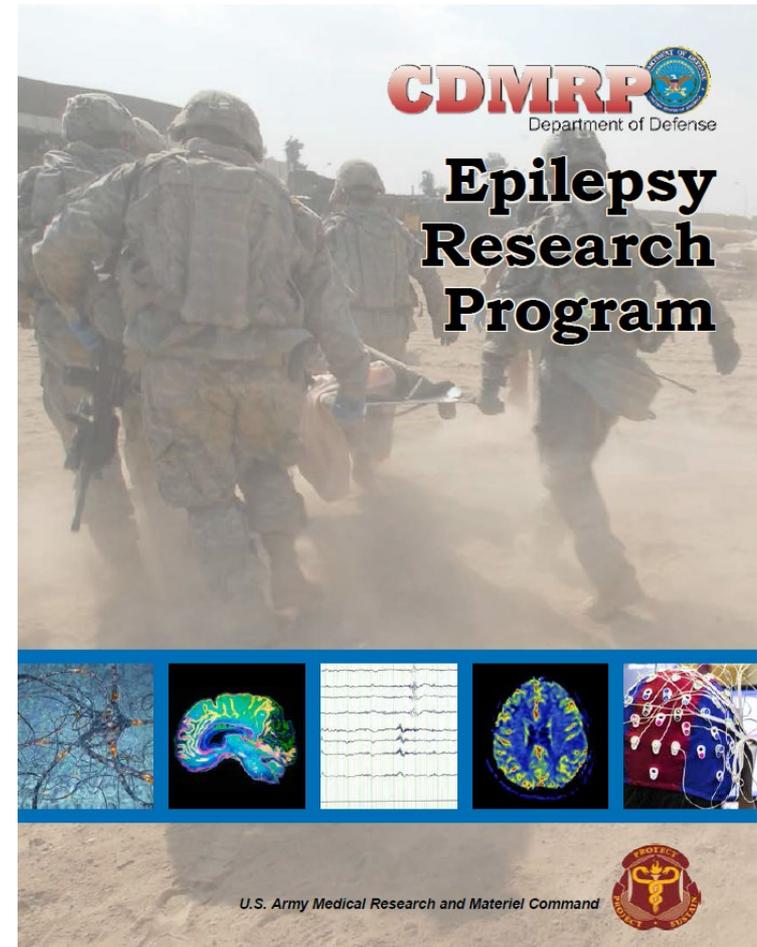




Congressionally Directed Medical Research Programs Epilepsy Research Program

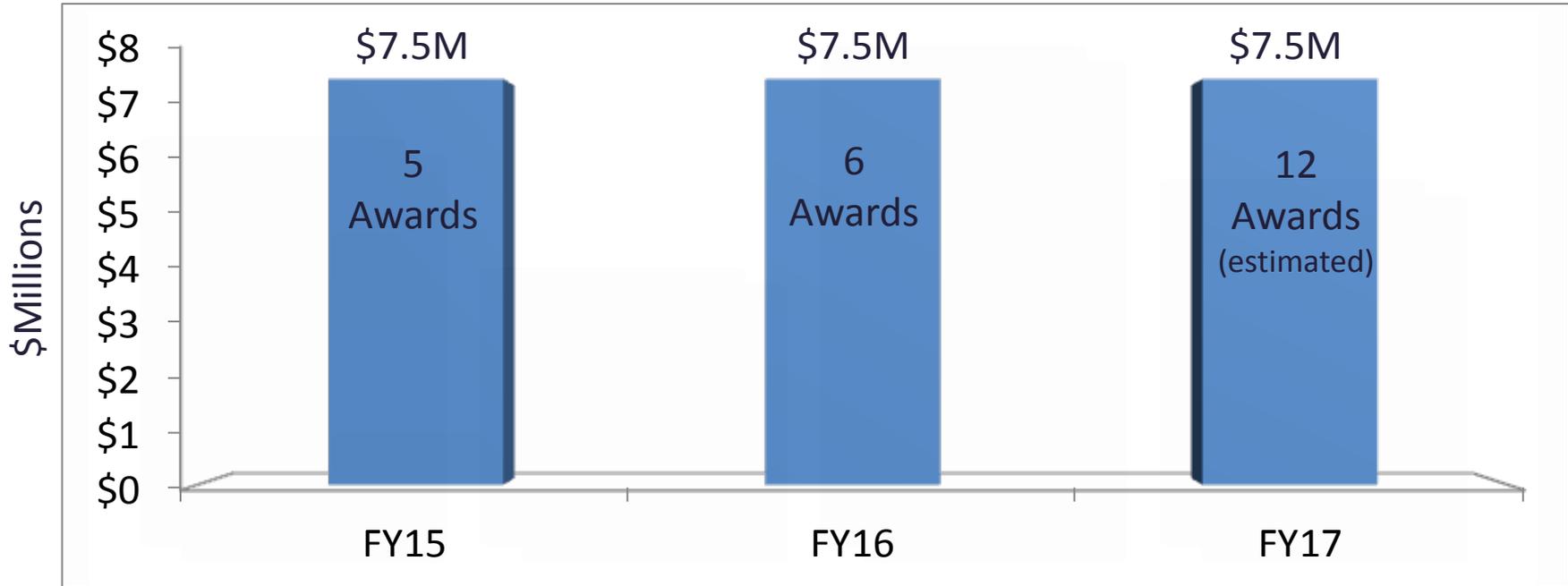
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Program Manager

- » **History:** The ERP was initiated in 2015 to develop an understanding of the magnitude of post-traumatic epilepsy (PTE) within the military and to expand research into the basic mechanisms by which traumatic brain injury (TBI) produces epilepsy
- » **Vision:** The ERP envisions a time when the causative links between TBI and epilepsy are understood and post-traumatic epilepsy is preventable
- » **Mission:** The ERP's mission is to advance research to understand the mechanisms underlying the genesis and progression of PTE, especially in Service members and Veterans.





Defense Health Program (DHP) Congressional Special Interest (CSI)



- » **Total Congressional appropriations: \$22.5M**
- » **Total applications received (through FY15): 64**
- » **Total awards made (through FY16) 11**

» Health Impact of Epilepsy

- » Hirtz, et al, estimated 2.1M cases, with 142K new cases per year in 2005¹
- » 4th most common neurological disorder¹
- » Incidence (new cases) is highest in children and the aging²
- » 2015 costs were estimated between \$9.6B and \$12.5B (Institute of Medicine Report²)
- » Surveillance report of active duty military (1998-2012) reported 11,295 incident cases of epilepsy among active component Service members (incidence rate: 52.8 per 100,000 person-years)³
- » Study also reported gender-based differences; concluded that traumatic brain injury (TBI) could not account for increased incidence of epilepsy during the surveillance period³

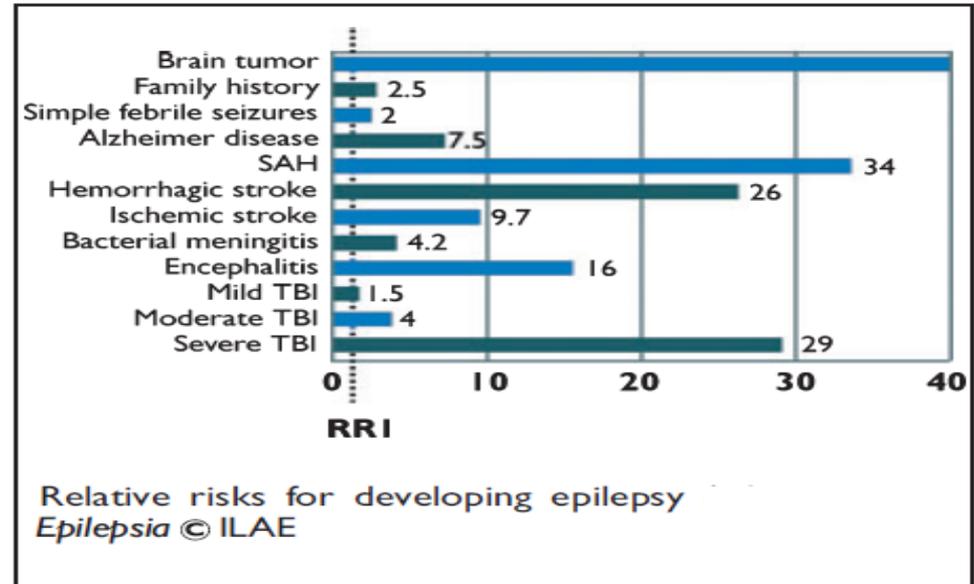


Figure 1: Adapted from Lowenstein et al. 2009⁴

¹Hirtz, et al. 2007. How common are the “common” neurologic disorders? *Neurology*. 68(5):326-337

²England et al. 2012. Epilepsy Across the Spectrum: Promoting Health and Understanding. Institute of Medicine Report Brief.

³Medical Surveillance Monthly Report. 2013. Vol 20, Number 5, 19-23.

⁴Lowenstein. 2009. *Epilepsia*. 50 (Suppl. 2):4-9.



Scope of the Problem (cont.)



» Health Impact of TBI

- » Defense and Veterans Brain Injury Center (DVBIC) reported roughly 350K cases since 2000¹
- » Centers for Disease Control and Prevention (CDC) reports 716 emergency department visits/92 hospitalizations per 100,000 U.S. population (2010)²
- » Number of civilian TBIs increased between 2001 and 2010²
- » CDC reported cost estimate for domestic TBI medical costs in 2010 at \$76.3B³
- » Study on Vietnam-era Veterans showed 53% had post-traumatic epilepsy after penetrating TBI (n=421) (Salazar)⁴
- » Salazar study is confirmed by several older TBI studies from World War I and World War II

¹<http://dvbic.dcoe.mil/dod-worldwide-numbers-tbi>

²<http://www.cdc.gov/traumaticbraininjury/data/rates.html>

³<https://www.cdc.gov/cdcgrandrounds/pdf/grtbi20sep2011.pdf>

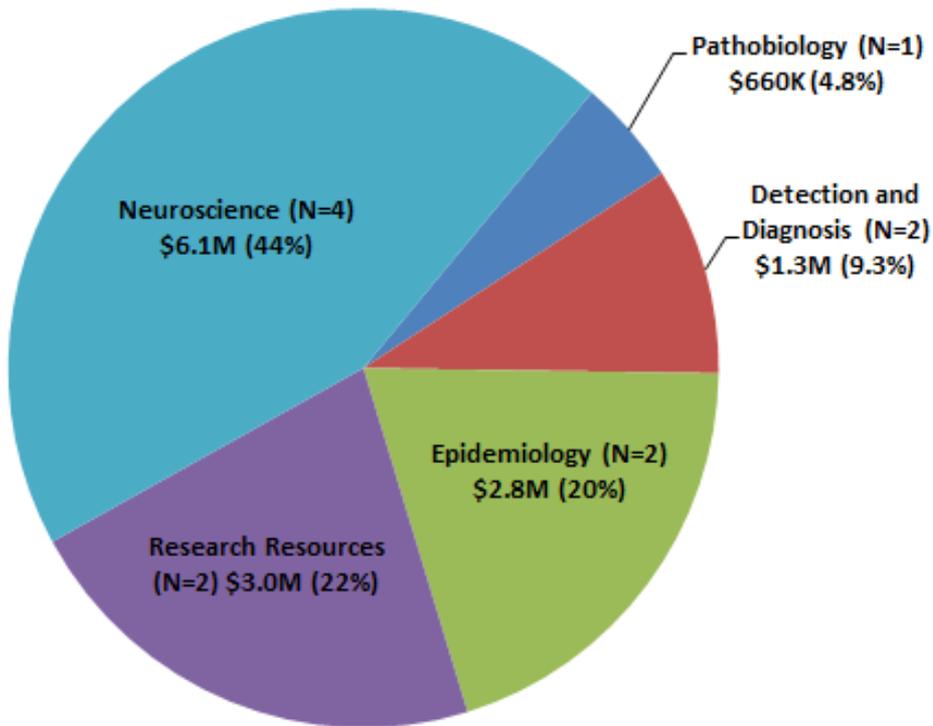
⁴Salazar, et al. 1985. Epilepsy after penetrating head injury. I. Clinical correlates: a report of the Vietnam Head Injury Study. *Neurology*. Oct;35(10):1406-14.



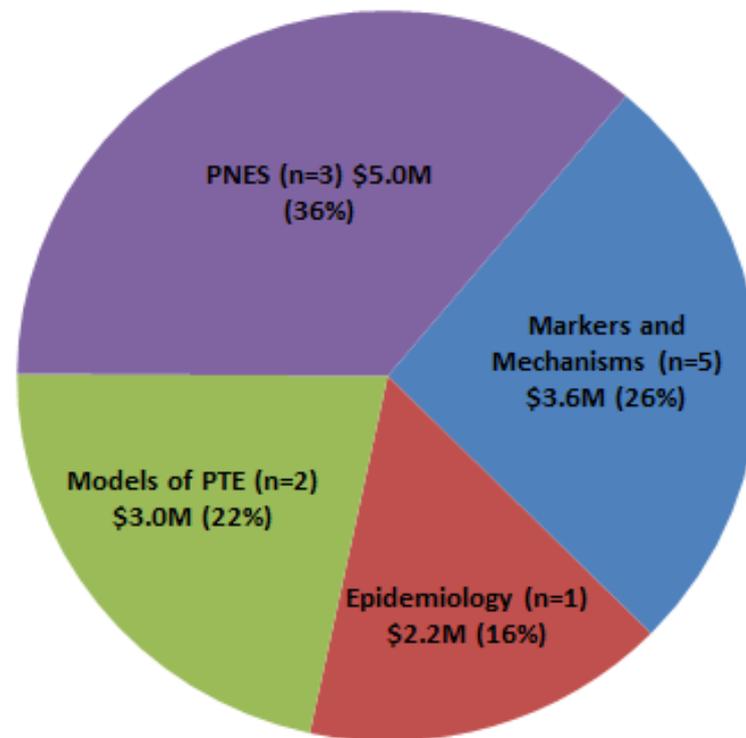
FY15-FY16 by CDMRP Scientific Classification System (SCS) Code



By SCS



By Focus Area



*Subject to final budget negotiations



Challenges and Successes



» Challenges

- » Limited amount of research completed on the epidemiology of PTE
- » Early studies of TBI-epilepsy concentrate on penetrating head injuries

» Successes

- » Focus Areas have helped identify novel research areas and unique projects for funding
- » Program is well-balanced to address both program needs and congressional intent



FY18 Focus Areas: Contingent on Receipt of Funding



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

- » Risk factors such as demographics, genetic factors, organic head injury factors, or type of insult
- » Differentiation of PTE and Psychogenic Non-Epileptic Seizures (PNES)
- » Outcomes including latency to epilepsy, morbidities and comorbidities, and mortality
- » Pre-existing conditions including psychological and psychiatric risk factors
- » Treatment

Markers and Mechanisms: Identifying markers or mechanisms (via clinical prospective or preclinical models) that address PTE which may include:

- » Early detection
- » Diagnosis
- » Prognosis
- » Morbidity
- » Comorbidity
- » Mortality
- » Risk stratification



Focus Areas (cont.)



Longitudinal Studies: Studies of the natural evolution of PTE which may include:

- » Seizure frequency and severity
- » Comorbidities (e.g., depression, functional deficits, sleep disorders, major illness)
- » Latency between injury and PTE
- » Mortality
- » Treatment
- » Quality of Life of individuals with PTE



FY18 Funding Mechanisms: Contingent on FY18 Funding



Award Mechanism	Eligibility	Key Mechanism Elements	Funding
Longitudinal Risk Factors Award	Assistant Professor or Above	<p>Intent: To facilitate high-impact, systematic, population-based research investigating the natural evolution of PTE from TBI.</p>	<ul style="list-style-type: none"> » Maximum funding of \$2,500,000 for direct costs (plus indirect costs). » Maximum period of performance is 4 years.
Idea Development Award	<p>Level I: The Principal Investigator must be at or above the level of postdoctoral fellow (or equivalent), but below the level of Assistant Professor (or equivalent).</p> <p>Level II: Assistant Professor or Above</p>	<p>Intent: To solicit research to understand the magnitude and underlying mechanisms of PTE, especially in Service members and Veterans, while also benefitting the civilian community.</p> <ul style="list-style-type: none"> » Level I is intended to support high-risk or high-gain research from researchers at or above the level of a post-doctoral fellow (or equivalent). » Level II is intended to support a more mature, hypothesis-driven research project. 	<p>Level I:</p> <ul style="list-style-type: none"> » Maximum funding of \$300,000 for direct costs (plus indirect costs). » Maximum period of performance is 2 years. <p>Level II:</p> <ul style="list-style-type: none"> » Maximum funding of \$500,000 for direct costs (plus indirect costs). » Maximum period of performance is 3 years.



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www.cdmpc.army.mil or EBRAP.org