

Alzheimer's Research Program



Advancing Alzheimer's Research for the Military

Congressionally Directed Medical Research Programs

The Congressionally Directed Medical Research Programs was created in 1992 when, following a powerful grassroots effort led by the breast cancer advocacy community, Congress first appropriated funds to the Department of Defense for biomedical research. The CDMRP has evolved into a global funding organization that fosters novel approaches to biomedical research in response to the needs of the American public, the military and Congress. The DOD allocates funds for the CDMRP annually to support individual programs via specific guidance from Congress. Over the course of its history, the CDMRP has managed \$15.9 billion in Congressional appropriations for military and domestic health research programs. The research spectrum supported by the CDMRP extends from basic science to large, multi-institutional consortia.

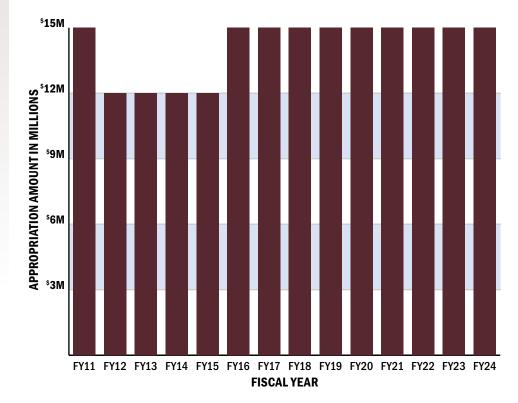
Like all programs at CDMRP, the PRARP uses a two-tiered review system to ensure research supported by the PRARP is both scientifically meritorious and addresses the vision and mission of the program.

PEER REVIEWED ALZHEIMER'S RESEARCH PROGRAM

PROGRAM HISTORY

Congress started the Peer Reviewed Alzheimer's Research program in fiscal year 2011 to address the long-term consequences of traumatic brain injury and military service as they pertain to Alzheimer's disease in civilian and military communities. In FY16, the program expanded to include AD-related dementia, ADRD, research related to TBI. Appropriations for the PRARP from FY11 through FY24 totaled \$198 million.

PRARP Funding History (\$198M in Total Appropriations)





At age 19, Anitra "Nia" Mostacero joined the Air Force, rising through the ranks to Senior Master Sergeant. During her service, Mostacero earned an MBA and various certifications before retiring in 2017 after 22 years of military service. That same year, Mostacero was diagnosed with younger-onset Alzheimer's disease at the age of 42, and later with Chronic Traumatic Encephalopathy dementia and traumatic brain injury. Mostacero has found a new calling to increase the concern and awareness of dementia because Black Americans are twice as likely as older white Americans to have Alzheimer's or other dementias. Her goal is to educate and raise awareness about how dementia symptoms can appear decades before "senior age." She has shared her story with local media and audiences and served on a local Dementia Friendly community group. She also served on the Alzheimer's Association's 2021-2022 National Early-Stage Advisory Group, Memory Gala committees and is an avid fundraiser. She is also an active member of National Council of Black Dementia Minds.

Senior Master Sgt. Anitra Mostacero, M.B.A.,

U.S. Air Force Retired; National Council of Black Dementia Minds; Alzheimer's Association

VISION:

Mitigate the impact of Alzheimer's and related dementias associated with military and diverse risks.

MISSION:

Fund person-centered research to address critical needs and improve quality of life for people living with Alzheimer's disease and related dementias.

THE PRARP RESEARCH PORTFOLIO



EPIDEMIOLOGY & RISK FACTORS

QUALITY OF LIFE FOUNDATIONAL SCIENCE

\$40.9M 40 AWARDS \$27M 20 AWARDS \$26.1M 31

AWARDS

\$54.2M 77 AWARDS

PROGRAM PRIORITIES



Increase representative research populations to reduce health disparities



Understand mechanisms, pathways, and causes of AD/ADRD



Improve quality of life for people living with dementia diagnoses, families, caregivers, and communities



Improve diagnosis and prognosis now



Reduce risk and prevent AD/ADRD

TRANSFORMING RESEARCH TO IMPROVE THE LIVES OF PEOPLE AFFECTED BY DEMENTIA

ACCELERATING UNDERSTANDING OF KEY FOUNI



ApoE4 and Lipid Metabolism – What Makes Neurons Vulnerable? Laura Beth J. McIntire, Ph.D., Weill Cornell Medical College

RISK FACTOR IDENTIFICATION AND REDUCTION



Late-Life Consequences of TBI and Military Service: A Population-Based Study Kristen Dams-O'Connor, Ph.D., Mount Sinai

IMPROVING DIAGNOSIS



A Highly Scalable & Cost-Effective Sampling & Testing Solution for Brain Health & Injury William Haskins, Ph.D., Gryphon Bio, Inc.

INDIVIDUAL, FAMILY, CARE-PARTNER QUALITY O



Teaching Self-Management Skills to Improve Self-Efficacy and Quality of Life for Caregiver Dyads in TBI and Dementia Populations Denise Krch, Ph.D., Kessler Foundation The PRARP actively funds research that spans a spectrum from increasing understanding of AD/ADRD risk and development to refining diagnostic is technology and accessibility. With a focus on tackling critical unmet needs to enhance the well-being of people supporting or living with dementia, the PRARP executes a person-centered mission supporting impactful research.

DATIONAL MECHANISMS

From synaptic transmission, myelin sheath to phagocytic activity of microglia, lipid metabolism plays an important role in the essential brain functions. PRARP-funded research is propelling lipidomic studies in TBI-AD/ADRD with more refined spatial and temporal resolutions that could pave the way for targeted therapy in AD/ADRD.

Epidemiological data and donated brains from the Adult Changes in Thought study identifies the chronic health consequences of traumatic brain injury and military service in individuals over 65 years old. Recent analyses show that traumatic brain injury with loss of consciousness contributed to an increase in cellular death in the cerebral cortex but not AD-related neuropathologic outcomes such as vascular pathology, Lewy bodies, tau and amyloid.^{2,3} These studies suggest that processes underlying post-TBI neurodegeneration may be distinct from the sporadic pathologies of Alzheimer's disease.

This project aims to develop a first-of-its-kind, highly scalable and cost-effective sampling and testing solution for brain health and injury in pre-hospital, hospital and post-hospital environments. The solution combines point-of-care, minimally invasive sampling methods for saliva or capillary blood and high sensitivity offline testing methods for acute, substitute and chronic biomarkers. Observational clinical studies to demonstrate the benefits of this novel solution for early detection and monitoring of brain health and injury are underway. Combined with other modules and factors including cognitive and age, this solution is a potential gamechanger to address the unmet medical needs of traumatic injury, mild cognitive impairment and Alzheimer's disease.

F LIFE AND SUPPORT

This study involves a clinical trial testing the Wellness, Coping, and Adaptation for Neurocognitive Conditions program, known as WeCAN, is a 12-session treatment that teaches self-management skills of coping, stress management and problem solving for individuals living with moderate-to-severe TBI, chronic mild TBI and dementia diagnoses. The research teams at three recruitment sites – Kessler Foundation, University of Michigan and Franciscan Health – assesses participants, both caregivers and those with the diseases, at baseline, post-treatment, and at six months after treatment, with a primary focus on measures of self-efficacy and quality of life.

UNDERSTANDING MECHANISMS LEADING TO ALZHEIMER'S DISEASE AND OTHER DEMENTIAS

Many questions remain unanswered on the biology of TBI and Alzheimer's disease. The PRARP invested in a range of foundational research to support accelerating our understanding of AD/ADRD to design better drugs and treatments and to improve the lives of those living with dementia today.



Presynaptic Protein Bassoon Contributes to Tau-Seed Propagation:

Cristian Lasagna-Reeves, Ph.D., Indiana University

The Lasagna-Reeves research team at Indiana University discovered a

breakthrough regarding the role of the pre-synaptic scaffold protein bassoon in facilitating the trans-synaptic propagation of pathologic tau (phospho-tau) in a prion-like manner during the early stages of tau pathology. This discovery sheds light on how the pathologic tau protein spreads along anatomical pathways in the brain in AD/ADRD. Furthermore, downregulating bassoon led to a decrease in tau spreading and rescued synaptic and cognitive behavioral impairment in a mouse model of tauopathy, highlighting the therapeutic potential of bassoon for treating tauopathies.

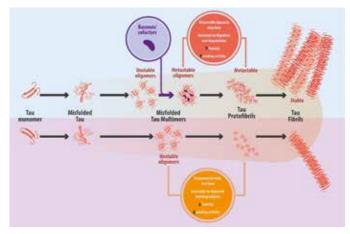


Illustration of how tau can seed propagation using the bassoon scaffold protein.

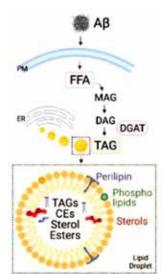


Impaired Lipid
Metabolism and
Phagocytosis of
Microglia Induced
by Amyloid-beta in
Alzheimer's Disease:

Gaurav Chopra, Ph.D., Purdue University

Researching the role of brain cells known as microglia in AD pathogenesis is crucial. Monitoring how microglia phagocytize,

or take in materials from the outside environment in both cell and mouse models, provides insights into their function in AD. By utilizing pH-sensitive amyloid β-proteins that change fluorescence color depending on whether they are inside or outside the cell, in combination with lipidomics, the research team discovered the accumulation of lipid droplets in microglia displaying impaired phagocytosis upon Aβ exposure. Inhibiting a key enzyme for lipid droplets, known as diacylglycerol O-acyltransferase 2, improved microglial uptake of AB, potentially paving the way for a novel therapeutic avenue for AD.5



DGAT2 inhibition reduces lipid droplet formation and improves microglial uptake and subsequent cleanup of AB, a key pathological ADrelated protein.⁵



Cerebral Organoids as a Drug-Screening Platform for Protection Against Neurodegeneration:

Justin Ichida, Ph.D., University of Southern California

The Ichida research team identified early changes to how neurons create and regulate the glutamatergic signaling pathway prior to neurodegeneration. Using induced pluripotent stem cell-derived cerebral organoids, or simplified mini-brain structures, harboring mutations from the ADRD, frontotemporal dementia, the research team screened potential drugs for neuroprotection after traumatic injury using the organoids. In this

system, they found that inhibiting the lipid kinase, PIKFYVE, which regulates endo-lysosomal trafficking, potently reduced neuronal vulnerability. PIKFYVE inhibition was also found to be neuroprotective in another neurodegenerative disease, amyotrophic lateral sclerosis. This groundbreaking research by Ichida and colleagues may lead to further promising therapeutic targets for ADRD.

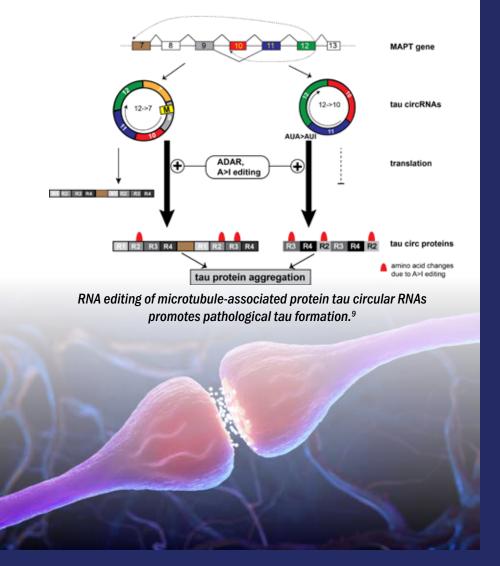


Translational Products from Tau Circular RNA Promotes Tau Tangle Formation in AD/ ADRD:

Stefan Stamm, Ph.D., University of Kentucky

The unique structure of the human microtubule-

associated protein tau gene facilitates the generation of tau circular RNA, or circRNA. Under physiological conditions, exon 12 back-loops with exon 7 or exon 10, generating two forms: tau12 7 and tau12 10 circRNAs. The less abundant tau12 7 circRNA is able to initiate a continuous translation of RNA to protein while the predominant form tau12 10 circRNA is only translated under the circumstances of a frontotemporal dementia tau mutation. Epigenetic adenosine to inosine base changes, caused by adenine deaminase acting on RNA, ADAR, enzymes, strongly activate translation of both circRNAs. Inflammation, injury and ischemia increase the activity of ADAR enzymes. Translational products from the tau12 7 and tau12 10 circRNAs form aggregates similar to neurofibrillary tangles. Stamm's group further found a linear relationship between circular RNA and AD disease severity in brains from people with AD.8 These novel insights into fundamental understanding of tauopathy and open new frontiers for biomarker and therapeutic development for AD/ADRD.



Recently funded projects advancing understanding of how TBI contributes to AD and other dementia:

Contribution of Thrombin Signaling to Alzheimer's Disease Pathology Following TBI: The thrombin signaling pathway may serve as a central mediator for AD cerebrovascular dysfunction following TBI. Understanding this pathway may lead to acute therapeutic targets for reducing neurodegeneration after TBI. Jaclyn lannucci, Ph.D., Texas A&M University

Do Microbiome-Derived Cell Fragments in the Brain Accelerate Transition from TBI to AD/ADRD? Understanding of the role of inflammation induced by microbiota-derived cells or cell fragments brings up an unprecedented opportunity of active and passive vaccinations that target the conserved microbial surface polysaccharide PNAG to prevent AD/ADRD. Colette Cywes-Bentley, Ph.D., Brigham and Women's Hospital; Michael Whalen, M.D., Massachusetts General Hospital

Protecting Neural Circuitry Underlying Memory-Dependent Learned Behavior: With the songbird as a novel animal model whose singing mimics the human language, Soderstrom is investigating the efficacy of cannabidiol in preserving learning and memory after TBI. Kenneth Soderstrom, Ph.D., East Carolina University

Role of Obesity and Glucose Homeostasis in the Regulation of Brain Perineuronal Net Reorganization in Alzheimer's Disease: Neurons are surrounded by specialized extracellular matrix lattices crucial to their proper function and health. This project explores the hypothesis that metabolic disorders such as obesity and diabetes may increase the risk of AD/ADRD through protein component changes in this extracellular matrix network. Kimberly Alonge, Ph.D., University of Washington

Microglial NOX2/NLRP3 Inflammasome
Activation Drives Tau Pathology and Cognitive
Impairments in Chronic Traumatic Brain Injury:
Through genetic manipulation of the key molecules in the inflammatory pathway in mice undergoing severe or mild brain injury, this project aims to elucidate the role of microglial inflammatory dysregulation in neurodegeneration following TBI.

Joseph Ojo, Ph.D., The Roskamp Institute

TBI AS A RISK FACTOR FOR AD/ADRD:

One of the strongest risk factors for the development of cognitive decline is a history of a TBI, which is an incredibly common event for both military personnel and civilian athletes or those involved in traumatic accidents. A meta-analysis of thirtytwo population-based epidemiology studies showed that TBI is associated with a nearly 70% increased risk for dementia. U.S. Veterans with a history of TBI were twice as likely to develop dementia compared to the general U.S. population.¹⁰ Recent findings from PRARP studies show that specific factors such as cardiovascular health, genetics, injury timing, race, sex and socioeconomic status, all influence this relationship. 11, 12, 13, 14, 15,

¹⁶ These PRARP-funded studies have potential to change how we approach prevention and treatment for TBI-related cognitive decline.

IDENTIFYING AND MITIGATING RISK FACTORS FOR THE DEVELOPMENT OF AD/ADRD

The PRARP is dedicated to funding research **Biological** that identifies risk factors that lead to the development of cognitive decline as individuals age. Vascular Genetics The goal of this portfolio disease is to develop culturally competent strategies to reduce controllable AD/ Healthcare Military ADRD risk and prevent Risk Factors for Environmental service Structural cognitive decline. Risk AD/ADRD factors for AD/ADRD Location generally fall into four Injury (TBI) categories: biological, environmental. psychosocial and structural. These risk exposure Socioeconomic status factors can further be categorized as modifiable factors, variables that an Depression individual can change or influence, or unmodifiable factors. **Psychosocial**

NON-MODIFIABLE RISK

- Genetics
- Age
- Gender
- Ethnicity/Race
- Family history



MODIFIABLE RISK

- Toxin exposure (e.g., smoking, alcohol)
- Cardiovascular health
- Diet and activity
- Depression and stress

Recently Funded Epidemiological / Risk Factor Projects:

Alzheimer's Disease Blood-Testing Initiative: Accelerating Blood-Based Diagnosis of AD/ADRD in Veterans: To achieve better and more accurate screening and diagnosis of AD, this study will test novel amyloid and tau blood biomarkers and identify clinical predictors of cognitive decline in Veterans. Raquel Gardner, M.D., Sheba Medical Centre

The Role of Environmental Stressors on Veteran's Neurocognitive Aging: This research examines the relationships among exposure to environmental stressors, brain structure,

inflammation, cognition and blood biomarkers in Veterans with a history of cognitive decline and/or TBI. Sharlene Newman, Ph.D., The University of Alabama

Facilitators and Barriers to the Use of Homeand Community-Based Clinical Services: An ongoing epidemiological study to record the use of community-based services of Veterans with or at risk of early-onset cognitive decline, and to identify novel and unique strategies to meet the needs of Veterans and their caregivers. Erin Bouldin, Ph.D., The University of Utah

Neural Imaging and Machine Learning Approaches to Estimate Brain Age and Post-TBI Decline:

Andrei Irimia, Ph.D., University of Southern California

This study leveraged machine learning to identify risk factors for cognitive decline and AD/ADRD progression using brain scans in older adults. Mild TBI experienced by individuals between 57 and 79 years old led to changes in neural activity identical to AD patterns as early as six months post-TBI. These data suggest that the age of injury is an important factor for cognitive decline. The team recently demonstrated that the machine learning approach can identify differences between chronological age and MRI-derived brain age to systematically identify other risk factors for decline post-TBI. In individuals with mild cognitive impairment, brain age estimates are significantly better than chronological age in capturing dementia symptom severity, functional disability and executive function. This technology's early detection of neural changes post-TBI and will allow for earlier detection and intervention.

Risk Factors and Cognitive Decline in U.S. Veteran Populations:

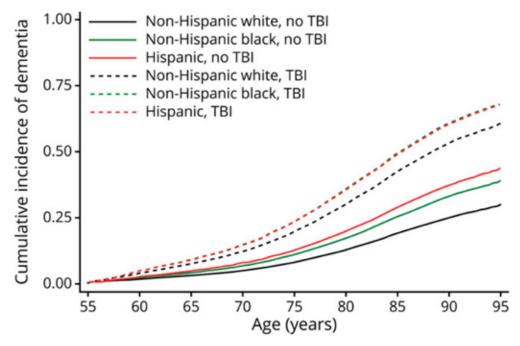
Kristine Yaffe, M.D., University of California, San Francisco

The Yaffe research team lead several PRARP-funded studies that leverage two large, established datasets to examine how TBI, sex, race, ethnicity and socioeconomic status contributes to developing cognitive decline and dementia in Veterans, civilians and twin pairs.

Genetics: Data from the twin studies suggest that TBI increases the risk of all cause dementia when controlling for genetic and environmental factors.¹⁷

Socioeconomic: A retrospective analysis of data from the Veterans Health Administration examined the impact of socioeconomic status on dementia incidence using the publicly available area deprivation index. Veterans living in more economically disadvantaged areas had a significantly increased risk of dementia.¹²

Health Disparities: An analysis of Veterans receiving care from the VHA shows that Hispanic and Black Veterans have a higher incidence of dementia diagnoses than any other ethnic group.¹⁴



Adjusted Cumulative Incidence of Dementia by Race and TBI Status. Mortality by age at dementia diagnosis with and without TBI, in White, Black and Hispanic Veterans. Data are adjusted for demographic and mortality health characteristics.¹⁴



70% increased risk of dementia after traumatic brain injury across thirty-two population studies.¹⁰



2X as likely to develop dementia post-TBI for Veterans than the general U.S. population.¹⁰



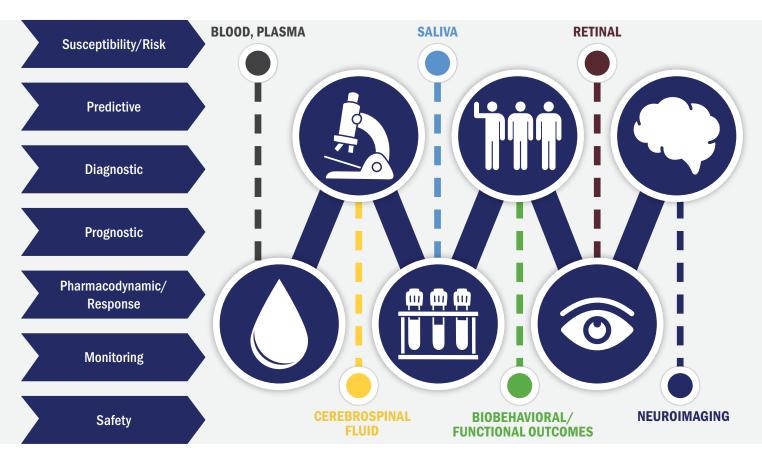
Reprioritizing Sex and Race Inclusivity in Risk Factor Research:

Out of 38 PRARP-funded risk factor research studies, only 13 incorporated efforts to sample a diverse population within their research strategy. PRARP is committed to improving these numbers and reducing health disparities in current and future epidemiological dementia research.

IMPROVING DIAGNOSIS NOW

Currently, physicians diagnose AD/ADRD by exclusion, which means individuals must go through many tests to first rule out other conditions. PRARP aims to change this by supporting projects that make diagnosis easier to achieve and by improving how we monitor AD/ADRD to help better care decisions.

TYPES OF AD/ADRD BIOMARKERS AND HOW THEY ARE MEASURED



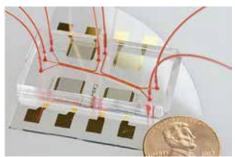


Acoustofluidic Multimodal Diagnostic System that Transforms the Diagnosis of AD/ADRD:

Tony Huang, Ph.D., Duke University

A new diagnostic technology supported by PRARP uses an acoustofluidic multimodal system to detect Alzheimer's disease biomarkers in human plasma. This approach first uses sound

to remove microscopic contaminants from the raw plasma to preserve incredibly small, nanosized particles in a matter of seconds. The integrated system incorporates Alzheimer's disease-specific antibodies also known as anti-Aß42 and anti-tau to significantly improve the sensitivity, specificity, and accuracy of detection of nanosized Alzheimer's disease-associated particles.



Picture of the acoustofluidic separation chip for isolating biomarkers from biofluids such as plasma samples.



Increasing the Sensitivity and Specificity of Classical Biomarkers for AD/ADRD:

Jeff Debad, Ph.D., Meso Scale Diagnostics, LLC

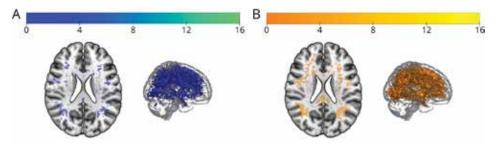
A diagnostic device assesses brain injury using ultra-sensitive immunoassays. These tests reliably detect site-specific tau phosphorylation in Service Members following blast-related TBI.



Advanced Neuroimaging for Detection of Early, Subtle Changes of Neurites, Micro-Vasculature and Inflammatory Changes of Different Brain Regions after TBI:

Christopher Rowe, M.D., University of Melbourne

Enlarged perivascular spaces seen in MRI images are associated with reduced verbal memory performance in the chronic, post-TBI period. These images suggest that impairments in glymphatic system function may be involved in the development of dementia following TBI.¹⁸



(A) ePVS overlap image for control participants (n = 75). (B) ePVS overlapmap for Participants With TBI (n = 100). (C) Case example of ePVS in a participant with TBI. Red circles denote a region of ePVS. ePVS = enlarged perivascular space; TBI = traumatic brain injury.

Virtual Reality-Based Diagnostic Tests to Capture Cognitive Decline in Everyday Scenarios:

Michael Barnett, Ph.D., The University of Texas at Tyler

The Virtual Environment Grocery Store and Virtual Apartment assessments use real-life scenarios, such as shopping from a list and budgeting, to diagnose cognitive impairment in aging adults. These tests show similar results to more traditional and abstract penand-paper tests used in a clinic setting.¹⁹







Recently funded projects:



Modifications Related to Cognitive Decline in Type 2 Diabetes and Preclinical Alzheimer's Disease:

Elevated plasma triglyceride/HDL cholesterol ratios and plasma ApoA1 are associated with worse cognitive outcomes in MCI and dementia participants, indicating their potential as promising prognostic markers to evaluate and predict the course of cognitive decline. *Jagan Pillai, M.D., Ph.D., Cleveland Clinic*



Blood-Based Biomarkers of TBI and Related Vascular Dementia:

To understand the relationship between TBI-related neurodegeneration and vascular dysfunction, Lippa leads an effort to analyze multi-panel blood and neuroimaging biomarkers related to neurovascular changes after TBI that could predict future cognitive decline in Service Members and Veterans. Sara Lippa, Ph.D., Walter Reed National Military Medical Center



Development of Blood-Based Biomarker of Blood Brain Barrier Dysfunction in Traumatic Brain Injury:

An investigation into the potential of the protein sPDGFR-ß for prognosis of long-term cognitive outcomes in individuals who have a TBI. Danielle Sandsmark, M.D., Ph.D., University of Pennsylvania



Detection and Characterization of Alpha-Synuclein Aggregates in Patients with ADRD:

This study uses the misfolding cyclic amplification technique to detects levels of the abnormal α-synuclein protein in biofluid samples of patients with AD/ADRD. Mohammad Shahnawaz, Ph.D., The University of Texas Health Science Center at Houston

LIVING WITH A DEMENTIA DIAGNOSIS

A cornerstone of the PRARP is the dedication to solutions that improve the lives of those living with a dementia diagnosis, their caregivers and families. Significant research is needed to develop new and improved approaches, interventions and resources to best support those whose everyday reality is living with AD/ADRD.



Prioritizing Community Engagement

In FY22, PRARP required funded clinical research to include community engagement and collaboration. Doing so supports equitable relationships among the researchers, community members and representatives. This gives an important seat at the table for those affected by dementia, giving them a platform to guide to guide the most impactful research through patient advocacy.

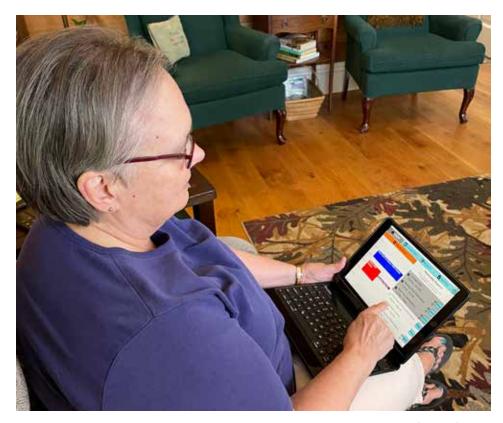
An Innovative Supportive Care Model for Dementia and Traumatic Brain Injury: Carol Manning, Ph.D., University of Virginia

This clinical trial examines how effectively a 12-month telehealth-delivered dementia care coordination program can improve the quality of life for both care partners and people living with a dementia diagnosis. The support sessions are designed to give easy-to-understand education on dementia, community resources, behavioral symptom management and counseling that meet a client's specific needs. By making the intervention available via telehealth, the hope is that this will improve access to TBI and dementia care in underserved communities.

Digital Technologies to Improve Memory and Everyday Functioning in Persons with Cognitive Decline:

Maureen Schmitter-Edgecombe, Ph.D., Washington State University

The Electronic Memory and Management Aid is a digital application that tracks activity and prompts individuals to complete everyday tasks in the home, promoting independence and reducing reliance on caregivers while managing life with a dementia diagnosis.²⁰



An individual living with cognitive impairment accessing the EMMA software for activity prompting and reminders to help with daily tasks.



Telehealth-Based Mind-Body Interventions to Improve Cognition and Quality of Life in Individuals with MCI and Their Caregivers:

Linda Chao, Ph.D., University of California, San Francisco

The Moving Online Together Investigation of Neurocognition study, or MOTION, is a telehealth mind-body intervention to improve the quality of life for older adults living with cognitive decline and their care-partners. The study focuses on group exercises that incorporate principles like learning-by-doing, staying active, setting goals, staying mindful, breathing exercises, fostering positivity and promoting social connections.

In earlier research funded by PRARP, the Chao research team found that older adults with mild cognitive impairment who took part in the program experienced better brain function, improved cognitive skills, better emotional regulation, increased wellbeing and felt less lonely.²¹

The current MOTION study includes a randomized clinical trial via telehealth delivery that directly compares the effects of T'ai Chi Chih to a standard health and wellness educational program in older adults with MCI. Additionally, the MOTION study is investigating how these interventions affect the neural mechanisms in the brain by conducting in-person follow-up assessments.

One of the most important aspects of Chao's MOTION study is the partnership with Together Senior Health, a community-based information technology company that delivers livestreaming mind-body group programs to people living with memory loss. For MOTION, they deliver the interventions virtually to study participants. The study team also leverages relationships with the Los Angeles County Department of Mental Health Services for older adults to reach minority groups and those with the most need. This type of research approach is called community-based participatory research as it engages community groups to be equitable partners in the research, making MOTION more accessible to diverse populations, and setting the stage for future outreach in assisted-living facilities, retirement homes and clinics.



TSH Telehealth platform for intervention delivery with video streams and chat functionality.

Recently Funded Quality of Life Projects:

Wellness, Coping, and Adaptation for Neurologic Conditions, WeCAN:
A 12-session wellness-based program that teaches self-management techniques for stress, coping skills and problem solving for people with TBI or dementia diagnoses. Denise Krch, Ph.D.. Kessler Foundation

Minds Navigating the Diagnosis of Mild Cognitive Impairment (MIND-MCI): A 9-session, group-based telehealth intervention that includes training on compensatory strategies, coping skills and health behavior self-management techniques in Veterans living with MCI diagnoses. Patricia Pilkinton, M.D. and Mary Lindsey Jacobs Dodson, Ph.D., Tuscaloosa VA Medical Center

Supporting Caregivers of Veterans with TBI and Mixed Dementia: The REACH Hope Behavioral Intervention: This randomized clinical trial is testing the ability of the individualized support intervention Resources for Enhancing All Caregivers Health, REACH, combined with the DOD's Virtual Hope Box smartphone application, REACH-HOPE, to improve caregivers' quality of life, depression and anxiety symptoms, and confidence in themselves as caregivers. Linda Nichols, Ph.D., Memphis VA Medical Center

"I am honored to be a part of the Peer-Reviewed Alzheimer's Research Program. As the wife of a Veteran with Alzheimer's Disease, I appreciate the need for innovative approaches to study traumatic brain injury in relation to dementia. The impact of studying the relationship between military risk factors and the devastation of brain degeneration as well as possible disease modifiers, caregiver support, and progress toward treatment/prevention will be life changing. Our Veterans and their Families will greatly benefit from this vital process."

Sarah Hornback,

Greater Kentucky and Southern Indiana Chapter, Alzheimer's Association

FY24 PROGRAMMATIC PANEL

The Programmatic Panel guides the investment strategy to address the mission and vision of the PRARP.

Heather Snyder, Ph.D. (Chair) *Alzheimer's Association*

Peter Bayley, Ph.D.Stanford University

Sarah Hornback

Greater Kentucky and Southern Indiana Alzheimer's Association

Michael Jaffee, M.D. University of Florida

Terrance Kummer, M.D., Ph.D. Washington School of Medicine

Erin Long, M.S.W.

U.S. Department of Health and Human Services, Administration for Community Living

Capt. Andres Martin, U.S. Marine Corps Retired

Senior Master Sgt. Anitra Mostacero, M.B.A., U.S. Air Force Retired National Council of Black Dementia Minds/Alzheimer's Association

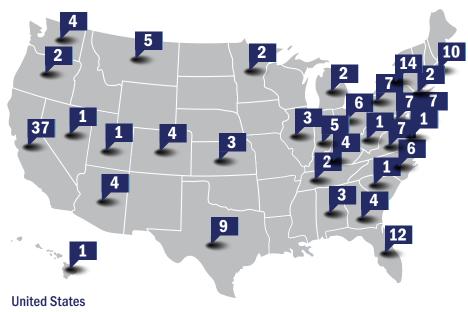
Lucien Richardson

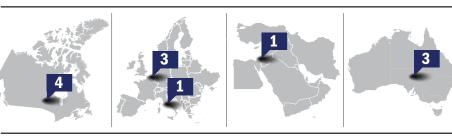
South Carolina Alzheimer's Association

Andrea Schneider, M.D., Ph.D. Penn Neuroscience Center, University of Pennsylvania

Andrew Teich, M.D., Ph.D.
Columbia University Medical
Center

FY11-FY23 Awards by Organization Location

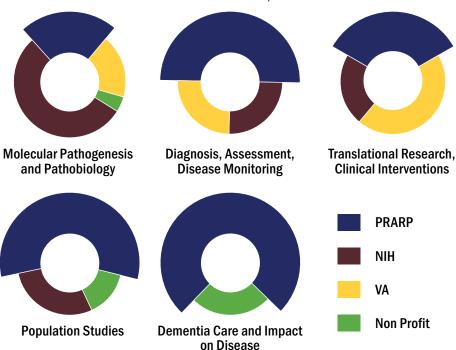




Canada Belgium & Italy

Israel Australia

Investment in TBI-focused AD research, 2008-2021



ENDNOTES

- ¹ Miranda, André Miguel, et al., "Effects of APOE4 allelic dosage on lipidomic signatures in the entorhinal cortex of aged mice," Translational Psychiatry 12, no. 1 (2022): 129, https://doi. org/10.1038/s41398-022-01881-6.
- ² Gibbons, Laura E., et al., "Association of Traumatic Brain Injury with Late Life Neuropathological Outcomes in a Community-Based Cohort," Journal of Alzheimer's Disease 93, no. 3 (2023): 949-961, https://doi.org/10.3233/JAD-221224.
- ³ Postupna, Nadia, et al., "The Delayed Neuropathological Consequences of Traumatic Brain Injury in a Community-Based Sample," Frontiers in Neurology 12 (2021): 624696, https://doi.org/10.3389/fneur.2021.624696.
- ⁴ Martinez, Pablo, et al., "Bassoon contributes to tau-seed propagation and neurotoxicity," Nature Neuroscience 25, no. 12 (2022): 1597-1607, https://doi.org/10.1038/s41593-022-01191-6.
- 5 Prakash, Priya, et al., "Amyloid β Induces Lipid Droplet-Mediated Microglial Dysfunction in Alzheimer's Disease," bioRxiv [Preprint].
- ⁶ Bowles, Kathryn R., et al., "ELAVL4, splicing, and glutamatergic dysfunction precede neuron loss in MAPT mutation cerebral organoids," Cell 184, no. 17 (2021): 4547-4563, https://doi.org/10.1016/j.cell.2021.07.003.
- ⁷ Hung, Shu-Ting, et al., "PIKFYVE inhibition mitigates disease in models of diverse forms of ALS," Cell 186, no. 4 (2023): 786-802, https://doi.org/10.1016/j.cell.2023.01.005.
- ⁸ Arizaca Maquera, et al., "Alzheimer's disease pathogenetic progression is associated with changes in regulated retained introns and editing of circular RNAs," Frontiers in Molecular Neuroscience 16 (2023): 1141079, https://doi.org/10.3389/fnmol.2023.1141079.
- ⁹ Welden, Justin Ralph, et al., "RNA editing of microtubuleassociated protein tau circular RNAs promotes their translation and tau tangle formation," Nucleic Acids Research 50, no. 22 (2022): 12979-12996, https://doi.org/10.1093/nar/gkac1129.
- ¹⁰ Gardner, Raquel C., et al., "Systematic Review, Meta-Analysis, and Population Attributable Risk of Dementia Associated with Traumatic Brain Injury in Civilians and Veterans," Journal of Neurotrauma 40, No. 7-8 (2022): 620-634, https://doi.org/10.1089/neu.2022.0041.
- ¹¹ Akushevich, Igor, et al., "Vulnerability to Hypertension Is a Major Determinant of Racial Disparities in Alzheimer's Disease Risk," American Journal of Hypertension 35, no. 8 (2022): 745-751, https://doi.org/10.1093/ajh/hpac063.
- ¹² Dintica, Christina S., et al., "Dementia Risk and Disadvantaged Neighborhoods." JAMA Neurology 80, no. 9 (2023): 903-909, https://doi.org/10.1001/jamaneurol.2023.2120.

- ¹³ Irimia, Andrei, et al., "Acute cognitive deficits after traumatic brain injury predict Alzheimer's disease-like degradation of the human default mode network," Geroscience 42, no. 5 (2020): 1411-1429, https://doi.org/10.1007/s11357-020-00245-6.
- ¹⁴ Kornblith, Erica, et al., "Sex, race, and risk of dementia diagnosis after traumatic brain injury among older veterans," Neurology 95, no. 13 (2020): e1768-e1775, https://doi.org/10.1212/wnl.000000000010617.
- ¹⁵ Yashkin, Arseniy P., et al., "Differences in Risk of Alzheimer's Disease Following Later-Life Traumatic Brain Injury in Veteran and Civilian Populations," The Journal of Head Trauma Rehabilitation 38, no. 6 (2023):E384-E393, https://doi.org/10.1097/htr.0000000000000865.
- ¹⁶ Yin, Chenzhong, et al., "Anatomically interpretable deep learning of brain age captures domain-specific cognitive impairment," Proceedings of the National Academy of Sciences of the United States of America 120, no. 2 (2023): e2214634120, https://doi.org/10.1073/pnas.2214634120.
- ¹⁷ Plassman, Brenda L., et al., "Traumatic brain injury and dementia risk in male veteran older twins Controlling for genetic and early life non-genetic factors," Alzheimer's & Dementia: The Journal of the Alzheimer's Association 18, no. 11 (2022): 2234-2242, https://doi.org/10.1002/alz.12571.
- ¹⁸ Hicks, Amelia J., et al., "Associations of Enlarged Perivascular Spaces With Brain Lesions, Brain Age, and Clinical Outcomes in Chronic Traumatic Brain Injury," Neurology 101, no. 1 (2023): e63-e73, https://doi.org/10.1212/wnl.0000000000207370.
- ¹⁹ Barnett, Michael D., et al., "Comparison of Traditional and Virtual Reality-Based Episodic Memory Performance in Clinical and Non-Clinical Cohorts," Brain Science 12, no. 8, (2022): 1019. https://doi.org/10.3390%2Fbrainsci12081019.
- ²⁰ Schmitter-Edgecombe, Maureen, et al., "Partnering a Compensatory Application with Activity-Aware Prompting to Improve Use in Individuals with Amnestic Mild Cognitive Impairment: A Randomized Controlled Pilot Clinical Trial," Journal of Alzheimer's Disease 85, no. 1 (2022): 73-90, https://doi.org/10.3233/jad-215022.
- ²¹ Chao, Linda L., et al., "Preventing Loss of Independence through Exercise (PLIÉ): A Pilot Trial in Older Adults with Subjective Memory Decline and Mild Cognitive Impairment," Journal of Alzheimer's Disease 82 (4): 1543-1557, https://doi.org/10.3233/jad-210159.



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