

Epilepsy Research Program

The linkage between head injuries and post-traumatic epilepsy (PTE) has been evident since World War I. PTE currently affects an estimated 2,187 Iraq/Afghanistan Veterans, with a 5 times higher mortality than others receiving Department of Veterans Affairs care. Many of the pathological mechanisms linking traumatic brain injury (TBI) to PTE remain a mystery. Studies to understand the linkages between TBI and PTE are therefore needed to understand how brain circuitry is altered in response to TBI. There are also a number of prominent comorbidities, such as psychogenic non-epileptic seizures (PNES), that need to be better characterized. An improved understanding of the basic mechanisms of PTE and its comorbidities will ultimately result in better treatment, care and prevention choices.

VISION

The ERP envisions a time when the causative links between traumatic brain injury and epilepsy are understood and post-traumatic epilepsy (PTE) is both preventable and treatable.

MISSION

To understand post-traumatic epilepsy and associated comorbidities to improve quality of life, especially in Service members, Veterans, and caregivers.

PROGRAM HISTORY

The Department of Defense Epilepsy Research Program (ERP) was established in fiscal year 2015 (FY15) to develop an understanding of the magnitude of PTE within the military and to expand research into the basic mechanisms by which TBI produces PTE. Epilepsy is the fourth most common neurological disorder, with annual domestic healthcare costs of roughly \$10 billion. Mild, moderate, and severe

TBI are all linked to epilepsy, but the nature of the connection remains vastly unexplored. Mechanisms and markers of pathology and population-based research are needed in order to understand the connection between TBI and epilepsy. The ERP received \$30 million from FY15 to FY18 to fund research in PTE, which has resulted in 32 awards.

ERP RESEARCH FOCUS

FY19 FOCUS AREAS

- Basic Research
- Markers and Mechanisms
- Epidemiology
- Longitudinal Studies

ERP-FUNDED RESEARCH

- Epidemiology of PTE
- The relationship between PTE and PNES using neuroimaging
- State-of-the-art preclinical and translational neuroscience

ERP PARTNERSHIPS

- Citizens United for Research in Epilepsy
- National Institute of Neurological Disorders and Stroke
- International League Against Epilepsy

DATA SHARING

- Federal Interagency TBI Research Information Registry (FITBIR)
- National Institutes of Health, Common Data Elements



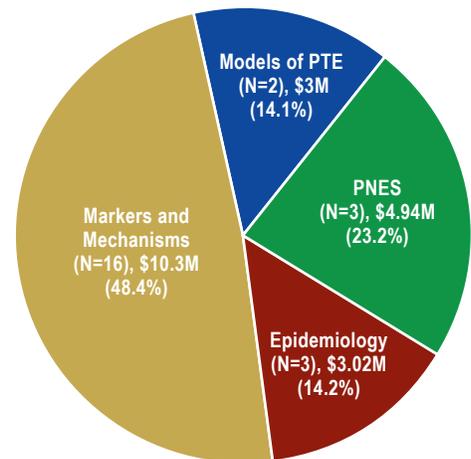
ERP RESEARCH INVESTMENT

FY18 is the first year that the ERP emphasized the need for longitudinal, population-based research studies. These studies may help the ERP understand how issues such as comorbidities figure into patient care and quality of life.

ERP STRATEGIC PLAN

At the start of FY18, the ERP developed a strategic plan to define the goals and direction of the program. The ERP strategic plan was developed in partnership with the ERP Programmatic Panel and outlines the near-, medium-, and long-term goals of the ERP. In addition, the strategic plan reviews the progress and investments made by the ERP through to the start of FY18 and emphasizes the ERP Focus Areas.

FY15-FY17 ERP Investment by Focus Area



THE EPIDEMIOLOGY OF EPILEPSY AND TRAUMATIC BRAIN INJURY: SEVERITY, MECHANISM, AND OUTCOMES

Mary Jo Pugh, Ph.D., R.N., South Texas Veterans Health Care System

While the link between severe TBI and epilepsy is well known, the long-term consequences of mild TBI (mTBI), the most common brain injury among post-9/11 Veterans, remain unclear with regard to PTE. To address this, Dr. Mary Jo Pugh was awarded an FY15 ERP Idea Development Award (IDA) to examine the association between TBI and PTE in Veterans who were deployed in post-9/11 conflicts. By comparing the medical records of post-9/11 Veterans, Dr. Pugh and her team found that Veterans with mTBI were twice as likely to have epilepsy as Veterans without TBI. In addition, Dr. Pugh's group is conducting a national survey to examine the unique effects of mTBI and epilepsy on the social, emotional, and physical functioning of our Veterans. Dr. Pugh and her team will also collect advanced clinical, cognitive, and neuroimaging data from a subset of participants. Importantly, this study seeks to identify populations at highest risk for developing PTE after mTBI, which may lead to earlier identification and treatment. Additional outcomes may include identifying individuals who may benefit from non-pharmacological therapy such as cognitive or lifestyle interventions. These types of interventions may benefit patients with PTE by improving their ability to manage their epilepsy, leading to better health outcomes for both patients and their families.



NEUROIMAGING BIOMARKER FOR SEIZURES

William Curt LaFrance, M.D., M.P.H., Ocean State Research Institute

Soldiers are exposed to a number of physical and psychological stressors in combat that can have long-term consequences. TBI, commonly seen in Veterans, can lead to PTE, where patients suffer from epileptic seizures that are the result of aberrant neuronal activity. In addition, Veterans may suffer from seizures that are non-epileptic (PNES), which lack epileptiform activity on an electroencephalogram, but are otherwise comparable to epileptic seizures. PNES is thought to be the result of traumatic experiences such as those seen in combat. With the help of an FY16 ERP IDA, Drs. William LaFrance, Jerzy Szaflarski, and their colleagues are investigating the neural circuitry of PTE and PNES through a longitudinal neuroimaging study of Veterans. Specifically, Dr. LaFrance's team will perform magnetic resonance imaging before and after patients receive cognitive and behavioral therapy for seizures, which in preliminary studies reduced the seizure burden in patients with PNES. In addition, these findings will be compared to patients who have received a TBI, but have not had PTE or PNES. Dr. LaFrance and his team are working to find neural signatures that differentiate PNES from PTE and TBI in Veterans with the hope that these discoveries may lead to better treatments for both PNES and PTE.