



Congressionally Directed Medical Research Programs

Peer Reviewed Alzheimer's Research Program Overview

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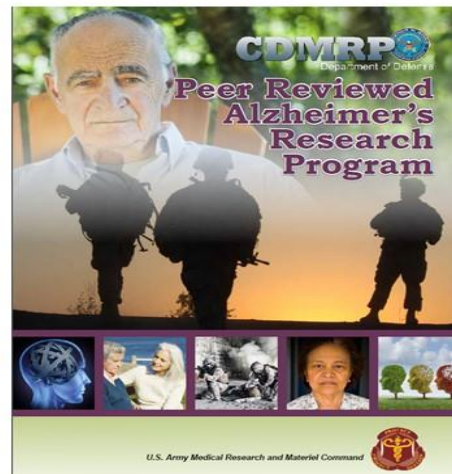
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Program Overview: Introduction



- » History: Initiated in 2011 to address the long-term consequences of traumatic brain injury (TBI) as they pertain to Alzheimer's disease (AD). In fiscal year 2016 (FY16), the program was expanded to include research on AD-related dementias (ADRD) as they pertain to TBI.
- » Vision: To address the long-term consequences of traumatic brain injury as they pertain to Alzheimer's disease and Alzheimer's disease-related dementias.
- » Mission: The PRARP's mission is devoted to (1) understanding the association between TBI and AD/ADRD and (2) reducing the burden on affected individuals and caregivers, especially in the military and Veteran communities.





Defining the Scope of the Problem



» Health Impact of AD

- » U.S. – Prevalence of AD is between 2.6 and 5.4 million cases, depending on the study; prevalence increases with age^{1,2}
- » Globally – Estimated 27 million cases³; 5% of European population (37 million!)⁴
- » Diagnosis rate is hard to estimate; cases are often missed¹
- » Centers for Disease Control and Prevention (CDC) reports 94,000 deaths in 2014 (6th leading cause of death)⁵
- » Estimated U.S. health care costs in 2010: \$157B to \$236B^{2,6}
- » No cure; treatments address only symptoms

¹Brookmeyer, et al. 2011. National estimates of the prevalence of Alzheimer's disease in the United States. *Alzheimers Dement.* Jan;7(1):61-73. doi: 10.1016/j.jalz.2010.11.007.

²Alzheimer's Association. 2016. 2016 Alzheimer's disease facts and figures. *Alzheimers Dement.* 2016 Apr;12(4):459-509.

³Brookmeyer, et al. 2007. Forecasting the global burden of Alzheimer's disease. *Alzheimers Dement.* Jul;3(3):186-91. doi: 10.1016/j.jalz.2007.04.381.

⁴Niu et al. 2017. Prevalence and incidence of Alzheimer's disease in Europe: A meta-analysis. *Neurologia.* 2017 Oct;32(8):523-532

⁵<http://www.cdc.gov/nchs/fastats/alzheimers.htm>

⁶Hurd, et al. 2013. Monetary Costs of Dementia in the United States. *N Engl J Med.* April 4; 368(14):1326-1334.

Health Impact of TBI

- » Defense and Veterans Brain Injury Center (DVBIC) reported roughly 380,000 cases since 2000¹
- » In 2014, there were approximately 2.87 million TBI Emergency Department (ED) visits/hospitalizations in the United States with 57,000 deaths²
- » Rates of TBI-related ED visits per 100,000 population were highest among older adults aged ≥ 75 years (1,682.0), young children aged 0-4 years (1,618.6), and individuals 15-24 years (1,010.1)²
- » CDC-reported cost estimate for domestic TBI medical costs in 2010 was \$76.3B³

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

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

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



Defining the Scope of the Problem (continued)



» Epidemiological Data Associating TBI with Dementia

- » Variety of studies, variety of outcomes
- » At least 20 published studies since 1984; odds ratios range from 1 to 14
- » Institute of Medicine report cites hazards ratio values based on length of loss of consciousness/post-traumatic amnesia at 2.3 for moderate and 4.5 for severe in Veterans with non-penetrating head injury¹
- » Yaffe et al. (2019) report a hazard ratio (HR) of 1.64 in female veterans (n=110K) with one or more additional comorbidities (PTSD or depression) increasing the HR up to 2.42²; similar but higher HR values for men (up to 3.8 for mod/severe TBI)³
- » Confounders include: self report, lack of robust autopsy data, age at injury, post-traumatic interval, operational TBI definitions at the time of the study (e.g., use of ever versus never), use of ICD codes...

» Common Symptoms

- » Memory disorders
- » Behavioral Symptoms
- » Executive functioning deficits

¹Plassman BL, et al. 2000. Documented head injury in early adulthood and risk of Alzheimer's disease and other dementia. *Neurology.* Oct 24;55(8):1158-1166.

²Yaffe K, et al. 2019. Military-related risk factors in female veterans and risk of dementia. *Neurology.* Jan 15; 92(3):205-211.

³Barnes, et al. 2018. Association of Mild Traumatic Brain Injury With and Without Loss of Consciousness With Dementia in US Military Veterans. *JAMA Neurol.* 2018 Sep 1;75(9):1055-1061.

■ TBI-AD/ADRD Risk Factors (or Comorbidities)

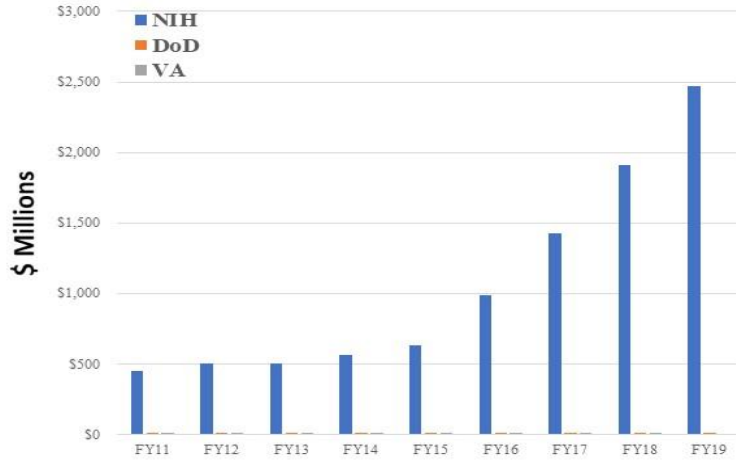
- Genetics
- Sleep, activity, nutrition
- Hypertension, diabetes
- Gender
- Age

■ Research Tools Used for Both

- Autopsy
- Radioimaging (plaques, Tau)
- Magnetic resonance imaging (MRI) (functional, diffusion tensor imaging, structural [hippocampal volume])
- Cerebral spinal fluid (Aβ42, Tau, and phospho-Tau), Blood, Saliva



NIH, VA, and PRARP Governmental Funding Landscape FY11-FY19 for AD/ADRD



	NIH	DoD [^]	VA
FY11	\$448M	\$15M	\$12.4M
FY12	\$503M	\$12M	\$13.4M
FY13	\$504M	\$12M	\$11.6M
FY14	\$562M	\$12M	\$11.2M
FY15	\$631M	\$12M	\$13.7M
FY16	\$986M	\$15M	\$12.8M
FY17	\$1,423M	\$15M	\$11.8M
FY18	\$1,911M	\$15M	\$11.9M
FY19	\$2,468M*	\$15M	N/A

PRARP “changes its course” yearly in order to leverage larger investments.

PRARP Total Congressional appropriations: \$123M

*Estimated (https://report.nih.gov/categorical_spending.aspx) [^]Before management and withhold costs.



Comparison of NIH[†] and PRARP Funding Using IADRP[‡] Data FY14-FY18[^]



	NIH (N=7,972 Projects*)	PRARP (N=83 Projects)	All IADRP Partners* (Non-DoD) N=11,429 Projects*)
Category A. Molecular Pathogenesis and Physiology of Alzheimer's Disease	4,113 (51.6%* [↓])	30 (36.1%* [↑])	5,753 (50.4%* [↓])
Category B. Diagnosis, Assessment, and Disease Monitoring	1,584 (19.9%* [↓])	21 (25.3%* [↓])	2,232 (19.5%* [↓])
Category C. Translational Research and Clinical Interventions	1,241 (15.6%* [↓])	8 (9.6%* [↑])	1,852 (16.2%* [↓])
Category D. Population Studies (Epidemiology)	547 (6.9%* [↑])	9 (10.8%* [↑])	727 (5.2%* ⁻⁻⁻)
Category E. Care, Support, and Health Economics of Alzheimer's Disease	487 (6.1%* [↑])	15 (18.1%* [↓])	865 (7.6%* [↑])

[†]National Institutes of Health

[‡]International Alzheimer's Disease Research Portfolio

[^]Data only for categories used by DoD PRARP

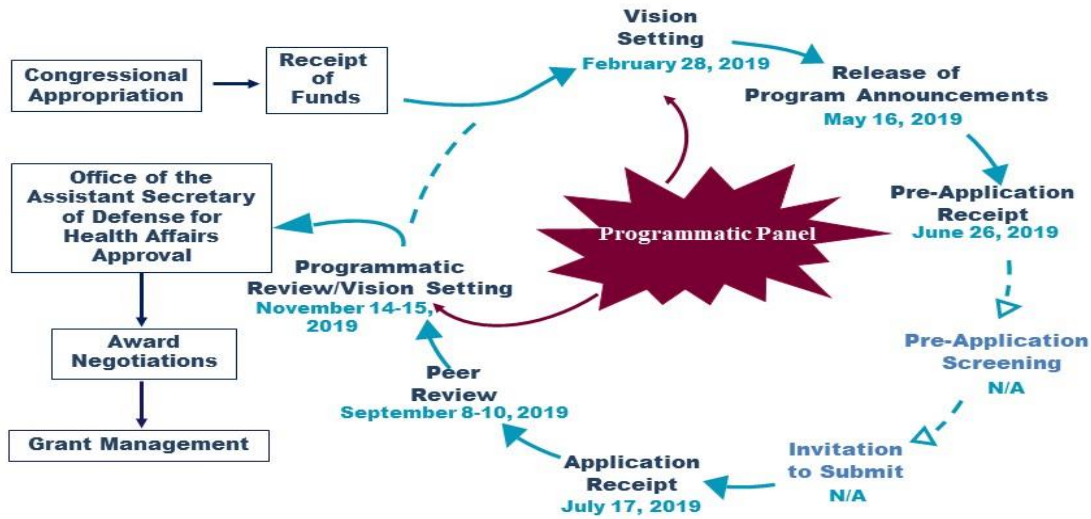
*0-1% Absolute change from FY13-FY17

[†]1-3% Absolute change from FY13-FY17

[‡]3-8% Absolute change from FY13-FY17



FY19/20 PRARP Program Cycle



PRARP Portfolio Investment Strategy: Through the Years



	FY15	FY16	FY17	FY18	FY19
Gaps/Priorities	Paucity of Clinical Studies; Diagnostics; Research Resources; Quality of Life; Caregiver Support	Paucity of Clinical Studies; Diagnostics; Research Resources; Quality of Life; Caregiver Support; Epidemiology	Paucity of Clinical Studies; Diagnostics; Research Resources; Quality of Life; Caregiver Support; Epidemiology	Paucity of Clinical Studies; Diagnostics; Research Resources; Quality of Life; Caregiver Support; Epidemiology	Paucity of Clinical Studies; Diagnostics and Prognostics; Research Resources; Quality of Life; Family and Care Support; Epidemiology
Funding Opportunities	Convergence Science Research Award Military Risk Factor Research Award Quality of Life Research Award	Convergence Science Research Award Epidemiology of Military Risk Factors Research Award Quality of Life Research Award Translational Research Partnership Award	Convergence Science Research Award Quality of Life Research Award Research Partnership Award New Investigator Award	Convergence Science Research Award Quality of Life Research Award Research Partnership Award New Investigator Award	Convergence Science Research Award Innovations in Care and Support Award Research Partnership Award
	16 Awards	15 Awards	18 Awards	18 Awards	21 Awards



Strategic Plan: FY20 PRARP Overarching Challenges



Paucity of Clinical Studies: The paucity of clinical studies to examine the interrelationship between TBI and subsequent AD/DRD for the military, Veteran, and civilian communities

Basic Research: Fundamental research to examine the interrelationship between TBI and subsequent AD/DRD for the military, Veteran, and civilian communities and to translate these findings

Diagnostics and Prognostics: The need for technologies, tests, surveys, questionnaires, devices, biomarkers, or analyses to detect TBI and sequelae to include AD/DRD utilizing new and/or pre-existing datasets

Epidemiology: The paucity of epidemiological research to examine the interrelationship between TBI, risk and resiliency factors, and subsequent AD/DRD for the military, Veteran, and civilian communities

Quality of Life: The need for technologies, assessments, interventions, or devices to benefit individuals living with the common symptoms of TBI and/or AD/DRD

Family and Care Support: The need for technologies, assessments, interventions, or devices that enhance the lives of those providing care and families of individuals living with the common symptoms of TBI and/or AD/DRD

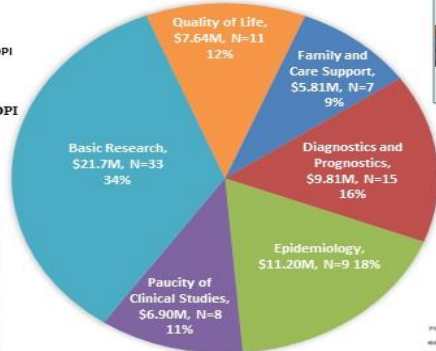
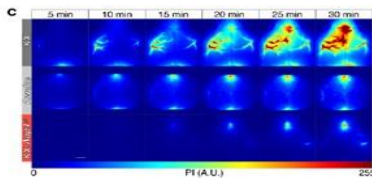
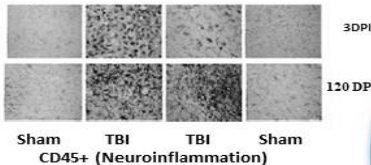
- » All are equally important as they address the PRARP's Mission and Vision
- » Address high-level research gaps
- » Mechanism-specific
- » All applications must address at least one Overarching Challenge
- » Meant to align with PRARP Focus Areas (Technical Challenges; e.g., Novel Target Identification, Bioinformatics)



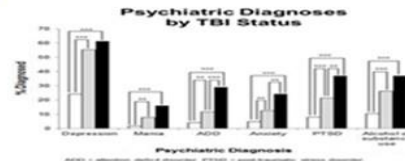
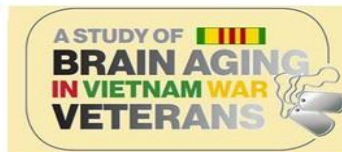
PRARP Research Investment FY14-FY18 by Overarching Challenge and Dollar Amount* (N=83; \$63.1M)



Non-TG R1.40 (Aβ+)



Nanobodies
(4 U.S. Patents granted/
applied for Diagnostics)





FY20 Award Mechanisms



Convergence Science Research Award (CSRA)

- » **Intent:** Support innovative or novel efforts to generate research resources, tools, or research efforts for researchers and/or practitioners in health sciences.
- » **Level I:** Investigators at the postdoctoral level (or equivalent) or above in any scientific discipline. (Mentor required.)
- » **Level II:** The Principal Investigator (PI) must be an independent investigator at or above the level of Assistant Professor (or equivalent).

Maximum funding of \$225,000 (Level I)/\$500,000 (Level II) for direct costs (plus indirect costs) over 3 years.



FY20 Award Mechanisms (*continued*)



Innovation in Care and Support Award

- » **Intent:** Support innovative research that improves the quality of life and care for individuals living with the common symptoms of TBI and/or AD/ABRD and/or their families and care providers.
- » **Level I:** Investigators at the postdoctoral level (or equivalent) or above in any scientific discipline. (Mentor required.)
- » **Level II:** The PI must be an independent investigator at or above the level of Assistant Professor (or equivalent).

Maximum funding of \$225,000 (Level I)/\$500,000 (Level II) for direct costs (plus indirect costs) over 3 years.



FY20 Award Mechanisms (*continued*)



Research Partnership Award (RPA)

- » **Intent:** To create an avenue for collaborative research partnerships between/among investigators to address a research problem or question in a manner that would be unachievable through separate efforts.
- » The PI and Co-PI(s) must each be an independent investigator at or above the level of Assistant Professor (or equivalent)

Maximum funding of \$1.3M in total costs over 3 years.



FY20 Award Mechanisms (*continued*)



NEW: Accelerating Diagnostics for Traumatic Brain Injury Research Award (ADTBI)

Intent: Supports high-impact, human-based, development of robust diagnostic and prognostic biomarkers for chronic TBI as they pertain to Alzheimer's disease and the related dementias.

The PI must be an independent investigator at or above the level of Assistant Professor (or equivalent).

- » The following biomarker types are encouraged:
 - » Imaging-Related
 - » Fluid-Based (e.g., Cerebrospinal Fluid [CSF], Blood, or Saliva)
 - » Retinal
 - » Wearable Devices
- » Studies focused on biomarker discovery are discouraged.
- » The biomarkers must correlate with clinical endpoints to include cognition and/or behavior.

Maximum funding of \$2.8M in total costs over 4 years.



FY20 Award Mechanisms (continued)



NEW: Leveraging Approaches for Innovation in Care and Support Award (LEAP-InCASA)

Intent: Supports multi-institutional, harmonized research approaches that will advance the quality of life and care for individuals living with the common symptoms of TBI and/or AD/ABRD and/or their families and care providers.

The PI and Co-PI(s) must each be an independent investigator at or above the level of Assistant Professor (or equivalent).

- » Requires a Coordinating Center and at least two Partnering sites.
- » The Coordinating Center provides overall leadership and infrastructure for all research projects.
- » Coordinating and Partnering sites work together to harmonize research protocols, analyze data and publish research findings.
- » Accrual for each of the research studies occurs at both the research site and coordinating center.

Maximum funding of \$2.8M in total costs over 4 years.



For more information regarding application deadlines, the full details for each award mechanism, and participation in future surveys, please register at:



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