Potential Relationship Between Military Exposures & Traumatic Brain Injury

Mental Health Effects of Toxic Exposures Among Veterans (Meeting 2)

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Learning Objectives:

- 1. How is traumatic brain injury (TBI) defined and diagnosed by VA in the clinic
- 2. Relationship of TBI to other mental health conditions (depression, suicide attempts and fatalities, and dementia) among Veteran populations.
- 3. Relationship of Military Exposures to TBI and related co-morbidities



VA Diagnostic Approach

- Both the VA TBI screening instrument and Comprehensive TBI Evaluation define TBI as an index event, either self-reported or witnessed.
- Screening is 4-question survey; positive response to all 4 questions = positive screen.
- Comprehensive evaluation is an evaluation by medical provider (physician, PA, Nurse Practitioner) to include 22-item neurobehavioral symptom inventory, comprehensive history, consultation as appropriate to specialists to address symptoms/complaints.
- Without an affirmative answer for a potential TBI index event on the screen, a comprehensive evaluation will not be requested for the Veteran.
- The latest VA/DoD Clinical Practice Guidelines (2021) suggests additional research to determine if repeated low-level blast exposures lead to TBI symptoms.





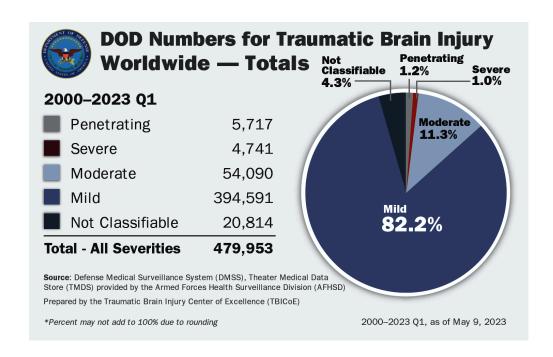
Diagnostics: VA-DoD Clinical Practice Guidelines for mTBI (2021)

- A traumatic brain injury (TBI) is defined as a traumatically induced structural injury and/or physiological disruption of brain function as a result of an external force. It is diagnosed by new onset or worsening of at least one of the following clinical signs immediately following the event:
 - Any period of loss of or a decreased level of consciousness
 - Any loss of memory for events immediately before or after the injury (post-traumatic amnesia)
 - Any alteration in mental state at the time of the injury (e.g., confusion, disorientation, slowed thinking, alteration of consciousness/mental state)
 - Neurological deficits (e.g., weakness, loss of balance, change in vision, apraxia, paresis/plegia, sensory loss, visual-spatial neglect, aphasia) that may or may not be transient
 - An intracranial lesion
- External forces may include any of the following events: the head being struck by an object, the head striking an object,
 the brain undergoing an acceleration or deceleration movement without direct external trauma to the head, a foreign
 body penetrating the brain, forces generated from events (e.g., a blast or explosion), or other forces
- The above criteria define the event of a TBI. Not all individuals exposed to an external force will sustain a TBI, but any person who has a history of such an event with immediate manifestation of any of the above signs and symptoms can be said to have had a TBI.
- No other diagnostic is recommended.





Current Number of Veterans with a Confirmed TBI Diagnosis Using the TBI Screen and Comprehensive TBI Evaluation



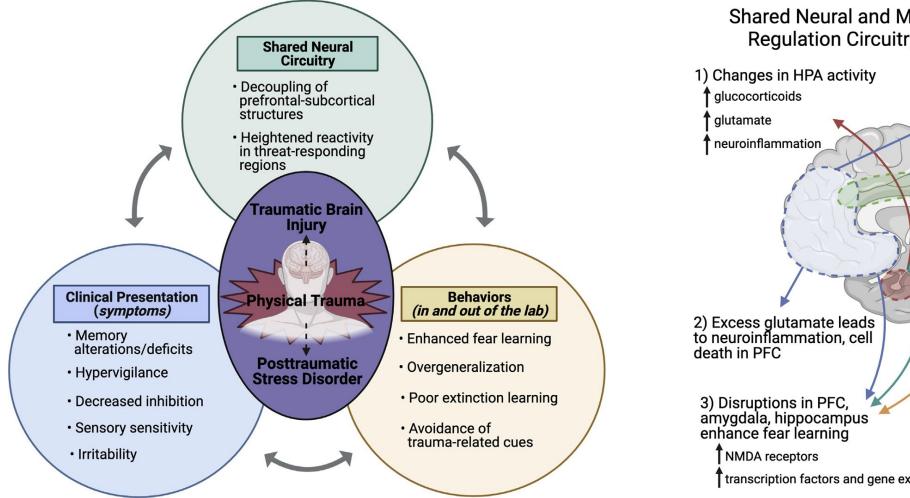
VHA TBI Numbers			
CTBIE Designation	Number of Veterans		
Number of Screens	1,704,154		
Number of Previous Positive Diagnosis	100,220		
Number of Positive Screens	306,913		
Completed Comprehensive Exams	175,934		
Positive for TBI Exams	107,474		
Total Confirmed TBIs	207,694		

Approximately 62% of Veterans utilize VA for healthcare.

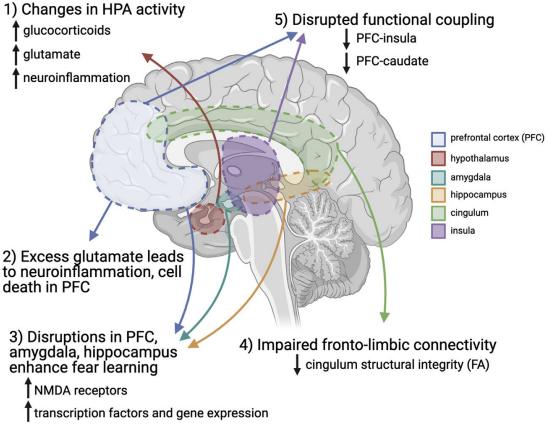




Overlap of Chronic TBI Symptoms and Mental Health Conditions



Shared Neural and Molecular Modifications of Emotion Regulation Circuitry Associated with PTSD and TBI



Weis CN, Webb EK, deRoon-Cassini TA, Larson CL. Emotion Dysregulation Following Trauma: Shared Neurocircuitry of Traumatic Brain Injury and Trauma-Related Psychiatric Disorders. Biol Psychiatry. 2022 Mar 1;91(5):470-477.





Association of TBI With Depression Status

TBI Severity, Depression Status, and Demographic Characteristics of Participants From Two Studies Included in Comparative Analyses (Mac Donald et al., 2019; Walker et al., 2016)

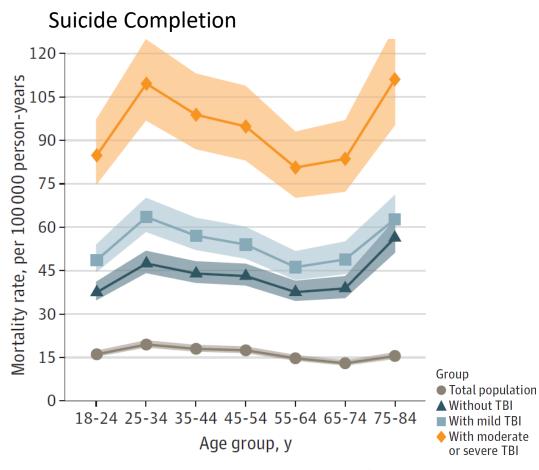
Value of outcome variable	Overall, $N = 1,633^{a}$	No TBI, $N = 326^{a}$	mTBI, $N = 1{,}307^{a}$
Depression			
Negative	468 (29%)	143 (44%)	325 (25%)
Positive	1,156 (71%)	181 (56%)	975 (75%)
Missing	9	2	7
Gender	•		·
Male	1,425 (87%)	257 (79%)	1,168 (89%)
Female	208 (13%)	69 (21%)	139 (11%)
Age category		(= - : -)	()
,25	30 (1.8%)	5 (1.5%)	25 (1.9%)
25–39	881 (54%)	183 (56%)	698 (54%)
40–49	444 (27%)	81 (25%)	363 (28%)
50–64	259 (16%)	50 (15%)	209 (16%)
65+	14 (0.9%)	5 (1.5%)	9 (0.7%)
Missing	5	2.	3
Race/ethnicity	Č	-	
Non-Hispanic White	929 (61%)	163 (53%)	766 (63%)
Other	595 (39%)	144 (47%)	451 (37%)
Missing	109	19	90
Population type	• • • • • • • • • • • • • • • • • • • •		· ·
Veteran/military	1,633 (100%)	326 (100%)	1,307 (100%)

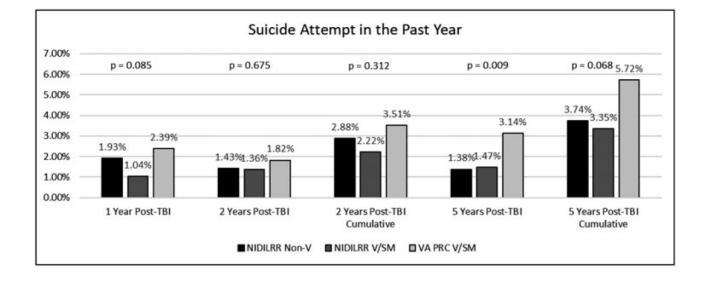
O'Neil, M. E., Krushnic, D., Clauss, K., Baker-Robinson, W., Hannon, S., Cameron, D. C., Cook, L., Niederhausen, M., Kaplan, J., & Brenner, L. A. (2024). Harmonizing federal interagency traumatic brain injury research data to examine depression and suicide-related outcomes. *Rehabilitation Psychology*. Advance online publication.





Long-term Risk of TBI to Brain and Mental in Veterans: Suicide



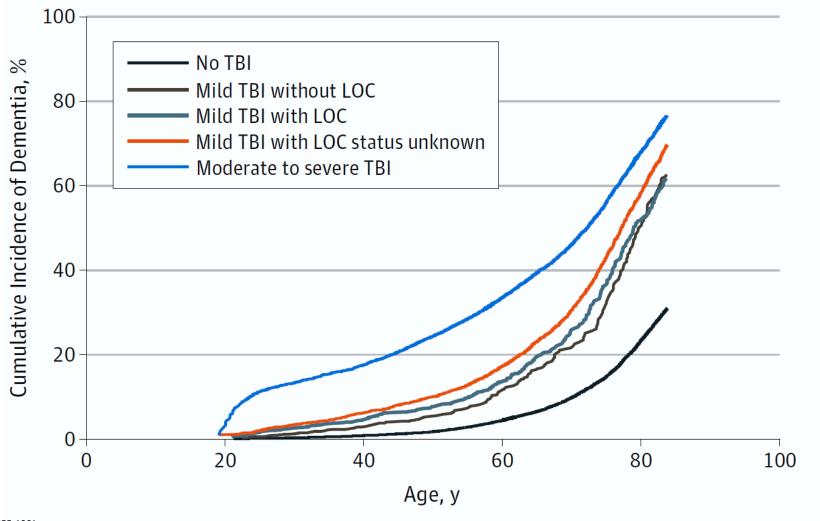


Howard et al., JAMA Network Open. 2022;5(2):e2148150. doi:10.1001/jamanetworkopen.2021.48150





Cumulative Incidence of Dementia by Traumatic Brain Injury (TBI) Severity



Barnes et al., JAMA Neurol. 2018;75(9):1055-1061.



TBI: Event vs Exposure

- Events can be exposures that occur repetitively over a lifetime, e.g., child abuse, contact sports, altercations, military service, assaults, or accidents.
- Alternatively, military exposures that are repetitive, subclinical injuries to the brain can accumulate over time without acute presentation of symptoms, e.g., loss of consciousness or alteration of consciousness.
- Focus of research has been on event-based TBI; however recent media reports have increased awareness of TBI from culminative military exposures.





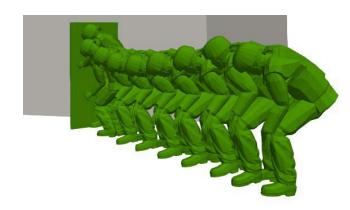
Types of Combat and Occupational Blast Exposures

Combat



Occupational













Raising Awareness to the Clinical Community

DOD Service Member Fact Sheet | July 2023 Information on Low-Level Blast Exposure Traumatic Brain Injury Center of Excellence

What is Low-Level Blast?
Blast generated from firing heavy weapon systems or explosives in combat or training environments. LLB exposure is not the same as a concussion/mild traumatic brain injury.

LLB Exposure May Cause

- · Concentration problems
- Irritability
- Memory problems
- · Slowed thinking/slow reaction time
- Decreased hand-eye coordination
- Difficulty hearing
- Headaches
- 207
 - . Tinnitus (ringing in the ears)

What Should Service Members Do?



Recognize

- There are specific military occupations at high risk for exposure.
- Certain heavy weapon systems have been identified as generating the most LLB exposure.
- There are ammunition firing limits for the weapon systems that you use.
- LLB exposure can vary depending upon your firing position and other environmental conditions.



Limit

Limit exposure to as low as reasonably achievable by:

- Keeping an appropriate distance from weapons being fired
- Turning in unused ammunition (i.e., avoid SPENDEX)
- Wearing appropriate protective equipment (e.g., helmet, hearing protection)
- Adhering to weapon system firing limits



Report

- Symptoms from LLB exposure typically resolve with time.
- If your symptoms persist and impact your daily function, inform your command and medical provider.
- Report to medical provider should include:
- Duration of exposure
- Number of blasts
- Years in high-risk occupation/ unit (e.g., MOS/NEC/AFSC)
 Symptom details and duration
- Refer to <u>health.mil/TBlfactsheets</u> for additional resources

DOD Service Member Fact Sheet | July 2023 Information on Low-Level Blast Exposure



Research is still emerging on the potential health effects of LLB exposure from heavy weapon systems. This fact sheet guidance is intended to raise LLB awareness and not meant to restrict mission-essential training.



4977.1.1.3 - Released July 2023 by the Traumatic Brain Injury Center of Excellence product is reviewed annually and is current until superseded. 800-870-9244 | Health.mil/TBICOE





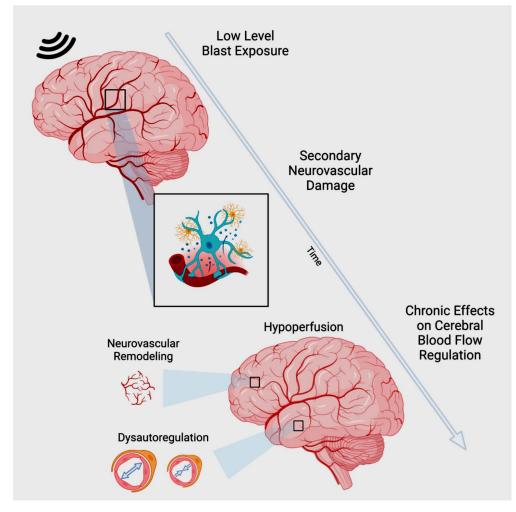


Prevalence in Service members and Veterans

- 98+ Military Occupational Specialty designations are considered to be at risk for occupation-related blast exposure.
- VA epidemiologists are collaborating with their DoD counterparts to get an estimate of the number at risk.
- The estimate of the potential number of Veterans who have been affected will provide the scope of the problem that may be encountered currently and into the future.

Cerebrovascular Effects of Blast Exposure

- Additional to the injury and dysfunction of neurons, various cerebrovascular pathologies are also present
- Loss of coupling of vasoreactivity to neuronal activity
- Aberrant neovascularization
- Dysfunctional blood-brain barrier



Kilgore, M.O.; Hubbard, W.B. Effects of Low-Level Blast on Neurovascular Health and Cerebral Blood Flow: Current Findings and Future Opportunities in Neuroimaging.Int. J. Mol. Sci. 2024, 25, 642.





Long-term Cerebrovascular Disruption

Cerebral hemorrhage

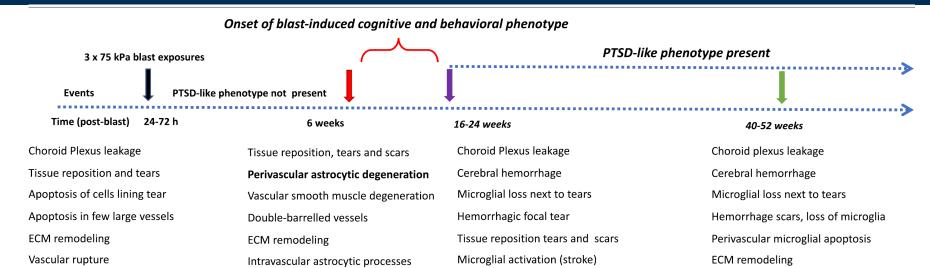
Vascular tunicae disruption

Vascular occlusion, attenuation

Vascular smooth muscle degeneration

Vascular strictures

- Local inflammation
 associated with vascular
 degeneration may be
 due to elevated
 permeability of the
 blood-brain barrier.
- Blood-Brain Barrier dysfunction could lead to greater influx and less efflux of toxins from the environment



Vascular tortuosity

Vascular occlusion, attenuation

Vascular smooth muscle degeneration

Perivascular astrocytic degeneration

ECM remodeling

Vascular strictures

Gama Sosa et al. acta neuropathol commun (2021) 9:167 https://doi.org/10.1186/s40478-021-01269-5

Vascular occlusion, attenuation

Migration of CD34⁺ adventitial

fibroblasts to lumen

Cerebral hemorrhage

Vascular dilation





Perivascular microgliosis

Vascular leakage

Tissue repositon, tears and scars

Vascular tortuosity and strictures

Vascular occlusion, attenuation

Intravascular astrocytic processes

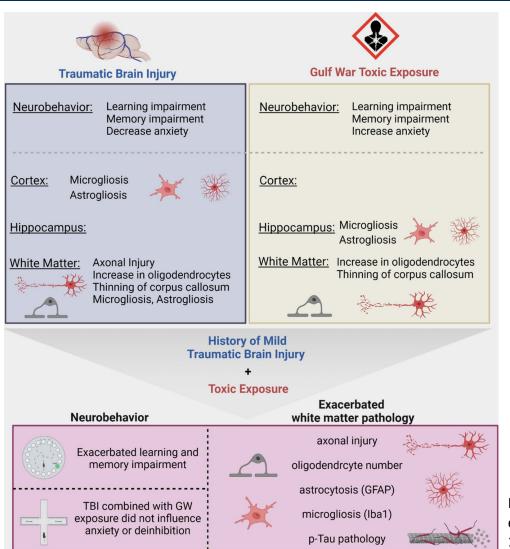
Perivascular astrocytic degeneration

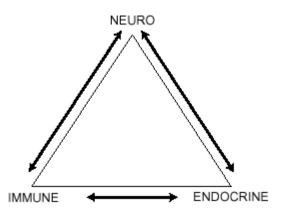
Perivascular microglial activation
Perivascular astrocytic apoptosis
Enlarged paravascular spaces

Perivascular astrocytosis

Vascular smooth muscle degeneration

Multi-system Effects of Both TBI and Military Exposures





- Gulf War Veterans, GWVs, show damage in all three of these areas. The consequences of such damage will not necessarily be limited to the area first affected by the chemical or biological insult.
- Post 9/11 Veterans with diagnosed TBI also have multisystem conditions that include neurobehavioral, immune, and endocrine.

Ferguson, S., McCartan, R., Browning, M. et al. Impact of gulf war toxic exposures after mild traumatic brain injury. acta neuropathol commun 10, 147 (2022).





Q&A

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