Scientific opportunities & key unknowns in TBI research

Defense and Veterans Brain Injury Center
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• The presenter does not intend to discuss the off-label/investigative (unapproved) use of commercial products or devices.

• The presenter has no relevant relationships to disclose.
**Mission:** to serve active duty service members, their beneficiaries, and veterans with traumatic brain injuries through state-of-the-art science clinical care, innovative clinical research and educational programs, and support for force health protection services as the DoD’s TBI Center of Excellence.
DVBIC Research Network

Walter Reed National Military Medical Center, Naval Medical Center San Diego (NMC San Diego), Camp Pendleton, Fort Belvoir
Exploring the Natural History of Traumatic Brain Injury within a Military Cohort-A Longitudinal Database and Blood Banking Study (15-year)

Fort Bragg, NC
A Psychometric Comparison of Brief Computerized Neuropsychological Assessment Batteries (Head to Head)

San Antonio Military Medical Center
Study of Cognitive Rehabilitation Effectiveness in Mild Traumatic Brain Injury (SCORE!)
Imaging support of Study of Cognitive Rehabilitation Effectiveness in Mild Traumatic Brain Injury (iSCORE)
Mission Essential Components

Research
- Clinical investigations
- Translation of research
- Congressionally mandated studies
- Epidemiological research
- Research analysis
- Program evaluation

Clinical Affairs
- Identification & sharing best practices
- Clinical guidelines & recommendations
- Care & consultation
- TBI surveillance
- Recovery support program
- TBI health outcomes
- Program evaluation and quality process improvement

Education
- Development of educational tools & resources
- TBI awareness and training
- Product distribution and dissemination
- Family caregiver program
- Regional education coordination
- Outreach
Bookends for Research

Gap Analysis

- Stakeholder needs assessment
- Maintain visibility on current TBI research
- Literature review, grade evidence
- Identify high priority focus areas; inform program announcements & research investment opportunities

Conduct Research

- Prioritize resource utilization for research based on identified gaps and clinical needs
- Programmatic and external scientific peer review of new studies

Translate Research – Dissemination & Implementation

- Share research findings with stakeholders through publications, presentations, reports, information papers
- Develop clinical recommendations based on evidence, clinical guidelines & expert clinical consensus
- Pilot, evaluate, revise, and implement clinical recommendations
TBI Research Priorities

National Research Action Plan – Interagency (Departments of Defense (DoD), Veterans Affairs (VA), Health and Human Services, and Education) response to Presidential Executive Order from August, 2012

Improving Access to Mental Health Services for Veterans, Service Members, and Military Families

The NRAP points out key areas of priority in TBI Research:

<table>
<thead>
<tr>
<th>Classification</th>
<th>More precise classification based on patient characteristics, injury characteristics, and signs/symptoms/deficits</th>
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<tbody>
<tr>
<td>Biomarkers</td>
<td>Imaging, proteomic, neurophysiologic tools for diagnosis, monitoring recovery, and predicting outcomes</td>
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<tr>
<td>Mechanisms</td>
<td>Increased understanding of neuropathology and recovery</td>
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<td>Treatment</td>
<td>Identify and validate pharmacologic, non-pharmacologic, and rehabilitation treatment options</td>
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<td>Long-term effects</td>
<td>Chronic effects of TBI; association between long-term effects and co-morbidities</td>
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</table>
How is DVBIC addressing the TBI research priorities?

**15 Year Longitudinal Study on TBI in OEF/OIF Service Members and Veterans and their Families**

- **In progress: 2011-2026**
- Walter Reed National Military Medical Center, Naval Medical Center San Diego (NMC San Diego), Camp Pendleton, Fort Belvoir
- This study will identify long-term physical, mental health, medical, and supportive care needs of OEF/OIF service members and veterans with TBI, and the effects of TBI on family members and caregivers
- Will provide information on the association of patient and injury characteristics and health/clinical services with outcomes and recovery; investigate blood biomarkers longitudinally after TBI; study co-morbidities as they relate to long term effects of TBI
- Bridges interagency investments via partnerships with the DoD/VA funded Chronic Effects of Neurotrauma Consortium and the NIDRR funded TBI Model Systems program
How is DVBIC addressing the TBI research priorities?

Study of Cognitive Rehabilitation Effectiveness in Mild Traumatic Brain Injury (SCORE!)

- Completed; publication in preparation
- San Antonio Military Medical Center
- This study will evaluate the effectiveness of six weeks (60 hours) of cognitive rehabilitation in OIF/OEF service members with a history of mild TBI and persistent cognitive complaints
- Will provide information on the association of patient and injury characteristics and with outcomes six months after cognitive rehabilitation
- In coordination with an imaging study (iSCORE), will correlate outcomes with anatomical and imaging data to better understand the neuroplastic changes in the brain associated with improvements in cognitive functioning
How is DVBIC addressing the TBI research priorities?

A Randomized, Double-Blind, Placebo-Controlled Study of the Safety and Efficacy of NNZ-2566 in the Acute Treatment of Adults with Mild TBI

- In progress: 2014-2016
- Fort Bragg - Womack Army Medical Center
- The randomized, double-blind, placebo-controlled study will evaluate the safety and efficacy of NNZ-2566 for the acute treatment of mTBI in adults.
- 132 service members are to be randomly assigned in a 1:1:1 ratio to receive treatment with one of two fixed dosages of an oral solution of NNZ-2566 or placebo for seven days.
- Subjects will be assessed for cognitive function, post-injury symptoms, postural stability, vision, psychological sequelae, general clinical status, ability to return to duty, and residual functional disability.
DVBIC Research Across the Continuum

Epidemiology
- Exploring the Natural History of Traumatic Brain Injury within a Military Cohort – A Longitudinal Database and Blood Banking Study
- Deployment Related Mild Traumatic Brain Injury (mTBI): Incidence, Natural History, and Predictors of Recovery in Soldiers Returning from OIF/OEF
- Epidemiology of Headache Disorders in a Military Cohort with and without TBI

Prevention/Screening
- A Psychometric Comparison of Brief Computerized Neuropsychological Assessment Batteries: Validity Study
- Structured Telephonic Testing 5 to 15 Years after TBI

Treatment/Management
- BRAVE Trial: Broad-spectrum Cognitive Remediation Available to Veterans–Effects of a Brain Plasticity-based Program in Mild Traumatic Brain Injury
- The Effect of Telephone Follow-up on outcome for Service Members with Mild TBI: Concussion Treatment after combat Trauma (CONTACT)
- A Randomized, Double-Blind, Placebo-Controlled Study of the Safety and Efficacy of NNZ-2566 in the Acute Treatment of Adults with Mild TBI

Rehabilitation/Reintegration
- Study of Cognitive Rehabilitation Effectiveness in Mild Traumatic Brain Injury (SCORE!
- Imaging Support of Study of Cognitive Rehabilitation Effectiveness in Mild Traumatic Brain Injury (iSCORE)
- A Demonstrated Program to Test the Efficacy of Peer Visitation for Caregivers of Veterans of OIF/OEF with Polytrauma/Blast-related Injury

Family Caregiver
- Health Related Quality of Life in Caregivers of Service Members with Military Related Traumatic Brain Injury

Research Highlights

- N = 35
- N = 6
- N = 10
- N = 7
- N = 2
Scientific opportunities

- Validation of standardized research outcome measures
- Validate advanced imaging applications in the mTBI population. Correlate imaging findings with functional impairment
- Is subclinical concussion exposure truly subclinical? What is the threshold for clinical? Does the threshold change after multiple “subclinical” exposures
- Environmental sensor threshold values to the level of injury-TBI
- Comparative effectiveness studies to evaluate current management standards of TBI
- Effectiveness of TBI educational efforts
- Collaboration on larger /multi-site trials to confirm pilot studies
- Blast pathophysiology, multiple TBI and CTE
- Long-term effects of traumatic brain injury
## Knowledge Translation: Implementation, and Evaluation of Clinical Guidance

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<tr>
<th>Develop Clinical Recommendations (CR)</th>
<th>Dissemination of CR Products</th>
<th>Implement CR</th>
<th>Evaluate and Refine</th>
<th>Sustainment</th>
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<td>Engage the services to identify needs/gaps</td>
<td>Communication plan for Military Healthcare System-wide roll-out of the CR</td>
<td>Conduct training and education events to promote understanding and use of the CR by providers</td>
<td>Analyze post-training survey</td>
<td>Continuous collaborations with TBI leaders and stakeholders to identify additional opportunities for implementation of the CRs</td>
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<td>Assemble multi-disciplinary team to synthesize and grade evidence</td>
<td>Leverage DVBIC network sites to promote DVBIC CRs at regional military treatment facilities and VA hospitals</td>
<td>Administer post-training Interactive Customer Evaluation (ICE) survey to assess the training and education</td>
<td>Initiate refinement of training and education based on feedback</td>
<td>Inform the development and implementation of policy related to the CRs</td>
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<td>Convene an expert working group to discuss current evidence and best practices to inform development of the CRs</td>
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<td>Administer post-training survey</td>
<td>Administer 3-month post-adoption survey to measure provider behavior change</td>
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<td>Analyze findings and refine CRs</td>
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<td>Conduct clinical trials to determine adoption and effectiveness of the CRs</td>
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Hero’s Highway

We thank our active duty service members, their families, beneficiaries, and veterans for their service & sacrifices

**DVBIC – HQ team**
- Saafan Malik, MD  Director of Research
- Felicia Qashu, PhD  Deputy Director of Research
- Gary Arasin  Senior Communications Manager (PAO)
Back up slides
DVBIC Network

DVBIC NATIONAL HEADQUARTERS

**MILITARY / DoD SITES**
- Fort Belvoir
- Fort Carson
- Fort Bragg
- Camp Pendleton
- Camp Lejeune
- Walter Reed National Military Med Center
- San Antonio Military Medical Center
- Naval Medical Center San Diego
- Joint Base Elmendorf-Richardson
- Fort Hood
- Landstuhl Regional Medical Center

**VA SITES**
- Richmond VAMC
- Tampa VAMC
- Palo Alto VAMC
- Minneapolis VAMC
- Boston VAMC
DVBIC Division of Research

**Mission:** Provide evidence-based knowledge through conducting and supporting clinically-focused research to improve treatment and outcomes for Service Members and Veterans who have sustained TBI

**Key Programs:**

- **Research Activities** – the DVBIC Research Portfolio of 60 studies addresses areas of focus across the continuum of care for TBI, including TBI screening and assessment, treatment and clinical management, and rehabilitation and reintegration, as well as foundational science/epidemiology/etiology of TBI

- **Clinical Translation** – catalyze the translation of promising clinical research through dissemination of findings to stakeholders in support of the development of evidence-based clinical and educational tools, and informing research gaps

- **Program Evaluation/Continuous Process Improvement** – provides a mechanism to measure the effectiveness of DVBIC’s programs by evaluating processes as they apply to specific projects/initiatives; assists DVBIC divisions and network sites in implementing performance improvement processes that enhance DVBIC programs, products, and services, and, ultimately, the health, wellness, and quality of life of Service members, veterans, and their families
Mission: Provide evidence-based knowledge through conducting and supporting clinically-focused research to improve treatment and outcomes for Service Members and Veterans who have sustained TBI

Key Programs:

• Research Network – Conducts clinical research at an integrated network of 11 different DoD, MTF and VA sites addressing areas of focus across the continuum of care for TBI, including: TBI screening and assessment, treatment and clinical management, and rehabilitation and reintegration, as well as foundational science/epidemiology/etiology of TBI

• Research Activities – Conducts, coordinates and supports clinical research studies across the DVBIC network. Tracks portfolio of 60 ongoing studies

• Clinical Translation – Catalyzes the translation of promising clinical research through dissemination of findings to stakeholders in support of the development of evidence-based clinical and educational tools, and informing research gaps

• Program Evaluation/Continuous Process Improvement – Provides a mechanism to measure the effectiveness of DVBIC’s programs by evaluating processes as they apply to specific projects/initiatives; assists DVBIC divisions and network sites in implementing performance improvement processes that enhance DVBIC programs, products, and services, and, ultimately, the health, wellness, and quality of life of Service members, veterans, and their families