TRAUMATIC BRAIN INJURY

CURRENT LANDSCAPE AND EMERGING RESEARCH

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HDIAC
Homeland Defense & Security Information Analysis Center

(*Image Sources: U.S. Army photo by Pfc. Nathaniel Newkirk)*

AGENDA

1. Baselining
2. Emerging Research
3. Diagnosis
4. Novel Treatments
5. Major U.S. Department of Defense (DoD) Research Initiatives
6. Conclusions

Important Missing TOPICS

Not discussing the following, but they are important:

- Laws directing military traumatic brain injury (TBI) research, specifically multiple National Defense Authorization Acts (NDAAs)
- Mild, moderate, and severe TBI definitions
- Protective equipment to prevent TBIs
- Medical imaging
- Chronic Traumatic Encephalopathy (CTE)

(Image Source: Shutterstock)

BASELINING

Establishing an individual's cognitive performance before any injury is sustained, allowing for more precise analysis after an injury.

(Image Sources: ARL, MARSOC, and. U.S. Space Force)

ANAM

Automated Neuropsychological Assessment Metrics (ANAM) is a standardized, computerized cognitive test used by the DoD for baselining.

(Image Sources: U.S. Space Force)

- DoD Instruction 6490.13: ANAM “is the DoD-designated neurocognitive assessment tool until evolving science and medical best practices inform a change in policy.”
- In use for predeployment since 2008; implemented DoD wide for initial entry trainees in 2024.

ANAM

Automated Neuropsychological Assessment Metrics (ANAM) is a standardized, computerized cognitive test used by the DoD for baselining.

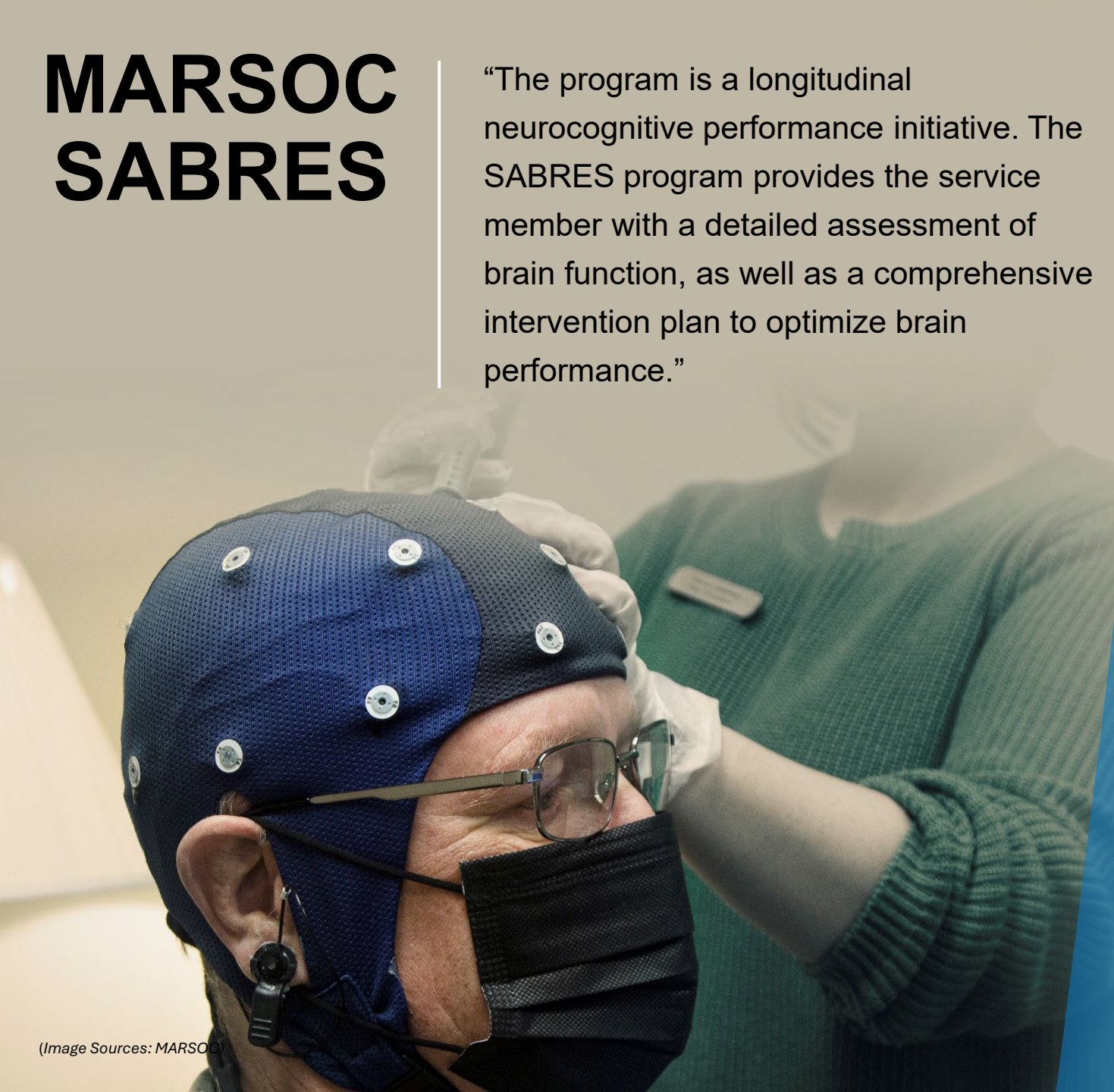
(*Image Sources: U.S. Space Force*)

Originally comprised of 7 tests - 3 more added in 2013:

- Simple Reaction Time (SRT)
- Code Substitution (Learning, CDS)
- Procedural Reaction Time (PRT)
- Mathematical Processing (MTH)
- Matching to Sample (MS2)
- Code Substitution (Delayed, CDD)
- SRT (repeated, SR2)
- Go/No-go (GNG, added 2013)
- Spatial Processing (SPD, added 2013)
- Memory Search (STN, added 2013)

MARSOC SABRES

"The program is a longitudinal neurocognitive performance initiative. The SABRES program provides the service member with a detailed assessment of brain function, as well as a comprehensive intervention plan to optimize brain performance."



(*Image Sources: MARSOC*)

SABRES uses qEEG, typically used to determine concussive effects, to establish a baseline and gauge brain health generally.

PURPOSE

- Improve general well-being and objective brain physiology.
- Give actionable, personalized feedback regarding performance.

MARSOC: Marines Special Operations Command
SABRES: Special Operations Assessment Baselining and Readiness Evaluation System
qEEG: Quantitative electroencephalogram

EMERGING RESEARCH

A New Understanding

(*Image Sources: U.S. Marine Corps*)

TBI CAUSATION

Low-Level Blast (LLB) Effects

- LLB from firing weapons.
- Concern for instructors and range personnel.
- Effects are proving to be more significant than previously thought.

Repeated Mild TBI (mTBI)

- Previously, there was difficulty conducting longitudinal studies (troops relocated, separated from service, etc.).
- NDAAs have called for longitudinal studies.
- Effects are long-lasting and, in some cases, severe.
- Exacerbates PTSD symptoms.

Blast Overpressure (BOP) From Weapons Firing

- Working to define the BOP from *firing* various weapons.
- Joint Technical Coordinating Group for Munitions Effectiveness developing risk estimated distances for blast-only weapons.
- Updating previous thresholds that used eardrum rupture for threshold.

Measuring Blast Accurately

- Sometimes you must “build a thing” to “test a thing.”
- Blast gauges – measure blast severity.
- Multiple receptors in one gauge can determine blast direction, measuring the time difference in fractions of a second.
- Used in INVICTA and CONQUER.

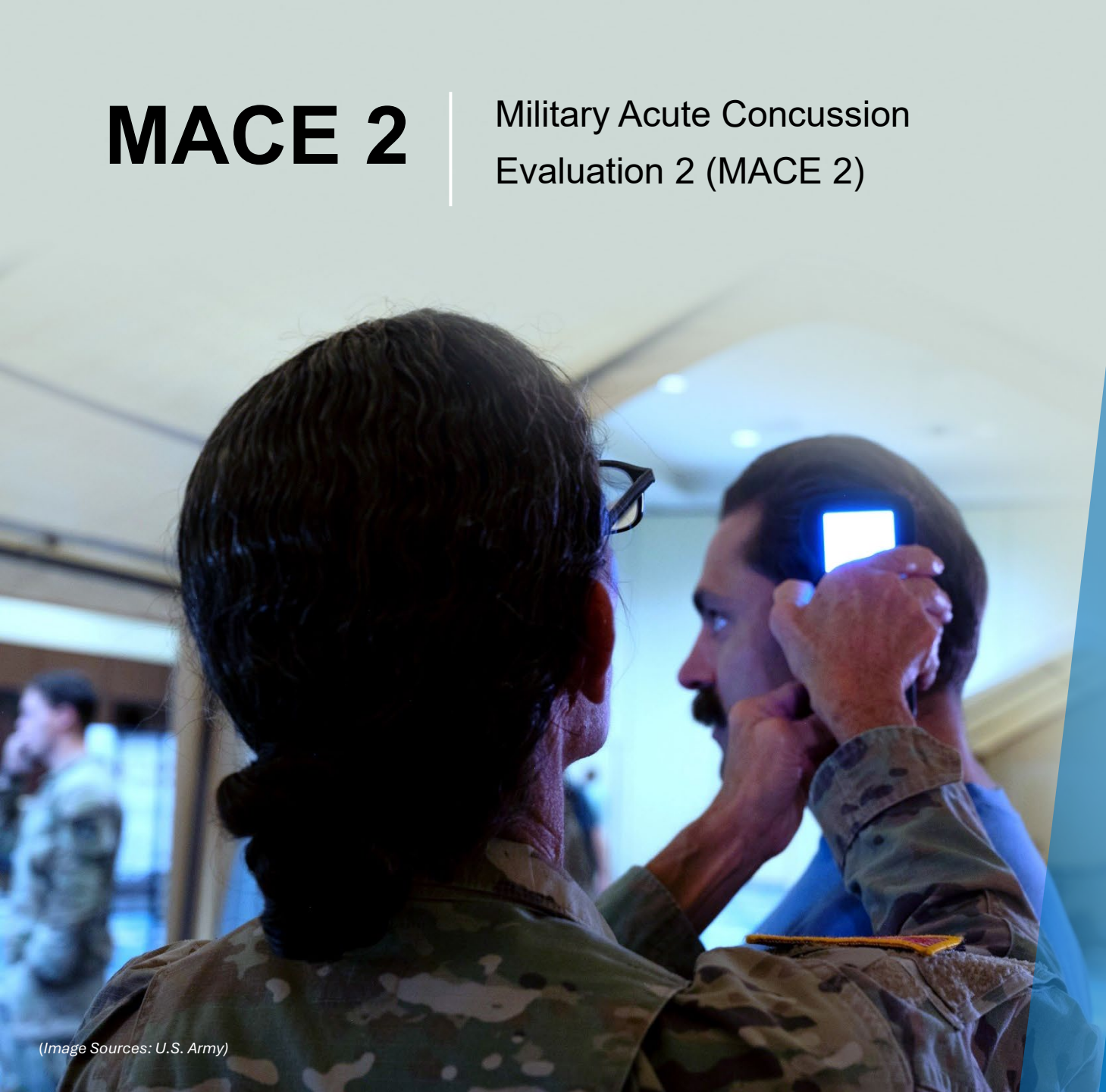
DIAGNOSIS

This involves a multifaceted approach, including screenings, medical evaluations, and potentially, specialized tests.

(*Image Sources: Defense Health Agency, U.S. Army, and. U.S. Air Force*)

MACE 2

Military Acute Concussion Evaluation 2 (MACE 2)



(*Image Sources: U.S. Army*)

- Performed by trained medic as close to time of injury as possible.
- Major red flags (double vision, repeated vomiting, etc.) requires immediate evacuation to care.
- Includes several field-expedient tests for cognition:
  - Cognitive exam
  - Neurological exam
  - Vestibular ocular-motor screening

MACE 2

Results are scored and entered into an Electronic Health Record (EHR), and medics initiate Progressive Return to Activity (PRA).

Stage	Objective	Environment	Physical/Vestibular Activity	Cognitive/Oculomotor Activity	Restrictions Stages 1–5
Stage 1*: Relative Rest	Avoid symptom provocation, and rest to promote recovery	• Minimize light and noise • Stay home/in quarters	• Daily activities that do not provoke symptoms • Limit large or sudden changes in head position • No exercise	• Limit screen time as needed to avoid symptom provocation • Very light leisure activity (e.g., reading, television, conversation)	• Do not go outside the wire in a combat zone
Stage 2: Symptom-Limited Activity	Introduce and promote mild exertion	• Calm and familiar environment with limited distractions	• Limit large or sudden changes in head position • Light routine exertion (e.g., walking on even terrain, light household chores, stationary bike) • No weight or resistance training	• Simple, familiar activities performed one at a time (e.g., routine computer use, leisure reading)	• Maintain or reduce pre-injury levels of caffeine/energy drinks and nicotine
Stage 3: Light Activity	Introduce occupation-specific exertion and environmental distractions	• Introduce environmental distractions during activity • Return to work on limited duty/profile without significant symptom provocation	• Initiate tasks requiring changes in head position • Light aerobic exercise without resistance (e.g., elliptical, stationary bike, walking on uneven terrain) • No lifting > 20 pounds • No resistance training	• Simple, unfamiliar tasks or complex familiar tasks (e.g., grocery shopping, technical reading)	• No alcohol** • No combatives or contact sports***
Stage 4: Moderate Activity	Increase activity intensity and duration	• Distracting or busy environment during activity as tolerated	• Attempt tasks requiring more significant or sudden changes in head position • Increase intensity and duration of activities (e.g., non-contact sports, hiking or running, push-ups, sit-ups) • Introduce resistance training as tolerated	• Increase intensity and duration of activities (e.g., navigate busy environments, recall and follow complex instructions)	• No driving until visual and vestibular symptoms have resolved
Stage 5*:** Intensive Activity	Introduce exertion of duration and intensity that parallels service member's typical role • Complete RTD Screening prior to advancement to Stage 6	• Typical daily environment EXCEPT listed restrictions	• Resume pre-injury exercise routine and training activities	• Complex problem solving or multitasking with exertion or distracting environment	• No weapons fire or blast exposure***
Stage 6: Return to Full Duty	Return to pre-injury activities	• Typical daily environment	• Unrestricted activity		

* Ensure service member adheres to Relative Rest guidelines and attempts to increase activity within 72 hours to avoid potentially detrimental effects of prolonged rest.

** Alcohol use can exacerbate post-concussive symptoms of headache, depression, and anxiety and can cause impaired cognitive functioning, dehydration, and sleep disturbances.

*** In Stage 5, the service member may gradually increase exposure to high risk activities in a supervised training environment based on mission requirements.

(*Source: Traumatic Brain Injury Center of Excellence*)

GCS

Glasgow Coma Scale (GCS) is a widely accepted test for TBI in the civilian sector

Vision: 1 (low) to 4 (high)

Verbal: 1 (low) to 5 (high)

Motor: 1 (low) to 6 (high)

Total Score: 15 pts

(Image Sources: Canva)

Tests and scores eye opening, verbal response, and motor response:

- 3-8: severe TBI, often with coma
- 9-12: moderate TBI
- 13-15: mild brain injury

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BLOOD-BASED BIOMARKERS (BBM)

Biomarker	Molecular Weight (kDa)	Primary origin	Location	Other Sources	Half-life (h)	Peak (h)
S100B	11	Astrocytes	Cytoplasm	Adipocytes, melanocytes, muscle, chondrocytes, enteric glial cells	0.5–2	<6
GFAP	50	Astrocytes	Cytoplasm	Schwann cells, chondrocytes, enteric glial cells liver, pancreas	24–48	20–24
UCH-L1	25	Neurons	Cytoplasm	Testis, ovary, kidney	8	7–9
NF-L	68	Neurons	Myelinated axons	Peripheral axons	Unknown	Unknown

GFAP: glial fibrillary acidic protein UCH-L1: ubiquitin C-terminal hydrolase L1 NF-L: neurofilament light chain

Source: Hossain et al.

Blood Biomarker (BBM)

WHOLE BLOOD TEST

USAMMDA* developed a deployable BBM test which can deliver results within 15 min - the iSTAT Allinity.

Uses whole blood vice blood plasma or serum.

No lab required.

Handheld devices with replaceable cartridges.

FDA approved in March 2024.

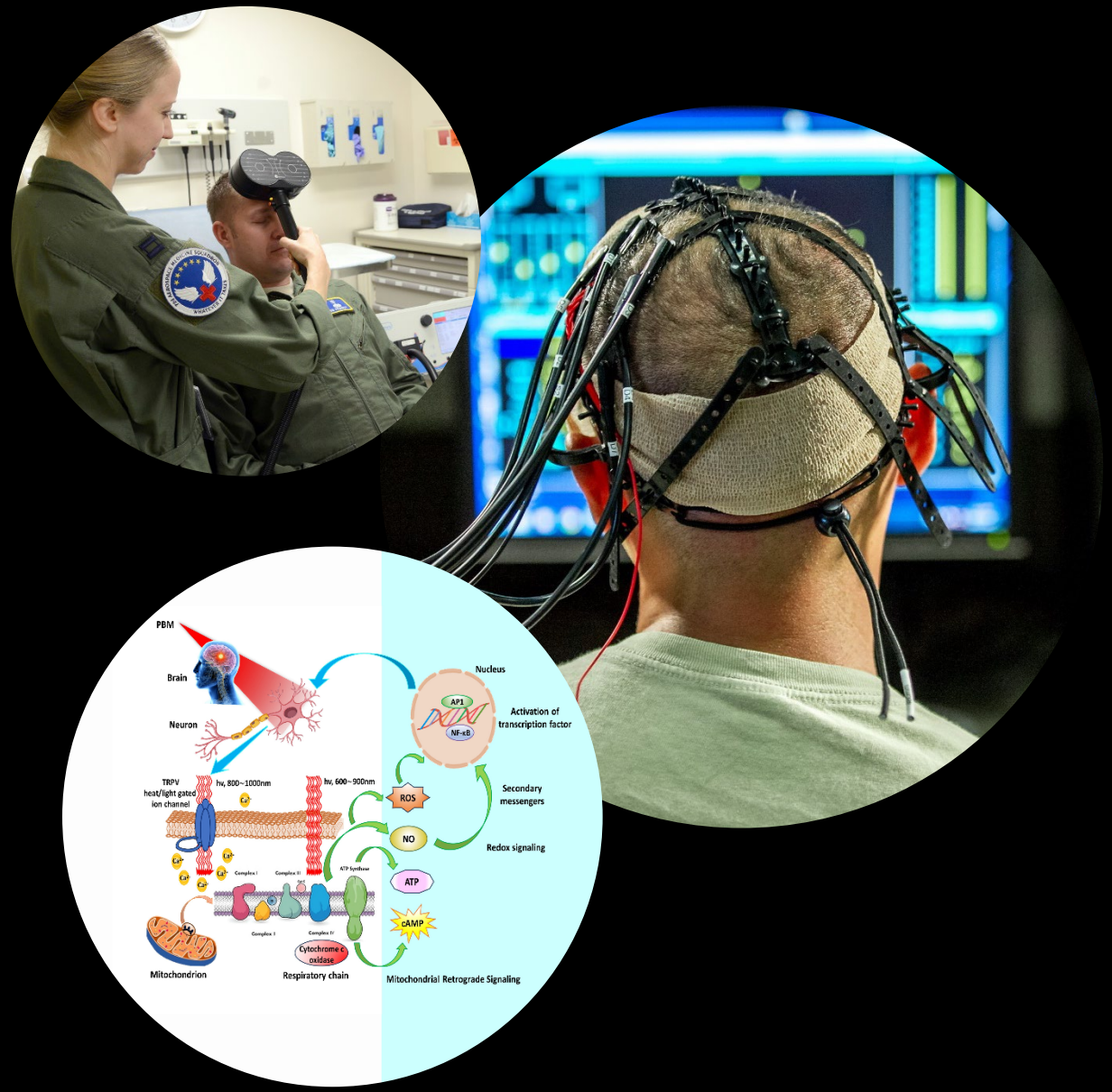
Significant correlation between BBM and TBI severity.

This may inform evacuation from a combat zone to definitive care.

Difficult to deploy neurosurgeons in significant numbers for large-scale combat operations, but quick evacuation could save lives.

*USAMMDA: U.S. Army Medical Materiel Development Activity

(*Image Sources: U.S. Army)*



NOVEL TREATMENTS

The following are some promising approaches for the treatment of TBI.

(*Image Sources: Nairuz et al. and. U.S. Air Force*)

Transcranial Photobiomodulation **(PBM)**

OVERVIEW	PBM is a relatively new and has not been extensively tested in humans for treating TBI.
STUDIES	From 2011 to 2023, 10 studies published, ~200 total subjects. • Each study used different parameters (wavelength, pulse intensity, pulse duration). • Success criteria often different.
PROS/CONS	✓ PBM promising as a safe, noninvasive TBI treatment. ✗ Studies are not comparable.
STATUS	Early work on humans ~proof of concept.

Transcranial Direct-Current Stimulation **(tDCS)**

OVERVIEW	tDCS, like PDM, is a relatively new idea for treating TBI.
STUDIES	Only seven studies published between 2014 and 2020, but all used similar parameters (2 mA for 20 min).
PROS/CONS	✓ "Most trials reported positive results in favor of the experimental group, which suggests that brain stimulation has a significant effect in outcomes in individuals with disorder of consciousness after TBI." ✗ Very small current sample size.
STATUS	More study needed, but very safe which may reduce timeline.

Transcranial Magnetic Stimulation **(TMS)**

OVERVIEW	It is safe and tolerable, cleared for use in other neuropsychiatric applications.
STUDIES	A study that hypothesized that mTBI would hamper TMS results was disproved.
PROS/CONS	✗ Only conceptual.
STATUS	This is not cleared for TBI treatment.

Low-Level Laser Therapy
(LLLT)

OVERVIEW	LLLT promotes cellular health and tissue repair, both within the brain and other cells.
STUDIES	(FIND A STUDY JOHN!)
PROS/CONS	✓ **Several noted benefits:** • Limits spread of brain cell death after TBI. • Anti-inflammatory and anti-edema effects. • Stimulates new blood vessels in brain. • Stimulates neurogenesis (growth of new brain cells) and synaptogenesis (new synaptic connections).
STATUS	Considered exceptionally safe, which could speed clinical trials.

Major DoD Research

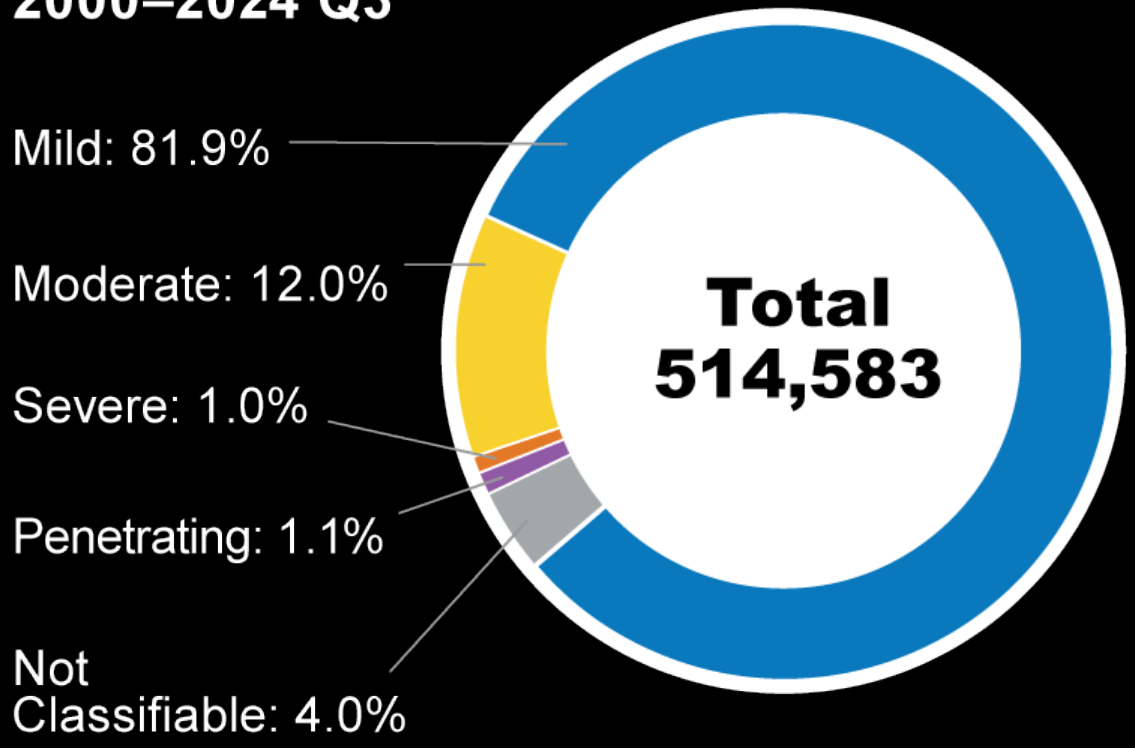
INITIATIVES

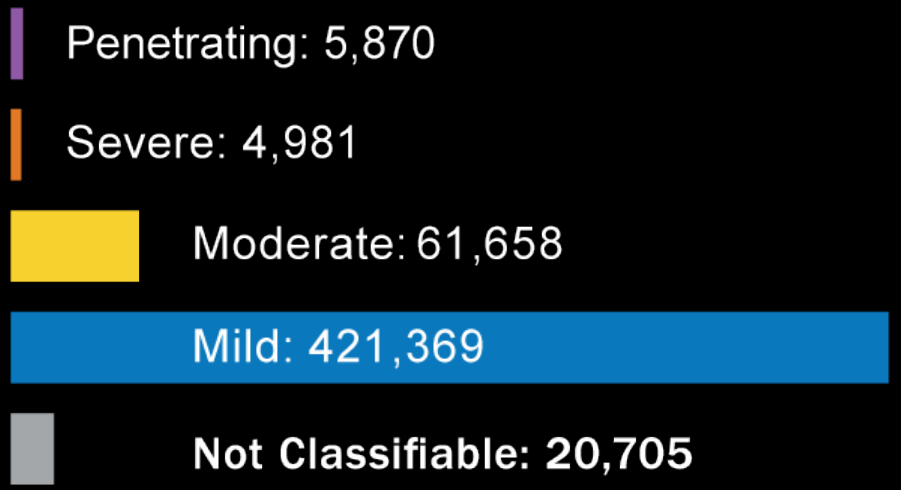
(*Image Source: Canva*)

Where We Stand

DoD NUMBERS FOR TBI WORLDWIDE

2000–2024 Q3





Source: Defense Medical Surveillance System, Theater Medical Data Store provided by the Armed Forces Health Surveillance Division.
Prepared by the Traumatic Brain Injury Center of Excellence.
*Percent may not add to 100% due to rounding.
2000–2024 Q3, as of November 8, 2024

DHA
Defense Health Agency

Warfighter Brain Health Initiative (WBH)

FOCUS AREAS

- Helping Warfighters think and move at their best.
- Checking up on brain health.
- Preventing and treating TBIs.
- Quickly spot TBIs to reduce their harm.
- Protecting Warfighters from things that may hurt their brains, like blast overpressure.
- Reducing long-term problems from brain injuries.
- Researching and learning more about how to keep Warfighters' brains healthy.

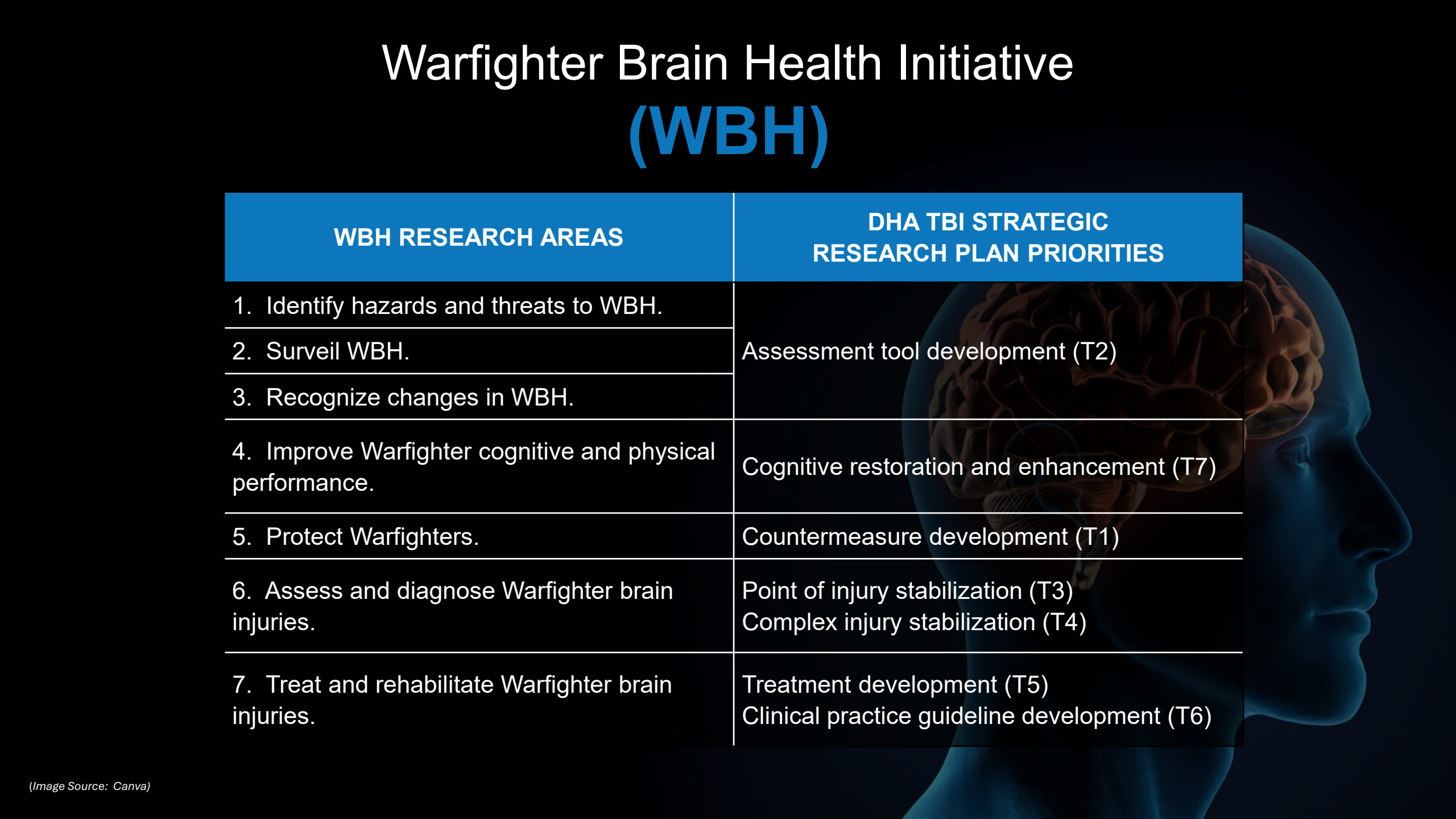
PROGRAM AIMS

- Maintain readiness.
- Optimize thinking.
- Enhance/ improve physical performance.

(*Image Source: Canva*)

Warfighter Brain Health Initiative (WBH)

WBH RESEARCH AREAS	DHA TBI STRATEGIC RESEARCH PLAN PRIORITIES
1. Identify hazards and threats to WBH.	Assessment tool development (T2)
2. Surveil WBH.	
3. Recognize changes in WBH.	
4. Improve Warfighter cognitive and physical performance.	Cognitive restoration and enhancement (T7)
5. Protect Warfighters.	Countermeasure development (T1)
6. Assess and diagnose Warfighter brain injuries.	Point of injury stabilization (T3) Complex injury stabilization (T4)
7. Treat and rehabilitate Warfighter brain injuries.	Treatment development (T5) Clinical practice guideline development (T6)



(*Image Source: Canva*)

TBI Center of Excellence
(TBICoE)

As the principal military organization to lead, translate, and advance brain health, TBICoE's work significantly impacts DoD operational and clinical communities, as well as other federal agencies and external stakeholders.

- A role in research and education.
- Publishes research studies on BBM, cognition, neuroimaging, vestibular balance, etc.
- Lead development of the MACE 2.

(*Image Source: Canva*)

Traumatic Brain Injury

CONCLUSIONS

(*Image Source: Shutterstock*)

PAST & FUTURE

Where We Were

TBI and brain health were not well understood.

Increase in weapons effects mixed with better PPE led to increase in brain injuries.

TBI came to the forefront in the 2000s.

Accelerated by the Global War in Terrorism.

Where We're Headed

Bedside/near point-of-injury blood tests for TBI.

Accurate baselining.

Eye tracking and pupillometry for TBI diagnosis.

Brain health incorporated into training.

Understanding LLB and repeated mTBI.

New techniques for recovery.

QUESTIONS?

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Check out our state-of-the-art reports at
https://hdiac.dtic.mil/state-of-the-art-reports/

(Image Source: Canva)