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EPILEPSY FOUNDATION
GREATER LOS ANGELES

Epilepsy Research Projects in Los Angeles Area being Supported by the Epilepsy Foundation of Greater Los Angeles

Eduardo Adonay Pineda, Ph.D.
Postdoctoral Fellow
University of California, Los Angeles

Title:

Long-Term Effects of Seizures in the Presence of Pre-Existing Inflammation

Postdoctoral Research & Training Fellowship

Award Amount: \$45,000 for one year

General Audience Summary:

The proposal examines the role of inflammation of the brain that occurs early in life, in the development of epilepsy. Using an animal model of epilepsy, we will study whether inflammation that coincides with early-life seizures exacerbates the course of epilepsy at an older age, and whether the use of anti-inflammatory drugs will prevent or alleviate the development of epilepsy. Our studies will be useful for the development of effective treatments for chronic epilepsy.

Technical Summary:

This proposal examines the long-term impact of neuroinflammation that coincides with early-life status epilepticus (SE). Immature rats will be administered lipopolysaccharide (LPS) and SE will be induced by pilocarpine 2 hr later. After weaning, they will undergo video/EEG monitoring for spontaneous seizures. Thereafter, sections of the hippocampus will be processed for both neuronal cell loss and dentate gyrus synaptic reorganization. In separate experiments, we will examine the effects of treatment with anti-inflammatory drugs on the long-term outcomes of LPS+SE. These animals will be injected with a combination of a selective Cyclooxygenase-2 inhibitor and a selective endogenous antagonist of interleukin-1 receptors and studied as described above. We hypothesize that the introduction of neuroinflammation in the early life SE will accelerate the onset and exacerbate the severity of epilepsy, will increase the extent of neuronal cell loss and promote synaptic reorganization in the hippocampus. At the same time, the anti-inflammatory therapy is expected to mitigate epilepsy, increase neuronal survival and hamper mossy fiber sprouting. If successful, our studies will contribute to the development of antiepileptogenic or disease-modifying strategies in the treatment of epilepsy which stems from precipitating epileptogenic insults with inflammatory components, such as prolonged febrile seizures or traumatic brain injury.

Zulfi Haneef, M.D.
Clinical Fellow in Epilepsy
University of California, Los Angeles

Title:

fMRI Identification of the Epileptic Network

Research & Training Fellowship for Clinicians

Award Amount: \$50,000 for one year

General Audience Summary:

This project studies the anatomy of epileptic networks with an aim to improve the results of brain surgery for epilepsy treatment. The epileptic network will be identified by using functional MRI (fMRI) to detect brain areas with activity that is similar to a known part of the network. This technique has previously identified brain networks for memory, language and movement. The visual images of the network will be more anatomically complete than those that are created using electrical signal changes.

Technical Summary:

Epilepsy surgery remains the most effective treatment for medication refractory temporal lobe epilepsy. However, outcomes are sometimes worse than predicted because the epileptogenic zone (EZ) is not identical to the ictal-onset zone or epileptogenic lesion identified by electroencephalography and imaging. One viewpoint holds that an underlying epileptogenic network (EN) forms the functional basis of EZ. Though intracranial EEG recordings help define the EN, they are disadvantaged by limited tissue coverage. A modality identifying the EN more completely is needed. Spontaneous functional coherences in functional MRI (SFC-fMRI) is a technique to identify brain networks utilizing spontaneous fluctuations of the fMRI Blood Oxygenation Level Dependent (BOLD) signal without a specific task or event. An area of interest is defined as a 'seed' and its BOLD signal fluctuations over time are correlated to all other brain voxels to detect other areas with similar temporal activity. This technique has successfully demonstrated somato-sensory, auditory, visual, and language networks at rest and possibly could identify the EN. Fast ripples (FR) are integral parts of the EN in the mesial temporal lobe and proposed sites of seizure onset. We plan to use the FR location identified using depth electrodes as a seed for our SFC-fMRI experiments to identify an EN. A better understanding of the EN would lead to better understanding of the EZ, and in turn to better surgical outcomes.