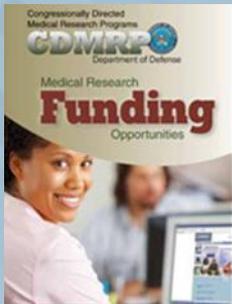


Epilepsy Research Program (ERP) 2019 ILAE Task Force on Post-Traumatic Epilepsy Update

CUTTING EDGE RESEARCH

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The views expressed in this presentation are those of the author and may not reflect the official policy or position of the Department of the Army, Department of Defense, or the U.S. Government



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2019 Mission and Vision

Vision:

A time when the causative links between Traumatic Brain Injury and epilepsy are understood and Post-Traumatic Epilepsy 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

FY20 Congressional Intent

The Committee is concerned about the large number of service men and women returning from combat zones who have sustained traumatic brain injuries [TBI] and the long term consequences of TBI. **These wounded warriors are at high risk for developing post-traumatic epilepsy, depression, cognitive difficulties, and post-traumatic stress disorder, which may be interconnected.** As current TBI longitudinal studies have not included epilepsy, the Committee encourages the Department to place greater priority and **invest more funding in longitudinal epidemiological research, including epilepsy surveillance, to better understand the magnitude of the problem and improve patient care and outcomes.** Additionally, the Committee urges the Department to **expand research into the mechanisms by which brain injury produces epilepsy and research directed at the prevention of epilepsy and concomitant comorbidities in those known to be at high risk.**

ERP Portfolio Strategy

	FY15	FY16	FY17	FY18	FY19
Focus Areas	<ul style="list-style-type: none"> Epidemiology Markers and Mechanisms Models of PTE 	<ul style="list-style-type: none"> Epidemiology Markers and Mechanisms Models of PTE Psychogenic Seizures 	<ul style="list-style-type: none"> Epidemiology Markers and Mechanisms Models of PTE Psychogenic Seizures 	<ul style="list-style-type: none"> Epidemiology Markers and Mechanisms Longitudinal Studies 	<ul style="list-style-type: none"> Innovative Research Epidemiology Markers and Mechanisms Longitudinal Studies
Mechanism	<ul style="list-style-type: none"> ERP Idea Development Award Level I/II 	<ul style="list-style-type: none"> ERP Idea Development Award Level I/II 	<ul style="list-style-type: none"> ERP Idea Development Award Level I/II Epilepsy Risk Factors Award 	<ul style="list-style-type: none"> ERP Idea Development Award Level I/II Longitudinal Risk Factors Award 	<ul style="list-style-type: none"> ERP Idea Development Award Level I/II Research Partnership Award Level I/II
Target	Mid and Large Capital (2) Projects	Mid and Large Capital (1) Projects	Small (4) and Mid Capital Projects; Young Investigators	Mid and Large Capital (1) Projects; Young Investigators	Mid and Large Capital (2) Projects; Young Investigators
	5 Awards	6 Awards	13 Awards	9 Awards	7 Awards (Estimated)

FY19 ERP Focus Areas

Innovative Research: Tools intended to better inform or improve upon how PTE research can be performed:

- **Hardware and/or software platforms that will improve seizure detection, characterization, or diagnosis**
- **Bioinformatics strategies, to include machine learning, that will improve access, annotation, curation and visualization of large and novel datasets from single or multiple sources**
- **Development of new models or better characterization of existing etiologically relevant models for PTE**
- **Improved characterization of the circuits involved in PTE**

Markers and Mechanisms: Identifying markers or mechanisms via preclinical models that address PTE, which may include the following:

- **Biomarkers**
- **Therapeutic targets for epilepsy prevention**
- **Early detection**
- **Diagnosis**
- **Prognosis**
- **Comorbidity**
- **Mortality**
- **Risk stratification**

FY19 ERP Focus Areas (Continued)

Epidemiology: Epidemiological characterization of PTE following TBI, which may include the following:

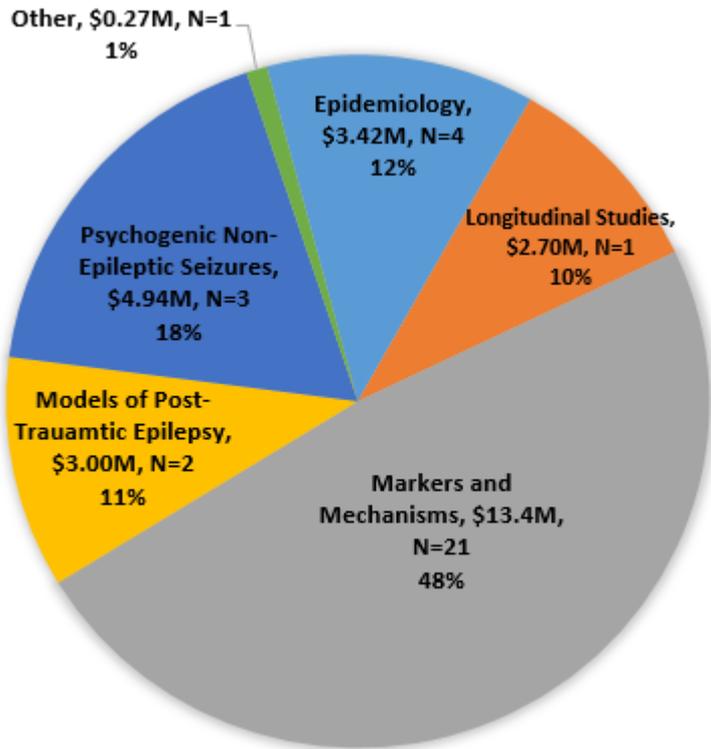
- Risk factors such as demographics, genetics, anatomy, pathology, or type of injury
- Differentiation of PTE and psychogenic non-epileptic seizures (PNES)
- Outcomes including latency to epilepsy, comorbidities, and mortality
- Pre-existing conditions including psychological and psychiatric risk factors
- Treatment and healthcare outcomes research

Longitudinal Studies: Studies of the evolution of PTE, which may include the following:

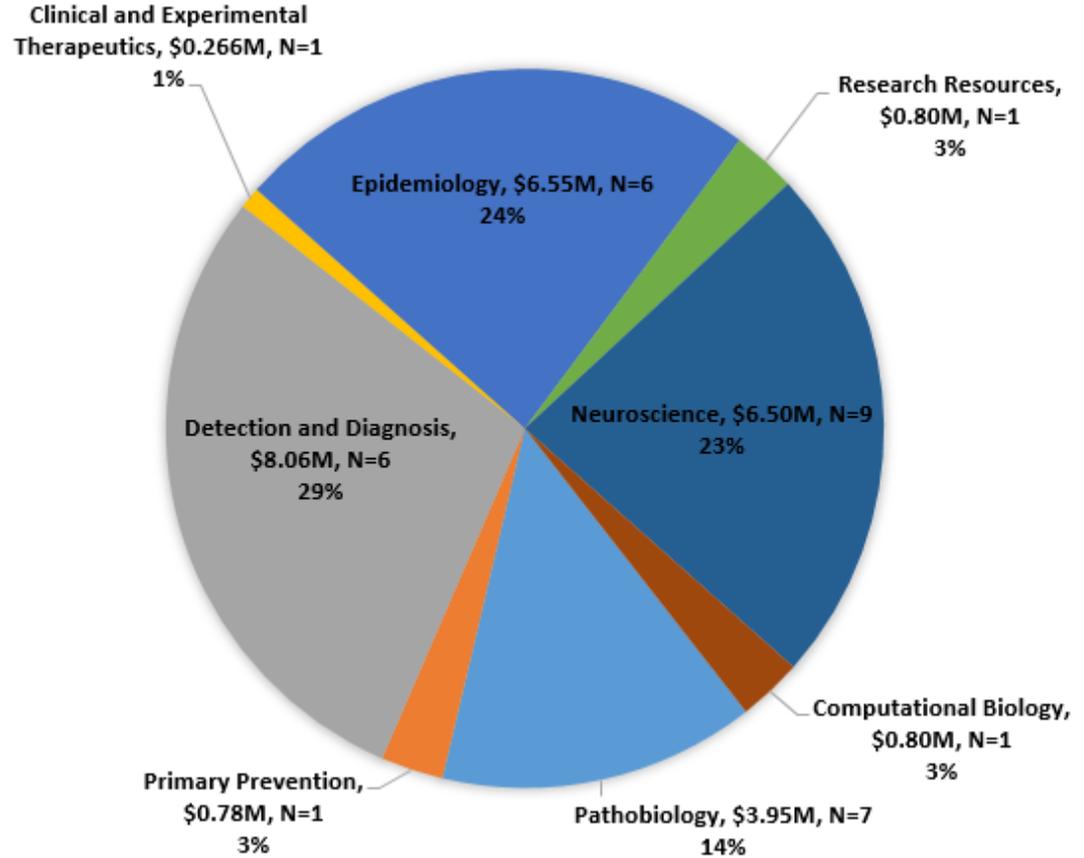
- Seizure frequency and severity
- Demographics, genetics, anatomy, pathology, or type of injury
- Comorbidities (e.g., depression, functional deficits, sleep disorders, major illness)
- Latency between type of injury and PTE
- Mortality
- Treatment and healthcare outcomes research
- Quality of life of individuals with PTE and their caregivers

FY15-18 By CDMRP Scientific Classification System (SCS) Code Series/Focus Area (N=32;\$27.7M)

By Focus Area



By SCS



Funded Projects FY15-FY18

Award Mechanism	FY15 (LVL II IDA=\$2.2M Total)	FY16 (LVL II IDA= \$3.7M Total)	FY17 (LVL II IDA= \$500K direct)	FY18 (LVL II IDA= \$500K direct)	Total
Idea Development Level I (High Risk/Gain)	3	5	2 (New Investigators)	2 (New Investigators)	12
Idea Development Level II (Advanced Studies/Collaborators)	2 (Barth/Pugh)	1 (LaFrance)	8	5	16
Epilepsy Risk Factors Award (Concepts)			3 (2 Epi/1 Tech Grant)		3
Longitudinal Risk Factors Award (TRACK-PTE)				1 (RDA)	1
Total	5	6	13	8	32

Animal/Human-Centered Studies by FY

	FY15	FY16	FY17	FY18	Total
Animal	4	3	6	4	17
Human	1	3*	7^	4**	15
Total	5	6	13	8	32

***(All PNES; 2 Functional Magnetic Resonance Imaging and 1 Epidemiology)**

^ Emphasis on seizure detection strategies.

****First large initiatives on Longitudinal cohorts/Biomarkers for PTE**

- **Research is mostly pre-translational; e.g. early studies to describe populations or novel mechanisms in animals**
- **Limited understanding of how TBI leads to seizures and then epilepsy**
- **Low conversion rates to PTE in animal models (12% or less) (few awards directly address this challenge)**

What's the (actual) size of the problem?



The PTE Landscape Ahead of Treatment/Prevention:

