy, can affect 1 to 2 per 1000 newborns. It is the single most important cause of brain injury and seizures in the neonatal period. Affected babies sometime die and the survivors can have severe long-term disabilities including seizures. Understanding how lack of oxygen injures the baby's brain and leads to seizures is essential for the development of effective treatments for this condition. Our studies indicate that a potassium channel may be involved in this phenomenon. In this work we are planning to test whether this channel represent a possible novel therapeutic target for the treatment of seizures caused by lack of oxygen in newborns. This will represent an important step towards developing more effective treatments to improve the outcomes of newborns with hypoxic-ischemic encephalopathy and resulting seizures.