

DEPARTMENT OF DEFENSE
BLAST INJURY RESEARCH PROGRAM COORDINATING OFFICE

Does Repeated Blast-Related Trauma Contribute to the Development of Chronic Traumatic Encephalopathy (CTE)?

3-5 NOVEMBER 2015

The VA Perspective on the State of the Problem and Policy Considerations:

Past, Present, and Future

November 3, 2015

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The Past



The Sphere is a large metallic sculpture by German sculptor Fritz Koenig, currently displayed in Battery Park, that once stood in the area between the World Trade Center towers in Manhattan.

To quote the artist at the Sphere's rededication: "It now has a different beauty, one I could never imagine. It has its own life – different from the one I gave to it".



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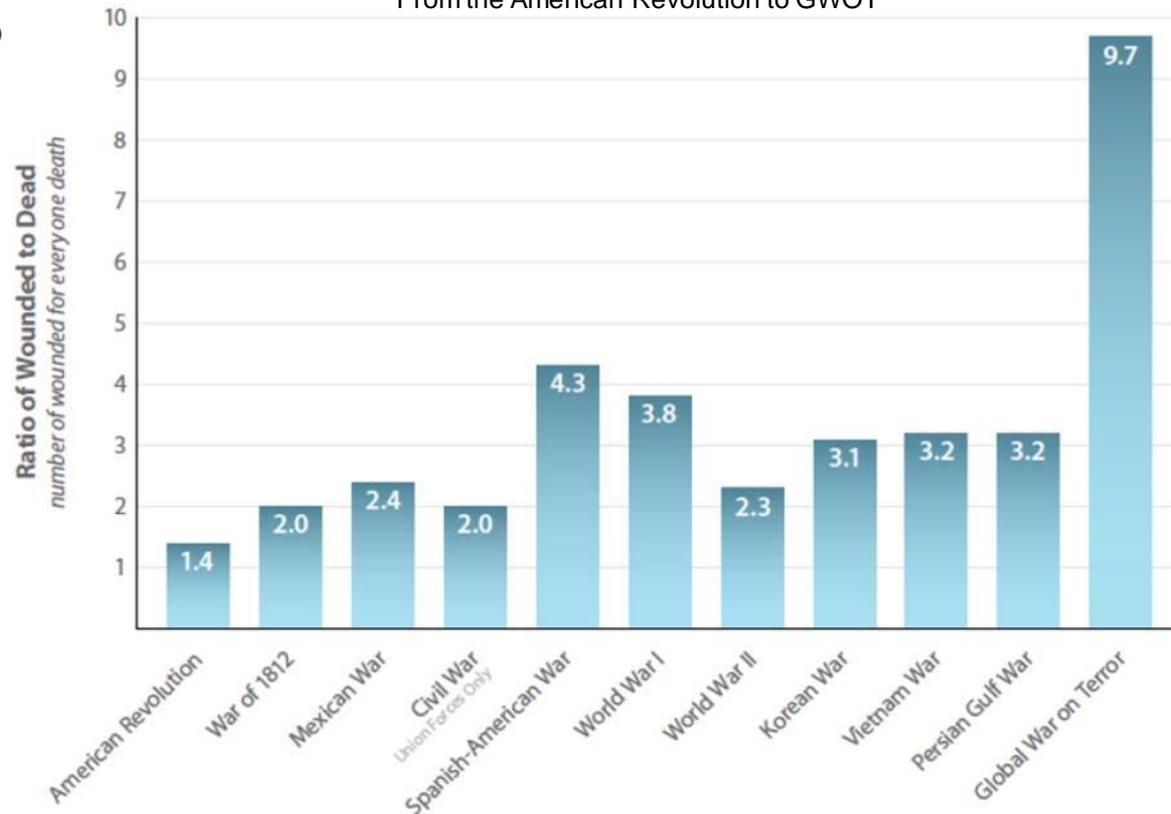
Background

Since September 11, 2001, more than 2.5 million service members have deployed to Iraq and Afghanistan in Operation Enduring Freedom, Operation Iraqi Freedom, and Operation New Dawn. Military forces sent to fight those wars have exhibited a number of unique features, including:

1. an all-volunteer military that has experienced multiple deployments to the war zone,
2. substantial use of the reserve components of the military and National Guard,
3. deployment of high numbers of women and parents of young children,
4. a high number of military personnel surviving severe injuries that in previous wars would have resulted in death.

Wounded to Dead Ratio

From the American Revolution to GWOT



IOM (Institute of Medicine), 2014



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Department of Veterans Affairs

“To care for him who shall have borne the battle, and for his widow and his orphan.”

Lincoln, 1865

Mission of VA Research and Development

The VA Office of Research and Development (ORD) aspires to discover knowledge, develop VA researchers and health care leaders, and create innovations that advance health care for our Veterans and the nation.



Does Repeated Blast-Related Trauma Contribute to the Development of Chronic Traumatic Encephalopathy (CTE)?

Present:

How do we get the Veteran re-integrated?



Inpatient

Caregivers/Family

Tele-Rehabilitation

Co-morbidities

Outpatient

Friends

Community Re-entry

Diagnostics

Re-integration

Job

Assistive Devices



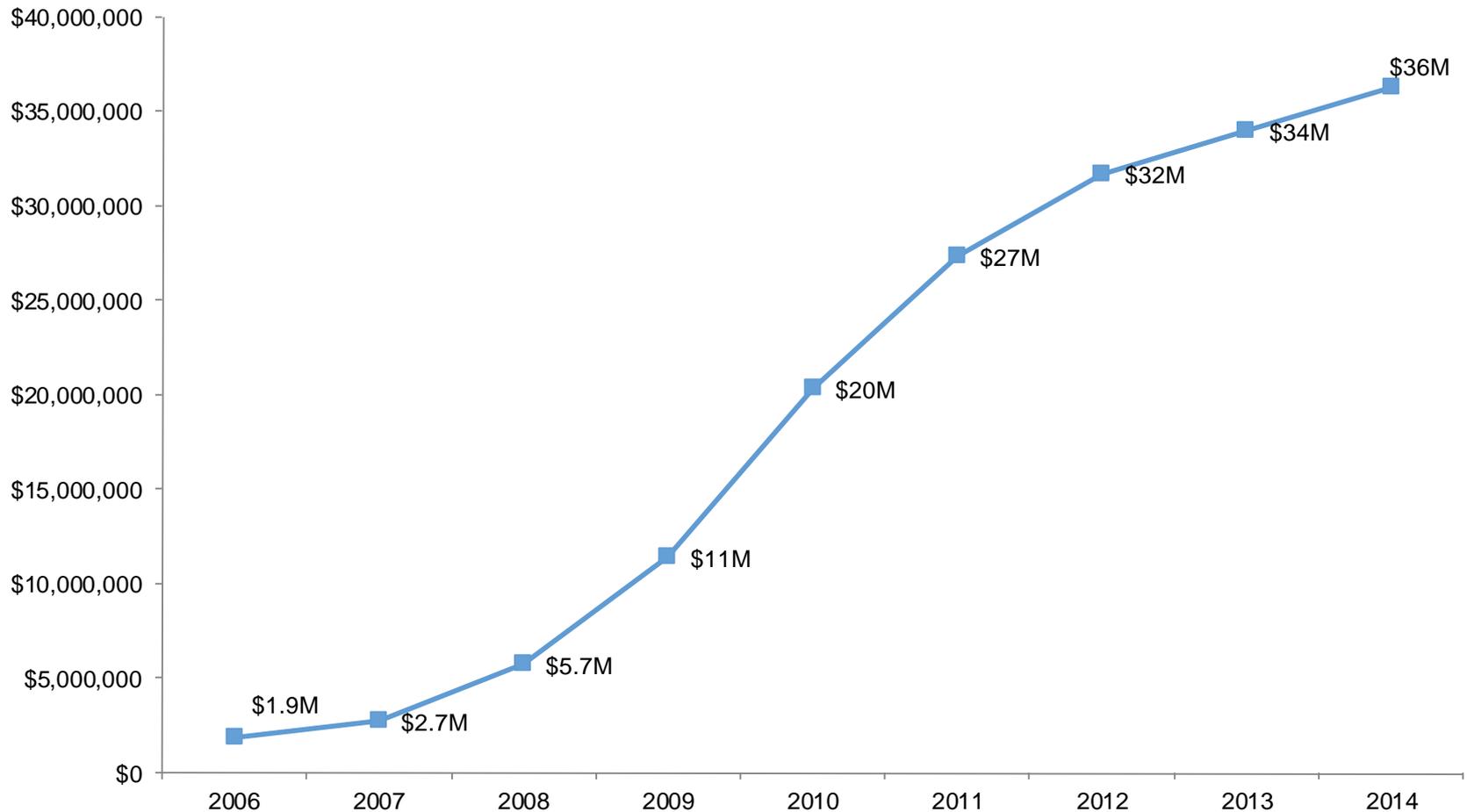
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Outcomes



Does Repeated Blast-Related Trauma Contribute to the Development of Chronic Traumatic Encephalopathy (CTE)?

Total Funding for TBI Research

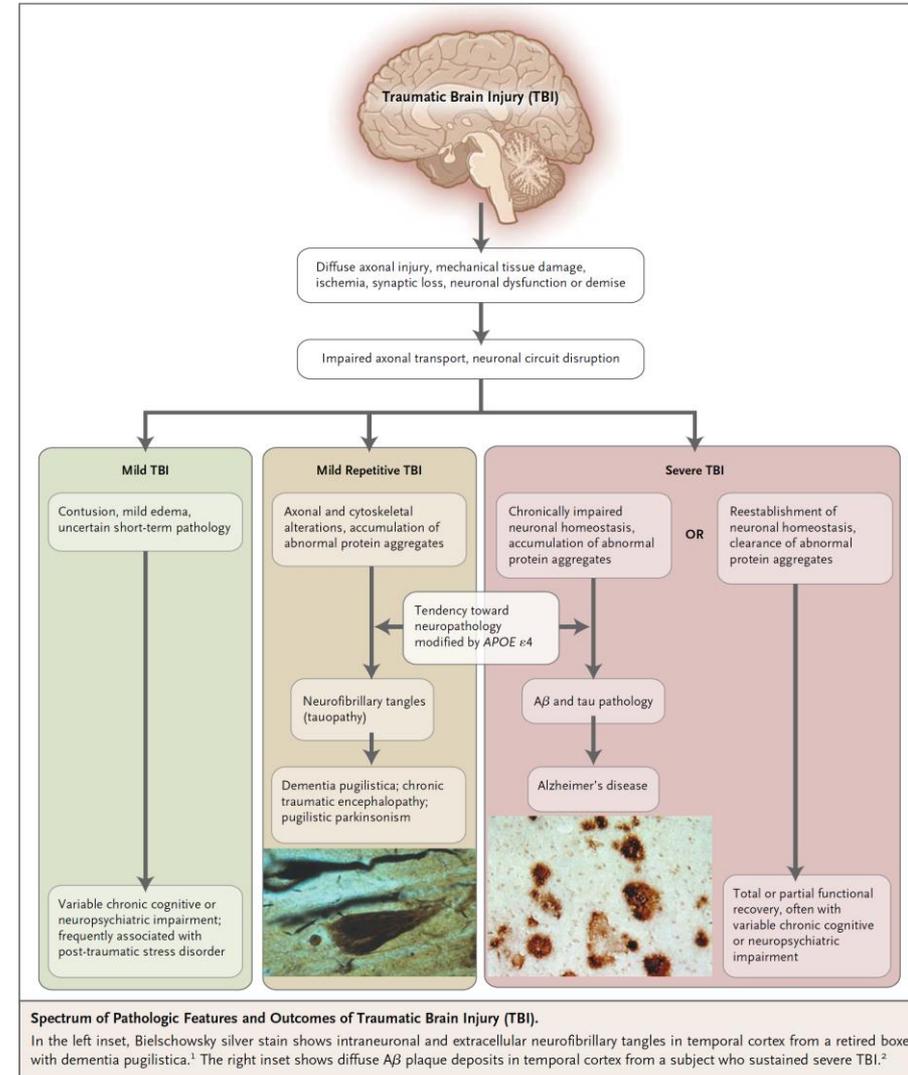




Does Repeated Blast-Related Trauma Contribute to the Development of Chronic Traumatic Encephalopathy (CTE)?

Making the connection between brain injury and CTE

- Multiple injuries BAD.
- Do multiple injuries lead to progressive degeneration?
- Are there necessary co-factors needed to trigger progressive degeneration, e.g., PEDS, gene variations, environmental exposures?





Does Repeated Blast-Related Trauma Contribute to the Development of Chronic Traumatic Encephalopathy (CTE)?

IMPROVING ACCESS TO MENTAL HEALTH SERVICES FOR VETERANS, SERVICE MEMBERS, AND MILITARY FAMILIES

Executive Order 13625 Sec. 5: PTSD, TBI, Suicide Prevention

The lack of full understanding of the underlying mechanisms of Post Traumatic Stress Disorder (PTSD), other mental health conditions, and Traumatic Brain Injury (TBI) has hampered progress in prevention, diagnosis, and treatment.

In order to improve the coordination of agency research into these conditions and reduce the number of affected men and women through better prevention, diagnosis, and treatment, the Departments of Defense, Veterans Affairs, Health and Human Services, and Education, in coordination with the Office of Science and Technology Policy, shall establish a National Research Action Plan within 8 months of the date of this order.



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Improving Access To Mental Health Services For Veterans, Service Members, And Military Families Executive Order 13625 Sec. 5: PTSD, TBI, Suicide Prevention: Goals

Requires development of National Research Action Plan (NRAP) with coordinated strategies for:

- Biomarkers for diagnosis and treatment
- Improved diagnostic criteria for TBI
- Mechanisms for PTSD, injuries and disorders following TBI
- New treatments based on mechanisms
- Improve data sharing & use of electronic health records (EHR)
- Collaborative research on suicide prevention
- DOD/DHHS comprehensive longitudinal mental health study
 - Enroll at least 100,000 service members by 12/31/12
 - Plan for long term follow up with enrollees through a coordinated effort with the Department of Veterans Affairs



Does Repeated Blast-Related Trauma Contribute to the Development of Chronic Traumatic Encephalopathy (CTE)?

National Research Action Plan

National Research Action Plan

Responding to the Executive Order
*Improving Access to Mental Health
Services for Veterans, Service Members,
and Military Families (August 31, 2012)*

Department of Defense
Department of Veterans Affairs
Department of Health and Human Services
Department of Education

August 2013

The image shows four circular seals arranged horizontally. From left to right: the Department of Defense seal, the Department of Veterans Affairs seal, the Department of Health and Human Services seal (featuring a stylized eagle), and the Department of Education seal (featuring a tree).



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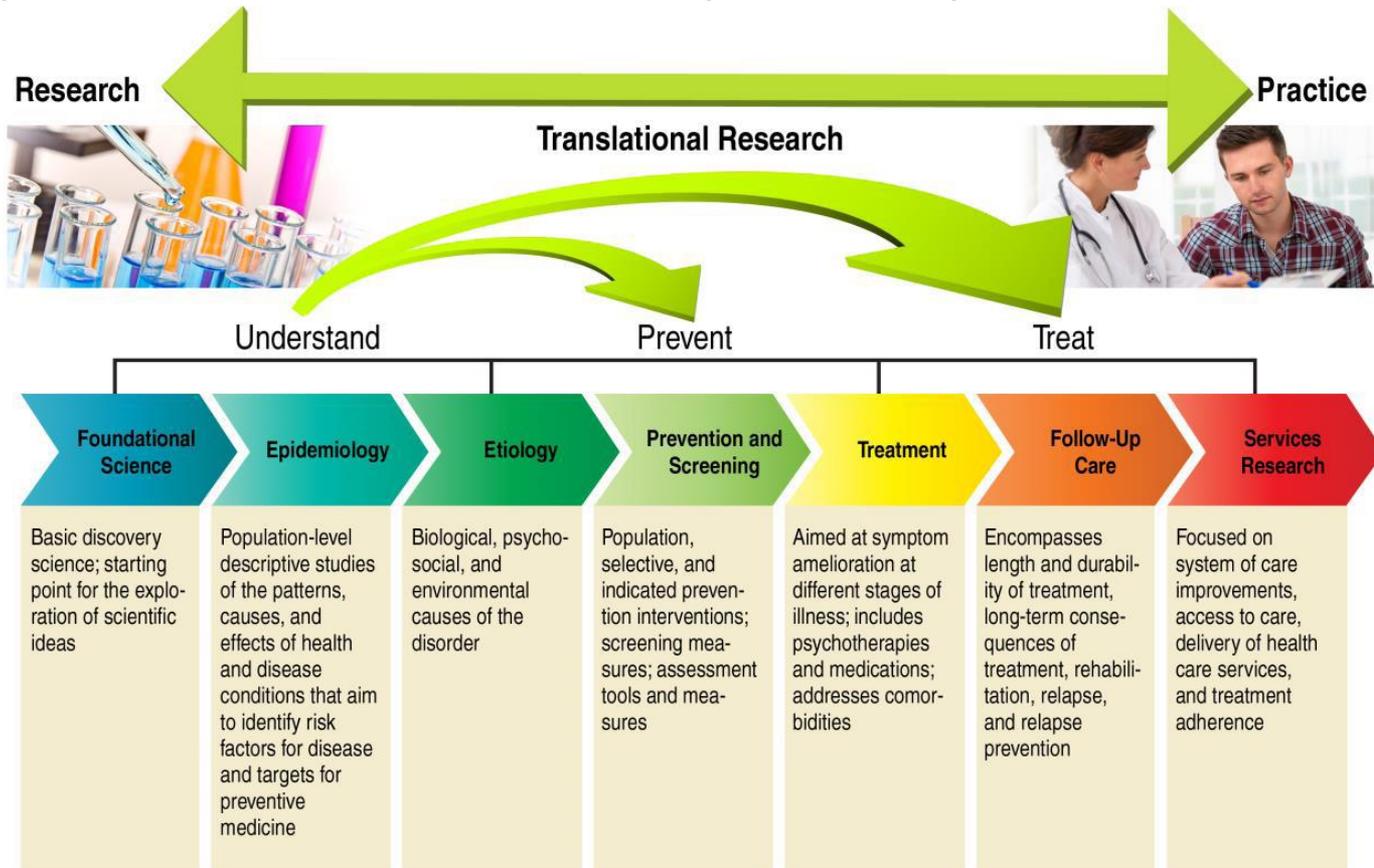




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NRAP Expectations

Continuum – from enhancing research capacity resources to funding strategic research and implementing promising practices





Does Repeated Blast-Related Trauma Contribute to the Development of Chronic Traumatic Encephalopathy (CTE)?



Chronic Effects of Neurotrauma Consortium

To establish the association (onset, prevalence, and severity) of the chronic effects of mild TBI (mTBI) and common comorbidities*

Determine whether there is a causative effect of chronic mTBI/concussion on neurodegenerative disease and other comorbidities*

Consortium Objectives

Identify diagnostic and prognostic indicators of neurodegenerative disease and other comorbidities associated with mTBI/concussion

Develop and advance methods to treat and rehabilitate chronic neurodegenerative disease and comorbid effects of mTBI/concussion

Goals

- Core facilities for common research efforts
- Alignment with DVBIC 15 Year Study for TBI
- Leverages
 - Multiple DoD and VA clinical sites
 - previously funded in-theater efforts for follow up data
 - DoD and VA Centers of Excellence
 - Nationwide expertise of established research networks
- Use of common data elements (CDEs) and entry of data into FITBIR
- Robust Peer Review Program to identify new projects

* Comorbidities include: psychological, neurological (memory, seizure, autonomic dysfunction, sleep disorders), sensory deficits (visual, auditory, vestibular), movement disorders, pain (including headache), cognitive, and neuroendocrine deficits

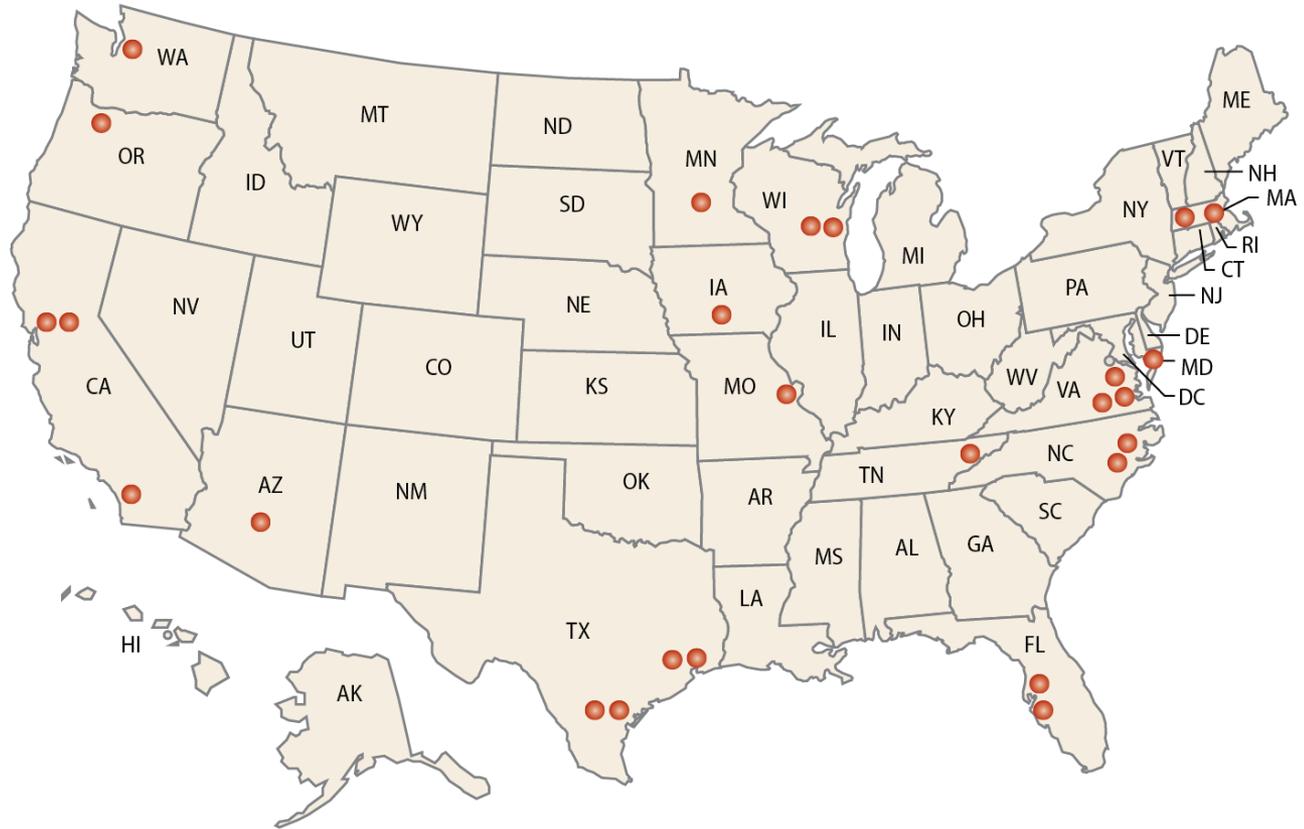


Does Repeated Blast-Related Trauma Contribute to the Development of Chronic Traumatic Encephalopathy (CTE)?



CENC Sites

- Barrows Neurological Institute, Phoenix, AZ
- Baylor College of Medicine, Houston, TX
- Boston University, Boston, MA
- Duke University School of Medicine, Durham, NC
- Fort Belvoir Community Hospital, Alexandria, VA
- Hunter Holmes McGuire VA, Richmond, VA
- James A. Haley Veterans Hospital, Tampa, FL
- Iowa City VA Health Care Center, Milwaukee, WI
- Michael E. DeBakey VA Medical Center, Houston, TX
- Milwaukee VA Medical Center, Milwaukee, WI
- Minneapolis VA Health Care System
- Mountain Home VA Medical Center, Mountain Home, TN
- Northern California Institute of Research and Education, San Francisco, CA
- Roskamp Institute, Sarasota, FL
- RTI International, Durham, NC



- San Antonio Military Medical Center, San Antonio, TX
- San Francisco VA Medical Center, San Francisco, CA
- South Texas Veterans Healthcare Center, San Antonio, TX
- Uniformed Services University of the Health Sciences, Bethesda, MD

- University of Missouri St. Louis, St Louis, MO
- University of Washington, Seattle, WA
- VA Boston Healthcare System
- VA Portland Health Care System
- VA San Diego Health Care System, San Diego, CA
- Virginia Commonwealth University, Richmond, VA



Does Repeated Blast-Related Trauma Contribute to the Development of Chronic Traumatic Encephalopathy (CTE)?

CENC Roadmap

Describe the common effects after mTBI

Research Question	Contributing Studies
Neurosensory Vision Hearing Vestibular	<ul style="list-style-type: none"> Observational Study on Late Neurologic Effects of OEF/OIF/OND Combat (Cifu) Assessment of Long-Term Outcome and Disability in Active-Duty Military Prospectively Examined Following Concussive TBI (MacDonald) Epidemiology of mTBI and Neurosensory Outcomes (Yaffe) Otolith Dysfunction and Postural Stability (Aiken) Visual Sensory Impairments and Progression Following Mild Traumatic Brain Injury (Kardon)
Neuroendocrine	<ul style="list-style-type: none"> Observational Study on Late Neurologic Effects of OEF/OIF/OND Combat (Cifu) Epidemiology of mTBI and Neurosensory Outcomes (Yaffe)
Seizures	<ul style="list-style-type: none"> Observational Study on Late Neurologic Effects of OEF/OIF/OND Combat (Cifu) Epidemiology of mTBI and Neurosensory Outcomes (Yaffe)
Sleep	<ul style="list-style-type: none"> Observational Study on Late Neurologic Effects of OEF/OIF/OND Combat (Cifu) Assessment of Long-Term Outcome and Disability in Active-Duty Military Prospectively Examined Following Concussive TBI (MacDonald) Epidemiology of mTBI and Neurosensory Outcomes (Yaffe) Novel White Matter Imaging to Improve Diagnosis of mTBI (Jak) Structural & Functional Neurobiology of Veterans Exposed to Blast Effects (Taber)
Pain	<ul style="list-style-type: none"> Observational Study on Late Neurologic Effects of OEF/OIF/OND Combat (Cifu) Assessment of Long-Term Outcome and Disability in Active-Duty Military Prospectively Examined Following Concussive TBI (MacDonald) Epidemiology of mTBI and Neurosensory Outcomes (Yaffe) Structural & Functional Neurobiology of Veterans Exposed to Blast Effects (Taber)
Cognitive	<ul style="list-style-type: none"> Observational Study on Late Neurologic Effects of OEF/OIF/OND Combat (Cifu) Assessment of Long-Term Outcome and Disability in Active-Duty Military Prospectively Examined Following Concussive TBI (MacDonald) Epidemiology of mTBI and Neurosensory Outcomes (Yaffe) Basic Science Tau Modification Study (Mufson/Crawford) Structural & Functional Neurobiology of Veterans Exposed to Blast Effects (Taber)

Research Question	Contributing Studies
Psychological	<ul style="list-style-type: none"> Observational Study on Late Neurologic Effects of OEF/OIF/OND Combat (Cifu) Assessment of Long-Term Outcome and Disability in Active-Duty Military Prospectively Examined Following Concussive TBI (MacDonald) Epidemiology of mTBI and Neurosensory Outcomes (Yaffe) Novel White Matter Imaging to Improve Diagnosis of mTBI (Jak) Structural & Functional Neurobiology of Veterans Exposed to Blast Effects (Taber)
Neurologic	<ul style="list-style-type: none"> Observational Study on Late Neurologic Effects of OEF/OIF/OND Combat (Cifu) Assessment of Long-Term Outcome and Disability in Active-Duty Military Prospectively Examined Following Concussive TBI (MacDonald) Epidemiology of mTBI and Neurosensory Outcomes (Yaffe) Basic Science Tau Modification Study (Mufson/Crawford) Novel White Matter Imaging to Improve Diagnosis of mTBI (Jak) Structural & Functional Neurobiology of Veterans Exposed to Blast Effects (Taber)

Define association between mTBI, common effects and neurodegeneration

Research Question	Contributing Studies
mTBI and Common Effects	<ul style="list-style-type: none"> Observational Study on Late Neurologic Effects of OEF/OIF/OND Combat (Cifu) Assessment of Long-Term Outcome and Disability in Active-Duty Military Prospectively Examined Following Concussive TBI (MacDonald) Epidemiology of mTBI and Neurosensory Outcomes (Yaffe) Basic Science Tau Modification Study (Mufson/Crawford) Otolith Dysfunction and Postural Stability (Akin) Novel White Matter Imaging to Improve Diagnosis of mTBI (Jak) Structural & Functional Neurobiology of Veterans Exposed to Blast Effects (Taber)
mTBI and Neurodegeneration	<ul style="list-style-type: none"> Observational Study on Late Neurologic Effects of OEF/OIF/OND Combat (Cifu) Assessment of Long-Term Outcome and Disability in Active-Duty Military Prospectively Examined Following Concussive TBI (MacDonald) Epidemiology of mTBI and Neurosensory Outcomes (Yaffe) Basic Science Tau Modification Study (Mufson/Crawford) Novel White Matter Imaging to Improve Diagnosis of mTBI (Jak) Structural & Functional Neurobiology of Veterans Exposed to Blast Effects (Taber)



Does Repeated Blast-Related Trauma Contribute to the Development of Chronic Traumatic Encephalopathy (CTE)?

Identify tools to measure the diagnosis and prognosis for common effects and neurodegeneration

Research Question	Contributing Studies
Tools to Diagnose and Prognosticate Common Effects after mTBI	<ul style="list-style-type: none"> • Observational Study on Late Neurologic Effects of OEF/OIF/OND Combat (Cifu) • Assessment of Long-Term Outcome and Disability in Active-Duty Military Prospectively Examined Following Concussive TBI (MacDonald) • Epidemiology of mTBI and Neurosensory Outcomes (Yaffe) • Otolith Dysfunction and Postural Stability (Akins) • Diffusion Tensor Imaging Standardization Using Novel MR Diffusion Phantoms (Wilde) • Novel White Matter Imaging to Improve Diagnosis of mTBI (Jak) • Structural & Functional Neurobiology of Veterans Exposed to Blast Effects (Taber) • Visual Sensory Impairments and Progression Following Mild Traumatic Brain Injury (Kardon) • Clinical and neuroimaging correlates of neurodegeneration in military mTBI (Davenport)
Tools to Diagnose and Prognosticate Common Neurodegeneration after mTBI	<ul style="list-style-type: none"> • Observational Study on Late Neurologic Effects of OEF/OIF/OND Combat (Cifu) • Assessment of Long-Term Outcome and Disability in Active-Duty Military Prospectively Examined Following Concussive TBI (MacDonald) • Epidemiology of mTBI and Neurosensory Outcomes (Yaffe) • Basic Science Tau Modification Study (Mufson/Crawford) • Diffusion Tensor Imaging Standardization Using Novel MR Diffusion Phantoms (Wilde) • Novel White Matter Imaging to Improve Diagnosis of mTBI (Jak) • Structural & Functional Neurobiology of Veterans Exposed to Blast Effects (Taber) • Clinical and neuroimaging correlates of neurodegeneration in military mTBI (Davenport) • Visual Sensory Impairments and Progression Following Mild Traumatic Brain Injury (Kardon)

Assess the efficacy of intervention for common effects and neurodegeneration after mTBI

Research Question	Contributing Studies
Assess Interventions for Neurosensory Common Effects	<ul style="list-style-type: none"> • Observational Study on Late Neurologic Effects of OEF/OIF/OND Combat (Cifu) • Assessment of Long-Term Outcome and Disability in Active-Duty Military Prospectively Examined Following Concussive TBI (MacDonald) • Otolith Dysfunction and Postural Stability (Akins)
Assess Interventions for Other Common Effects	<ul style="list-style-type: none"> • Observational Study on Late Neurologic Effects of OEF/OIF/OND Combat (Cifu) • Assessment of Long-Term Outcome and Disability in Active-Duty Military Prospectively Examined Following Concussive TBI (MacDonald)
Assess Interventions for Neurodegeneration	<ul style="list-style-type: none"> • Observational Study on Late Neurologic Effects of OEF/OIF/OND Combat (Cifu) • Assessment of Long-Term Outcome and Disability in Active-Duty Military Prospectively Examined Following Concussive TBI (MacDonald)



Does Repeated Blast-Related Trauma Contribute to the Development of Chronic Traumatic Encephalopathy (CTE)?

The VA TBI State-of-the-Art Conference

- The TBI SOTA was designed to be closely aligned to the National Research Action Plan.
- The VA TBI SOTA specifically addressed the research areas that were within its mission to improve the health and lives of our Veterans.
- The conference covered pre-clinical modeling, diagnostics, health services, co-morbidities, neurodegenerative conditions, caregiving, and CPGs.



Does Repeated Blast-Related Trauma Contribute to the Development of Chronic Traumatic Encephalopathy (CTE)?

The VA TBI State-of-the-Art Conference

- The TBI SOTA will have impact on VA research policy going into the future and will provide the basis for new RFAs.
- The SOTA demonstrated that research has the support of the VA leadership.



Does Repeated Blast-Related Trauma Contribute to the Development of Chronic Traumatic Encephalopathy (CTE)?

Recommendations for Future Research

- Effects of gender differences on TBI outcomes.
- Development of standardized animal injury models using common data elements.
- Various researchers discussed efforts to discern the effects of genetic markers upon injury responses, recovery, and resilience.
- Need for more research into the differing effects of injury type and number of insults has on the long-term mechanisms of degeneration.
- Improving the reach, efficacy, and acceptance of Telemedicine in terms of rehabilitation and clinical monitoring.



Does Repeated Blast-Related Trauma Contribute to the Development of Chronic Traumatic Encephalopathy (CTE)?

Conclusion

- VA has a committed policy on TBI research.
- VA recognizes the need to determine the long-term effects of repeated exposures to both blast and blunt trauma to the brain.
- VA research works closely with VA Patient Care Services in an integrative fashion to advance the care of the Veteran with TBI.